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**A multi-omics approach to advance precision medicine and study patient heterogeneity in amyotrophic lateral sclerosis**

Marriott, Heather

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# **A multi-omics approach to advance precision medicine and study patient heterogeneity in ALS**

**Heather Marriott**

A thesis submitted for the degree of  
*Doctor of Philosophy in Clinical Neuroscience*

Supervisors:

Professor Ammar Al-Chalabi

Dr Alfredo Iacoangeli

Dr Ahmad Al Khleifat

Institute of Psychiatry, Psychology and Neuroscience

King's College London

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## Abstract

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease caused by degeneration of both upper and lower motor neurons, with death from respiratory failure typically occurring 2-3 years after onset. More than 40 genes are definitively linked to ALS with a further 125 involved in either pathogenic processes or as modifiers of phenotype. However, the complex architecture of ALS has impacted negatively on further genetic variant discovery and the interaction of known and non-canonical variants with transcriptomic factors, such as alterations in gene expression. Despite identifying a number of pertinent risk loci in recent years, genome-wide association studies (GWAS) are plagued by issues. Single nucleotide polymorphism (SNP)-based microarray genotyping approaches can only explain 8.5-20% of the estimated 60% heritability of ALS as only common variants are tagged, leaving the remaining ~40% explicable by rare and low frequency SNPs, other classes of variation such as structural variants, transposable elements, post-transcriptional and splicing alterations, and changes in gene expression. Consequently, more research groups and dedicated ALS consortia such as Project MinE and TargetALS, are opting for next-generation sequencing (NGS) technologies such as whole genome sequencing (WGS) and RNA-sequencing (RNAseq), as they are capable of detecting variation missed by microarray technologies and therefore can be used to better understand the complexity of ALS. NGS can be utilised for precision medicine approaches, which involve harnessing big data and bioinformatics or machine learning frameworks to identify biologically homogeneous groups of individuals. It is therefore important to adopt NGS-based precision medicine strategies in ALS research to define people with ALS into biologically relevant subgroups to better inform biomarker discovery or future clinical trial design.

The overall focus of this thesis was to employ several bioinformatics and machine learning techniques which can exploit the potentialities of WGS and RNAseq to delineate the complex heterogeneity of ALS and provide new molecular insights into disease for the advancement of precision medicine. Chapter 4 reports the update of a previously published NGS bioinformatics pipeline developed by our group, which demonstrates enhanced detection, annotation and prioritisation of structural variants, including transposable elements and tandem repeats. In Chapter 5, I confirm that rare missense variants and in-frame deletions in the tail domain of the neurofilament heavy

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chain gene (*NEFH*) increase ALS risk, through a meta-analysis of previous reports from the literature, and variant screening and rare burden analysis of SNPs, indels and structural variants from the Project MinE WGS cohort. This is in agreement with previous reports using smaller sample sizes. Causal associations are also found for intronic SNPs and indels in the rod domain, and a protective effect is identified for a large 113 base-pair deletion in the tail domain; both identified in Project MinE with rare variant burden analysis. Despite these findings, these associations do not have large effect sizes and require more experimental follow-up studies to assess their functional impact before determining whether their inclusion in genetic screening panels is warranted. In Chapter 6, I investigate the molecular architecture of ALS by conducting a case-control differential gene expression analysis of post-mortem motor cortex RNAseq data from the KCL BrainBank (a subsidiary of Project MinE) and TargetALS, which identify genes in the neuropeptide signalling pathway as differentially expressed and enriched in both datasets. Analysis of neuropeptide-related genes and their receptors find that higher expression of *TACR1* and *NPBWR1* is associated with longer disease duration and lower age of onset, respectively, suggesting that neuropeptides could be used as diagnostic and prognostic biomarkers. Finally, in Chapter 7 I identify and characterise three molecular subtypes of ALS which reflect predominant molecular mechanisms of pathogenesis, using unsupervised hierarchical clustering of KCL BrainBank for initial discovery of the clusters, followed by linear discriminant analysis for validation in independent brain and blood datasets. I show that these molecular phenotypes are robust, with their expression signatures being able to distinguish people with ALS from controls, and the motor cortex from occipital cortex and cerebellum regions in the TargetALS cohort. Cell type analysis also reinforces the biological interpretation of the clusters. This demonstrates that these motor-cortex derived molecular phenotypes could be used to successfully stratify people with ALS into biologically relevant subgroups, although further work needs to be carried out to determine whether these subgroups are truly ALS-specific. Distinct cluster-related onset and progression measures in both motor cortex case datasets are also identified, which demonstrates the potential for future identification of subgroup-specific prognostic biomarkers.



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*“To my grandparents, who inspired my journey into neuroscience and provided immeasurable support and encouragement even in the face of adversity; to my late grandmother, who demonstrated great strength and courage whilst living with PSP; and to my grandfather, whose unwavering resolve and loyalty still spurs me on.”*

---

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## Chapter 1. Introduction

### 1.1 Introduction to ALS

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease which is caused by progressive degeneration of upper and lower motor neurons in the brainstem and spinal cord. There are two types of typical ALS, where individuals present with both upper motor neuron (UMN) and lower motor neuron (LMN) involvement at onset, usually between 50-65 years of age; spinal (70-75% of individuals), which causes limb and trunk weakness, and bulbar (25-30% of individuals), which presents as difficulty with speech, swallowing and chewing. As the disease progresses to end-stage, the majority of people with spinal-onset ALS will have some degree of bulbar involvement. Despite ALS being frequently described as a rare disease, the lifetime risk of ALS is approximately 1 in 350 for males and 1 in 400 for females (R. H. Brown & Al-Chalabi, 2017; Ryan et al., 2019), with the mean global prevalence and incidence of ALS currently estimated at 4.1-5.0 and 0.86-1.75 in 100,000 people, respectively (GBD 2016 Motor Neuron Disease Collaborators, 2018; Marin et al., 2017; L. Xu et al., 2020). Typically, ALS is diagnosed based on a combination of clinical and electrophysiological evidence based on the presence of mixed UMN and LMN signs, with several diagnostic classification guidelines, such as the revised El-Escorial, Awaji and Gold Coast criteria (Brooks et al., 2000; de Carvalho et al., 2008; Turner & UK MND Clinical Studies Group, 2022), created over the last three decades to increase diagnostic sensitivity (Costa et al., 2012; De Carvalho & Swash, 2009; Pugdahl et al., 2021) and reduce diagnostic delay, which is the time period between symptom onset and diagnosis. This is necessary as death typically occurs from respiratory failure 2 to 3 years after symptom onset, although this can vary based on site and age of onset, as well as the involvement of genetic and environmental factors.

Traditionally, ALS is defined as being either familial or sporadic. Sporadic ALS (SALS) accounts for approximately 90% of cases, where there is either no apparent family history of the disease or discernible genetic mutation attributed to its onset. The remainder of cases are classified as familial (FALS), which means that at least one first- or second-degree family member has to have previously been diagnosed with ALS, and the individual must harbour a mutation in a highly penetrant Mendelian ALS-linked gene; penetrance refers to the proportion of people carrying a genetic mutation

that will go on to develop ALS. Mutations in the 4 main ALS-linked genes *C9orf72*, *SOD1*, *FUS* and *TARDBP* account for approximately 60-80% of FALS, although these mutations are also present in up to 15% of people with SALS. As the heritability of SALS, which refers to the proportion of disease explained by genetic variation, is estimated at between 40 and 60% from twin and parent-offspring studies in European populations (Al-Chalabi et al., 2010; Ryan et al., 2019), it suggests that there are other types of variation, i.e. environmental exposures, gene expression levels, epigenetic alterations, additional genetic mutations, that are unaccounted for.

Indeed, there are now upwards of 40 genes that are causally linked to ALS, with a further 130 putatively associated with ALS risk or shown to modify onset or progression (Mejzini et al., 2019). Furthermore, ALS displays a complex disease architecture, with a combination of gene variants with varying effects in addition to environmental and lifestyle factors influencing its onset.

For instance, some genetic variants demonstrate age-related and incomplete penetrance. Age-related penetrance is a phenomenon where ALS onset is dependent on the age of the individual carrying an ALS-linked genetic mutation. This is demonstrated in country and global population-based epidemiological studies, which report that the prevalence and incidence of ALS increases until the peak age of 70-79 (Fontana et al., 2021; L. Xu et al., 2020), with males displaying higher incidence and prevalence rates than females (Fontana et al., 2021; Marin et al., 2017; L. Xu et al., 2020). One example of a genetic variant which displays this phenomena is the *C9orf72* hexanucleotide repeat expansion, whereby the cumulative incidence of people carrying the pathogenic expansion repeat size increases with age, with 50% penetrance occurring at 57 years of age, which is typically the mean age of onset. Furthermore, FALS and SALS demonstrate near identical incidence estimates, with male carriers and those with spinal onset ALS displaying a 2 year reduced median age of onset, reflective of the increased penetrance in those groups (Murphy et al., 2017). In contrast, incomplete penetrance is where not all carriers of a genetic mutation will be affected by the disease. This was recently exemplified from a recent penetrance analysis of *SOD1* carriers in the European population, which found that when aggregating all 180 pathogenic variants, the penetrance estimate was 0.70, although for individual variants, the penetrance is variable: the A5V mutation, which causes rapidly-progressive ALS, has a 100% penetrance, whereas the second most common

mutation, I44T, has a penetrance estimate of 0.64. The D91A mutation, which is associated with slower progression, has an estimated penetrance of 0, which is partly due to its mode of inheritance, as it can be inherited in a dominant, recessive or oligogenic fashion (Spargo et al., 2022).

Oligogenicity is another component of the complex disease genetics of ALS, which is where variants in multiple genes, with varying effects and population frequencies, contribute to the onset of ALS. The multistep model of ALS onset rationalises the oligogenic effects of ALS, whereby based on a least squares regression approach conventionally applied to cancer in 5 European ALS population registers, a strong linear relationship between log incidence and log age was found, with a slope estimate suggestive of a six-step process required for ALS onset (Al-Chalabi et al., 2014). Since then, support for the six-step multistep process has been strongly replicated in Italian, Irish, Australian, Danish and Japanese register-based population cohorts (Chiò et al., 2018; Garton et al., 2021; Vucic et al., 2019, 2020). Identification of these steps has been more challenging due to the complex nature of ALS. Indeed, for people with SALS, the impact of highly penetrant ALS risk genes on ALS onset is clear: individuals harbouring genetic variants in *TARDBP*, *C9orf72* and *SOD1* require 2-4 fewer steps for ALS to develop in Italian (Chiò et al., 2018) and South Korean populations (Choi et al., 2022), which corroborates with the finding that reduced age of onset in people with FALS is due to the presence of causal ALS gene variants (Mehta et al., 2019). However, it is clear that as there are still steps unaccounted for, and as there does not appear to be a striking difference in the number of steps needed for ALS onset between FALS and SALS, rare variants and multiple variants with medium to large effects will most likely make up most of the remainder of the steps. A multitude of molecular processes are also implicated in ALS onset and progression, including RNA metabolism, excitotoxicity, oxidative stress, axonal and vesicular transport, neuroinflammation, autophagy, mitochondrial function, nucleocytoplasmic transport and proteostasis (Mejzini et al., 2019), which means that it is hard to pinpoint the processes which induce motor neuron degeneration at a molecular level on an individual basis.

This complexity has posed many challenges pertaining to further gene and variant discovery and the characterisation of molecular processes which contribute to our understanding of pathogenesis and progression in apparently homogenous groups of

people with ALS. This is in part due to the traditional genome-wide association study frameworks and microarray technologies used to identify genes and characterise the effects of their mutations and changes in expression levels on the ALS phenotype. This has a consequential effect on the development of precision medicine approaches in ALS, which concerns the identification of effective biomarkers and therapeutic treatments both readily available and accessible via clinical trials for specific groups of people with ALS, based on their biological characteristics. It is therefore necessary to adopt frameworks capable of detecting a wide range of genomic variation as well as capturing subtleties in gene expression in order to define subgroups of people with ALS more accurately to speed up the discovery of novel biomarkers and allow earlier access to clinical trials.

This chapter will highlight current efforts to integrate precision medicine strategies into translational and clinical ALS research, before discussing issues faced by the ALS genomics community in deciphering the genetic and molecular heterogeneity of ALS. Finally, approaches which could be used to resolve the genomic heterogeneity of ALS and ultimately improve precision medicine strategies will be explored, through the adoption of next-generation sequencing (NGS) in combination with bioinformatics, statistical genetics and machine learning methods.

## **1.2 What is Precision Medicine?**

Precision medicine is described as the tailoring of treatment and symptom management to biologically homogeneous groups of individuals, identified through the analysis of omics data with artificial intelligence and machine learning methods. Various types of omics data such as genetic, transcriptomic, epigenetic, proteomic, and clinical information are utilised. The importance of this approach is that biomarkers which are indicative of differential treatment response or disease progression, which cannot be gathered from clinical assessment alone, can be identified (Ginsburg & Phillips, 2018). The creation of clinicogenetic and molecular patient stratification models can also be created for use in further genomic discovery and characterisation studies. In the last year, a large-scale precision medicine initiative, PRECISION ALS (McFarlane et al., 2023), has been established to identify genomic biomarkers and develop progression prediction models. Through a collaborative partnership with 9 academic sites and 7 industry partners throughout Europe, phenotypic and omics data will be collected from over 21,000 people with ALS via a dedicated data platform.

Longitudinal collection of multimodal data will also be achieved as the infrastructure allows the documentation of all stages of the individuals journey through the healthcare system. Although this collaboration is still in the initial data collection phase, it is hoped that this approach will be highly beneficial for ALS research. Despite this effort representing a major milestone in how cross-collaborative data infrastructure can improve patient stratification and biomarker identification, a lot remains to be explored at a more foundational level with regards to understanding the role of causal and modifier genes to molecular mechanisms of pathogenesis, as well as developing frameworks to identify biomarkers of said molecular mechanisms to use for patient stratification, biomarkers of clinical progression, and clinical trial recruitment based on the tested therapeutic's mode of action.

### **1.3 Barriers to Precision Medicine in ALS**

#### **1.3.1 The genetic classification of ALS is outdated**

As previously stated, the classification of ALS is heavily dependent on family history and the presence of causal gene mutations. However, this distinction is highly misleading and detrimental to both people with ALS and the ALS research community. International surveys evaluating clinical testing practices report that 27-49% of people with SALS are offered genetic testing, whereas approximately 90% of people with FALS are afforded this opportunity (De Oliveira et al., 2023; Klepek et al., 2019; Salmon, Anoja, et al., 2022; Vajda et al., 2017), despite FALS often being misdiagnosed as SALS due to small family sizes or age-dependent gene penetrance (Salmon, Kiernan, et al., 2022).

This has a consequential effect upon the identification of individuals who may be eligible for targeted clinical trials and therapies; recent genetic screening studies report that 11-14% of people with SALS carry a pathogenic or likely pathogenic variant in an ALS-linked gene (Ruf et al., 2023; Shephard et al., 2021; Van Daele et al., 2023), with an estimated 20% of UK individuals in one study having a clinically actionable result according to Genomics England guidelines (Mehta et al., 2022). This, along with the estimation that 54% of *SOD1* and 74% of *C9orf72* incident cases are likely to be SALS (C. A. Brown et al., 2021), and that upwards of 15% of people with SALS meet the eligibility criteria to be recruited into *SOD1* and *C9orf72* gene-therapy based clinical trials (Shephard et al., 2021), stresses the importance of making genetic testing available to the same percentage of people with SALS as with FALS, to

ultimately improve access to appropriate clinical trials and therapies. Although, genetic testing in the UK is currently offered to either those with FALS or young-onset SALS (below the age of 40), which is unjust given that this policy potentially misses 98% of SALS patients with a clinically actionable result (Mehta et al., 2022), as the age of onset of ALS can range from 45 to 75 years of age.

### **1.3.2 Genome-wide association studies and microarray technologies are falling out of favour for genetic discovery in ALS**

In the last two decades, there has been monumental progress in our understanding of how genes contribute to and modulate ALS onset and progression, largely through the application of genome-wide association studies (GWAS), which utilise genetic information from microarray technologies to identify genomic variants associated with ALS risk or phenotype.

Examples of tentative SALS susceptibility loci discovered using this approach in individuals of European ancestry include *DPP6* (rs10260404) (van Es et al., 2008), *ITPR2* (rs2306677) (van Es et al., 2007), *FGGY* (rs6690993) (Dunckley et al., 2007), a 175kb linkage disequilibrium block containing *SUNC1*, *HUS1* and *C7orf57* (rs2708909 and rs2708851) (Chiò et al., 2009), and a locus at chromosome 17q11.2 containing the tag-SNP for *KRT18P55* (rs34517613) (van Es et al., 2007). Several modulators of age of onset have also been discovered; the first being a 750kb spanning region on chromosome 1p34.1, with each copy of the minor allele of the intronic *ST3GAL3* tag-single nucleotide polymorphism (SNP) (rs3011225) conferring a 2.5 year earlier age of onset (Ahmeti et al., 2013). More recently, *CTIF* (rs2046243) and two genes containing SNPs at DNA methylation sites; a 144.7kb region tagged by rs9357140 (*C6orf10/LOC101929163*), and a 16kb region tagged by rs4970944 (*CTSS*). The presence of at least one copy of the major allele of *CTIF* reduces age of onset by approximately 1.3 years (C. Li et al., 2023), with the AA genotype of the *CTSS* SNP delaying onset by two years (M. Zhang et al., 2021). In patients harbouring *C9orf72* mutations, each A allele in *CTIF* delays onset by 1.6 years (C. Li et al., 2023), with the *C6orf10* AA genotype demonstrating a 6 year delayed age of onset (M. Zhang et al., 2018). Survival-associated SALS loci have also been reported, such as *KIFAP3* (rs1541160), where the CC genotype is associated with 14-months longer survival (Landers et al., 2009), as well as *CAMTA1* (rs2412208) and *IDE* (rs139550538), whose GG/GT and AA/AT genotypes correspond to a 4- and 8-month reduction in



survival, respectively (Fogh et al., 2016). Although, the only reproducible ALS SNP locus identified thus far has been *UNC13A* (rs12608932) (van Es et al., 2009), with a 5 to 33 month shorter survival in people with ALS carrying the homozygous CC genotype (Diekstra et al., 2012)

GWAS studies can also identify structural variants (SV) and copy number variants (CNV) which are associated with ALS. Structural and copy number variants comprise various forms of genomic imbalance, including insertion, deletion, inversion, duplication and inter-chromosomal translocation (Carvalho & Lupski, 2016; McCarroll & Altshuler, 2007; Roses et al., 2016), with SVs representing a major difference between individuals in health and disease (Lupski et al., 2010; Marshall et al., 2017; Weischenfeldt et al., 2013). The most well-defined ALS SV risk locus captured by GWAS is 9p21.2 (Laaksovirta et al., 2010; Shatunov et al., 2010; van Es et al., 2009), for which the haplotype was later identified as the intronic hexanucleotide *C9orf72* repeat expansion (DeJesus-Hernandez et al., 2011; Renton et al., 2011). Due to the elusive and heterogeneous nature of CNVs, many CNV susceptibility loci discovered with GWAS have been found to be inconsequential (Morello et al., 2018) - only duplications in the survival motor neuron gene *SMN1* consistently demonstrate an association with SALS risk (Blauw, Barnes, et al., 2012; X.-B. Wang et al., 2014).

Despite the wealth of SNP and SV loci discovered by GWAS, only those in *C9orf72*, *UNC13A*, *CAMTA1* and *SARM1* (Chiò et al., 2023; Su et al., 2022; van Rheenen et al., 2016a, 2021; Vidal-Taboada et al., 2015; Yang et al., 2019) have been consistently associated with ALS risk and survival. Many of the aforementioned previous GWAS associations have been lost in replication studies (Ahmeti et al., 2013; Cai et al., 2014; Y. Chen et al., 2012; Czell et al., 2017; Daoud et al., 2010; Fernández-Santiago et al., 2011; Fogh et al., 2011; Koçoğlu et al., 2021; van Doormaal et al., 2014), whilst for other loci, GWAS replication studies have not been performed. Therefore, it is uncertain whether these genes modulate ALS risk or phenotype, or if their preliminary associations are an effect of the study design. Furthermore, there are several methodological and technical aspects of GWAS and microarray technologies that have hindered both the discovery and replication of causal and modifier genes and their variants in ALS. These are discussed in more detail below.

### **1.3.2.1 Replicable and reliable associations can only be obtained with large sample sizes and appropriate control-to-case ratios**

The main reason why so many associations are refuted in independent replication studies is largely due to the effect known as the ‘winner’s curse’, which is where the estimates of variant effect sizes in discovery studies are often inflated. This means that replication studies will fail as they will be underpowered to detect such associations (Xiao & Boehnke, 2009). One of the reasons why this can occur is that there may be an inadequate case-to-control ratio in the cohorts used in these analyses. It is generally accepted that in order to improve power in genetic association studies, at least 4 controls to every case should be recruited, although this is rarely achieved in practice (Katki et al., 2023). Another reason is that the total sample size is not large enough to detect causal associations, even if they have smaller effect sizes i.e., odds ratio (OR) of 1.3-1.5 (Hong & Park, 2012). There are two recent examples of GWAS that illustrate the benefits of using large sample sizes and higher control-to-case ratios for ALS gene discovery. Using 12,577 cases and 23,475 controls, *MOBP*, *SCFD1*, and a locus fine-mapped for *C21orf2* (*CFAP410*), were discovered and validated in a replication cohort as novel ALS risk loci (van Rheenen et al., 2016a). When expanding this cohort to 27,505 cases and 110,881 controls, 15 risk loci were discovered. These included novel associations for *HLA*, *GPX-TNIP1*, *SLC9A8-SPATA2*, *ERGIC1*, *COG3* and *PTPRN2*, and replication of *SCFD1*, *TBK1*, *NEK1*, *KIF5A*, *C21orf2* (*CFAP410*), and *MOBP-RPSA* loci, alongside the well-defined associations at *C9orf72*, *UNC13A* and *SOD1* (van Rheenen et al., 2021).

### **1.3.2.2 The calculated genome-wide heritability of ALS is not accurate as GWAS studies and microarray technologies consider only common variation**

One important application of GWAS besides the identification of causal variants, is determination of the genetic architecture of ALS through SNP-based heritability estimates. Usually, linear mixed-model approaches are employed in the GWAS framework, which consider all SNPs regardless of their association to account for polygenic effects, which are the combined effects of multiple SNP-based associations in each locus. As a result, the calculated heritability estimates are considerably lower than what is observed in twin and parent-offspring studies; ranging between 12 and 21% (Fogh et al., 2014; Keller et al., 2014). This is because estimates derived from twin and family-based studies compare phenotypic similarities between either

monozygotic (identical) and dizygotic (non-identical) twins, or individuals within the family or inherited structure, therefore the genetic contribution of traits can also be influenced by indirect genetic effects from relatives, gene-environment interactions, and epistatic or non-linear effects, which are not captured in traditional SNP-based heritability estimates of unrelated individuals. Furthermore, it is assumed that identical and non-identical twins have similar environmental influences on the studied trait, and that the effects of population stratification and assortative mating are mitigated when using family-based measures of heritability, although these assumptions can be violated (Young et al., 2019; Matthews and Turkheimer, 2022).

More sophisticated methods to calculate SNP-based heritability, such as linkage disequilibrium score regression, which tangles out confounding effects such as population stratification and cryptic relatedness from polygenicity, estimate the heritability of ALS as 8.2% (McLaughlin et al., 2017), which despite replicating a previous population-based estimate of 8.5% identified with the standard GWAS approach (van Rheenen et al., 2016a), still inadequately captures the full genetic architecture of ALS. Therefore, the underestimation of SNP-based heritability ultimately lies within the inability for GWAS to consider rare variation (< 1% MAF), and the inability for microarray technologies to reliably tag low frequency (MAF 0.5-5%) and rare SNPs. In ALS, the drivers of phenotype are rare variants which have medium-to-large effects, therefore by calculating SNP-based heritability using standard GWAS approaches, estimates are constrained by the variance explained by the additive effects of common variants.

### **1.3.2.3 Variants other than SNPs are not reliably tagged and characterised by microarrays**

Whether microarrays are used for GWAS or for the screening of variants in potential ALS risk genes, they cannot characterise more complex variation i.e., small insertions and deletions (indels), SVs and copy number alterations. The genotype of a SNP is easily deduced as the intensity levels of each probe cluster into three groups, representing each of the three possible genotypes. However, as SVs and CNVs usually span multiple probes, intensities have to be either aggregated from adjacent SNPs or across samples to make consensus calls. Microarrays also often incur hybridisation-related biases as single fragments of genomic sequences can map to more than one probe. Furthermore, highly polymorphic regions and tandem repeats

are difficult to detect as a lower density of available probes map to those regions (Alkan et al., 2011). As the upper estimate for heritability explained by genetic information captured on genome-wide microarrays for SALS is approximately 20%, this implies that the remainder is in rare variants and other types of genetic variation such as copy number variation, short tandem repeats, post-transcription RNA editing, and epigenetic changes (DeJesus-Hernandez et al., 2011), that cannot be identified easily by microarrays.

### **1.3.3 Current ALS gene panels for use in diagnostic and research settings are not regulated**

Genetic panel screening in ALS is beneficial for not only evidencing an ALS diagnosis, but to also signpost individuals to appropriate therapeutic treatments and identify those best suited for enrolment in gene-mutation specific clinical trials. Despite these advantages, many of the ALS-defined gene panels used in diagnostic and research settings contain genes whose evidence mainly originates from traditional linkage and GWAS study designs, and often contain genes which have conflicting or no evidence to support their role with ALS risk or phenotype. For instance, the Genomics England PanelApp, which curates evidence on 42 genes included in the ALS/motor neuron disease genetic testing panel, finds that only 24 (57.1%) are classified as green, which means that there is sufficient evidence for those genes to explain the disease phenotype, as their variants are pathogenic and diagnostically reportable (Martin et al., 2019). One gene, *NEFH*, is classified as amber as there is borderline supportive evidence for a causal relationship, but there are not enough reported pathogenic or likely pathogenic variants in the literature to be deemed clinically actionable. Furthermore, there is not a well-defined consensus on which genes should be included in these panels, nor is there a rigorous procedure to standardise genetic panels in healthcare and laboratory settings nationwide. A recent worldwide survey of 14 widely used ALS clinical gene panels (Dillio et al., 2023) identified a total of 91 genes present in at least one panel, with 44% of those unique to only one panel. Furthermore, more than 90% of panels contained the causally linked ALS genes *ANG*, *FUS*, *OPTN*, *SETX*, *SOD1*, *TARDBP*, *UBQLN2*, *VAPB*, and *VCP*, with half of the panels offering the option to screen for the *C9orf72* repeat expansion. There was no relationship with ALS identified for 14 (15.4%) genes; *ABCD1*, *ABHD12*, *ATL1*, *BSCL2*, *GBE1*, *HEXA*, *HNRNPD*, *HSPD1*, *LMNB1*, *PRF1*, *PRPH2*, *PSEN1*, *REEP1*, *SPAST*.

## **1.4 Next-Generation Sequencing (NGS) Approaches to Advance Precision Medicine in ALS**

As previously mentioned, genotyping microarrays are the most widely used method for detecting SNPs and SVs, as well as quantifiable changes in gene expression, although next-generation sequencing (NGS) approaches (short-read WGS and RNAseq) are rapidly becoming the preferred choice as they can more reliably detect complex genetic variation (Majewski et al., 2011; Spielmann & Mundlos, 2013), multiple gene transcripts and lowly expressed genes, because they do not rely on the selection of known DNA and RNA probes. Instead, the whole genome and transcriptome is randomly sampled and sequenced into 150 base-pair fragments before being mapped to a reference genome, which achieves a consistent average read depth coverage (how many fragments overlap a genomic position) of 30-40x. Consequently, NGS is more sensitive for quantifying gene expression and calling genomic variants as the confidence of the presence of a genetic variant or level of gene expression from dedicated bioinformatics tools are determined from a read-count or abundance-based approach rather than a relative measurement of probe intensity at each gene or base pair (Alkan et al., 2011). Moreover, as NGS provides better distribution of sequencing position and coverage of the non-coding region of the genome and transcriptome, a hypothesis-free experimental design can be employed. The quantification of variation and expression for thousands of genes and regions at any one time is highly beneficial when trying to characterise the genetic and molecular landscape of a complex disease such as ALS.

### **1.4.1 Design aspects of NGS to consider**

#### **1.4.1.1 Tissue Types**

The most extensively utilised tissues to study genetic and transcriptomic alterations in people with ALS using WGS and RNAseq are the motor cortex and blood. The motor cortex is a valuable region to examine as regardless of inheritance or clinical phenotype, pyramidal cell degeneration and cytoplasmic phosphorylated TDP-43 inclusion pathology is observed in 97% of individuals (Nolan et al., 2020; Suk & Rousseaux, 2020). There is also substantial evidence that hyperexcitability of the motor cortex can precede UMN degeneration by propagating ALS pathology along the descending corticofugal axons of the corticospinal tract: the 'dying forward' hypothesis of ALS (Eisen, 2021; Eisen et al., 2017). Although, the collection and preparation of

motor cortex tissue can only occur post-mortem, and questions still emerge over whether any quantifiable changes are a consequence of the end-stage of disease or the differential contribution of various molecular processes throughout the disease course. Nevertheless, it remains a pivotal tissue to interrogate patient heterogeneity in SALS, particularly in transcriptomic studies. Nevertheless, from a precision medicine perspective, it can be more practical to utilise blood tissue as samples can be collected relatively non-invasively and you can more easily and confidently identify genetic and molecular biomarkers of progression and differential treatment response.

#### **1.4.1.2 ALS Sequencing Consortia**

As previously elucidated, collaboration between geneticists, bioinformaticians, and clinicians, and data sharing between research centres can be an effective strategy to study the genetic and molecular heterogeneity of ALS. Besides PRECISION ALS, there are already several smaller case-control research initiatives operating both nationally and internationally which have adopted this framework, via collection of NGS data from motor cortex and blood. The largest is Project MinE, which was developed in 2018 with the aim of collecting WGS genetic profiles of 15,000 people with ALS and 7,500 controls of European ancestry from 21 countries, as well as matching RNAseq and methylation data available for a proportion of individuals (Project MinE ALS Sequencing Consortium, 2018). Another notable consortium is TargetALS, which contains WGS and RNAseq data of hundreds of post-mortem brain tissue samples from five centres across the USA (*TargetALS*, n.d.). As these consortia recruit a very high percentage of people with SALS or apparent SALS i.e., people with no family history or mutations in Mendelian or FALS-linked genes, this means that any discoveries are more likely to generalise to the entirety of the ALS population. There is also considerably higher power for detecting novel and rare genetic variants and gene expression alterations as well as confirming or disputing previously identified modulators of ALS risk or phenotype, as a product of the large sample sizes acquired.

#### **1.4.1.3 Use of Bioinformatics Tools to Identify Genetic Variation**

One of the most crucial processes in NGS variant discovery is the application of various bioinformatic tools which utilise a range of calling algorithms that perform downstream genotyping and optional variant filtering. Unlike SNPs and indels, which have dedicated best practice guidelines i.e., the Genome Analysis Toolkit (GATK) (DePristo et al., 2011) and Global Alliance for Genomics and Health (Krusche et al.,

2019), structural variant calling is largely unregulated. Their intrinsic unpredictability makes it difficult for calling algorithms to distinguish between interspersed duplications and inversions, tandem duplications and insertions, and deletions and translocations (Mahmoud et al., 2019). Stringent benchmarking and evaluation studies of multi-purpose and specific SV callers on both real and simulated short-read WGS data can offer recommendations to researchers, although the general consensus is that there is no singular tool that offers a 'one size fits all' approach to the detection of SVs. For instance, Manta (X. Chen et al., 2016) performs best on non-reference insertions, small-to-medium deletion and duplication variants with micro-homology features ( $\geq 30\text{bp}$ ) and insertions with varying breakpoint sizes, whereas Wham (Kronenberg et al., 2015) and the GRIDSS rearrangement detection suite (Cameron et al., 2017) are suited towards deletion and duplication events (Cameron et al., 2019; Kosugi et al., 2019). Conversely, Delly cannot handle structural variants smaller than 300 base-pairs, and consistently miscalls inversion events (Cameron et al., 2019). Fortunately, in the last 5 years, there have been a proliferation of meta-callers, which integrate several different SV tools (Collins et al., 2020; O'Donnell & Fischer, 2020; Zarate et al., 2020) as well as more specialised SV calling algorithms, such as MELT for mobile element insertions (Gardner et al., 2017), ExpansionHunter and ExpansionHunter Denovo for known and novel tandem repeat expansions (Dolzhenko et al., 2019, 2020), TARDIS for interspersed duplications (Soylev et al., 2019), and for SVs which reside in low complexity regions (Delage et al., 2020; Kosugi et al., 2019).

## **1.4.2 Whole Genome Sequencing (WGS) Analysis Frameworks used in ALS**

### **1.4.2.1 Case-Control Variant Screening**

This approach consists of screening for specific classes of genetic variation in people with ALS and controls using variant calling tools, before determining their pathogenicity status and comparing their frequency in both populations to determine whether they contribute to ALS susceptibility. Generally, these studies will look for variants in genes present in clinical and laboratory-based testing panels or identified from the literature, as an unbiased genome-wide approach can be computationally exhaustive and time consuming.

As GWAS is suitable for screening of SNPs, WGS is used to offer populational insights on their contribution to the complexity of ALS. One of the most recent and most notable studies was a WGS analysis of 1043 Italian people with ALS who were screened for

variants in 42 ALS-linked genes, which identified that 26.9% of people with ALS, including 21.5% of people with SALS, carried a disease-causing variant. The same authors also found that 10.7% carried the *UNC13A* C/C survival modifier SNP genotype, with 24.2% more people with early onset ALS (< 50 years) carrying a causal mutation than late-onset ALS (> 75 years), consistent with the multistep model of ALS (Grassano et al., 2022). There have also been genetic screening studies of German (Krüger et al., 2016), Australian (McCann et al., 2021), and British (Morgan et al., 2017) populations which also report a significant proportion of people with ALS carrying more than one pathogenic variant in ALS-associated genes, with oligogenic SALS cases in the Australian population demonstrating earlier age of onset than those without a mutation (McCann et al., 2021).

There are a couple of instances where the advantages of using WGS to identify and genotype SVs comes into effect. Recently, two repeat expansions were associated with increased ALS susceptibility in individuals of European ancestry; a downstream tetranucleotide (TTTA) *NEK1* repeat of  $\geq 11$  from the largest ALS GWAS to date from Project MinE (van Rheenen et al., 2021), and a non-coding CA repeat of  $\geq 19$  in *STMN2*, using targeted PCR for ~390 SALS and 330 controls (Theunissen, Anderton, et al., 2021). Individuals harbouring the *STMN2* repeat were reported to have a 7.5 year earlier age of onset, with accelerated disease progression in people with bulbar-onset SALS. However, both of these associations were lost when applying ExpansionHunter to independent WGS cohorts with the same European genetic background: neurologically normal individuals also displayed *NEK1* and *STMN2* repeat lengths above their proposed pathogenic thresholds (Grima et al., 2022; Ross et al., 2022), which was likely detected as large population-based control cohorts were used.

The most encouraging result so far for the ALS community is the confirmation that the *C9orf72* repeat expansion modifies age of onset in bulbar-onset ALS, and that there are novel associations with a *VCP* inversion and *ERBB4* insertion in bulbar- and respiratory-onset ALS, respectively, for reduced age of onset and survival (Al Khleifat, Iacoangeli, van Vugt, et al., 2022). These were ultimately discovered because the large sample size used for screening (over 6,000 individuals from Project MinE) combined with the use of dedicated WGS variant calling tools and a bioinformatic validation protocol meant that the above associations had large effect sizes and the



variant calls were robust. The likelihood that screening for these variants in clinical and prognostic settings would be beneficial needs to be elucidated, especially as a possible synergistic interaction for ALS risk was found in *C9orf72* expansion carriers who also harboured the *VCP* inversion, and that since the discovery of *ERBB4* as a causative ALS gene in 2013, only missense mutations have been linked to ALS pathogenesis (Scarlino et al., 2020a; Takahashi et al., 2013, p. 4, 2019, p. 4).

#### 1.4.2.2 Meta-Analysis

Meta-analysis is a statistical framework which involves combining the findings from multiple independent genetic association studies in order to statistically determine the absolute effect of genetic variants to disease risk. The advantage of using this approach is that by pooling results from multiple smaller studies, you can more accurately estimate the effect sizes of the genetic variants being tested, therefore enhancing statistical power and making any findings highly generalisable as more appropriate sample sizes are utilised (Haidich, 2010). The benefits of meta-analysis in ALS are huge, as you can more credibly confirm or refute the association of a novel or putative ALS-linked gene, or causally linked genes whose association with ALS have long been established but no definitive evidence exists from replication studies.

Several multicentre case-control meta-analyses have been performed in recent years to validate the role of certain SVs in ALS risk. The validation of *NIPA1* polyalanine and *ATXN1/ATXN2* polyglutamine intermediate trinucleotide repeats through separate meta-analyses of the Project MinE cohort have been instrumental in further explicating their role as ALS susceptibility genes (Sproviero et al., 2017; Tazelaar et al., 2019, 2020); repeat expansions in *ATXN2* and *NIPA1* had previously been linked to ALS, albeit with conflicting results in GWAS and CNV genome-wide screens (Blauw, van Rheenen, et al., 2012a; Dekker et al., 2016; Elden et al., 2010). However, despite functional evidence indicating that these genes participate in analogous *C9orf72* processes, including defective intracellular RNA processing and endoplasmic reticulum transport (Martinez-Lage et al., 2012; Tazelaar et al., 2020), all three genes failed to show a modifying effect on age of onset or survival in both intermediate repeat-positive SALS cases and those harbouring *C9orf72* repeat expansions (Sproviero et al., 2017; Tazelaar et al., 2019, 2020). The recruitment of consanguineous European and American subjects within the Project MinE cohort could have contributed to this finding, as in Southern European, Korean, Japanese

and Northern Indian populations, large normal *ATXN2* repeat alleles have been linked to increased ALS susceptibility (Gonçalves et al., 2020; Y.-E. Kim et al., 2018; Narain et al., 2017; Naruse et al., 2019; Tavares de Andrade et al., 2018).

Another WGS study which utilised 8,747 European and American samples in addition to meta-analysing 9 previously studied populations, finally confirmed that *SMN1* and *SMN2* copy number is not determinant of survival or age of onset in people with ALS, nor is their copy number distribution on ALS susceptibility (Moisse et al., 2021), in accordance with previous reports on smaller datasets (Corcia et al., 2002, 2018). A further meta-analysis, which combined European and North American datasets from four recently published studies and British Project MinE samples, found 24-30 intermediate *C9orf72* hexanucleotide repeat expansions to be an adjuvant to ALS susceptibility, contrary to the long-held belief that only expansions 100-1000 repeats in size increase ALS risk (Iacoangeli, Al Khleifat, Jones, et al., 2019). Since then, this association has also been identified in the Finnish population, for compound heterozygous carriers of two intermediate length alleles where the longer allele is larger than 17 repeats, with an additional connection to reduced survival (Kaivola et al., 2020). Further studies need to address these results in more homogeneous populations, such as Ashkenazi and North African Jews, where only 0.52% of people carry intermediate repeat alleles (Goldstein et al., 2018), and Sardinia, where 13.6% of all ALS cases carry the *C9orf72* expansion (Borghero et al., 2014), as well as in a wider context; the only other support for *C9orf72* compound heterozygosity is in a British frontotemporal dementia report of someone with a 200-repeat long allele (Cooper-Knock et al., 2013) and a Belgian ALS-frontotemporal dementia cohort with homozygous repeats ranging from 8 to 21 units (Gijssels et al., 2016).

#### **1.4.2.3 Rare Variant Burden Analysis**

Burden analysis is a type of gene-based association test which collapses variants into gene- or regulatory region-based units. The purpose of this is to increase the power of identifying rare or low-frequency variants in case-control studies, which could be missed in a standard variant-by-variant screening approach, particularly if there are many variants which would not survive multiple testing correction (S. Lee et al., 2014). There are several types of burden methods that one can employ, with the most frequently used being the combined multivariate and collapsing (CMC) (B. Li & Leal, 2008), sequence kernel association test (SKAT) (Wu et al., 2011), the optimal unified

test (SKAT-O) (S. Lee et al., 2012), and Madsen-Browning (Madsen & Browning, 2009).

Each of these methods have their advantages. For instance, the CMC method is useful if all of the rare variants are assumed to be causal and have similar effect sizes, as the means of each variant are compared in different MAF categories. The Madsen-Browning test is similar but uses a combination of a weighted-sum test and permutation of case status to adjust for the variant weights and more reliably identify an excess of variants in a gene or region which contribute to disease. However, both SKAT tests are more commonly used, as because a variance component approach is adopted to evaluate the distribution of variants, they consider that there will be a large amount of non-causal variants, and causal variants who display different directions of effect.

In recent years, exome-wide variant burden analysis has been integral for the discovery of *NEK1* (Kenna et al., 2016), *GLT8D1* (Cooper-Knock et al., 2019), *DNAJC7* (Farhan et al., 2019), and *TUBA4A* (B. Smith et al., 2014) as causal and modifier ALS genes. Burden analysis frameworks have also been used in combination with WGS to identify novel associations between gene variation in *MYH15* (H. Kim et al., 2019), *CAV1* (Cooper-Knock et al., 2021) and *IL18RAP* (Eitan et al., 2022) with ALS susceptibility. Project MinE has also been an invaluable resource for refuting associations due to the sheer scale of WGS data available. The most recent example is tumor protein p73 (*TP73*), a transcription factor belonging to the p53 tumor suppressor gene family which is responsible for regulating apoptosis in the cytoplasm and mitochondria (Melino et al., 2004). It was initially identified as a potential SALS risk gene by initial exome screening of 87 cases and 324 controls with variant prioritisation tools and subsequent sequencing in two additional cohorts. Altogether, twenty-four rare nonsynonymous pathogenic variants were identified, at a similar frequency reported in other ALS-related genes (Russell et al., 2021). Although, the association of rare non-synonymous *TP73* variants was refuted in a much larger cohort of 8,230 cases and 9,671 controls obtained from Project MinE and the ALS Knowledge Portal, as a large number of controls carried these variants, therefore diluting the previous association (Dilliot et al., 2022). Another example is *CHCHD10*, a mitochondrial gene which was initially suggested as a new ALS gene after an initial report of a mutation carrier with mitochondrial disease who also displayed ALS-like

features and related phenotypes, such as myopathy and cerebellar ataxia (Bannwarth et al., 2014), and follow-up screening determining that pathogenic non-synonymous variants are present in people with FALS (Johnson et al., 2014). Although, analysis of all non-synonymous *CHCHD10* variants in 4,365 cases and 1,832 controls of Project MinE using a range of aggregate gene burden analyses methods did not find any additional evidence supporting their role in ALS, as burden analyses were insignificant and carriers of *CHCHD10* mutations did not exhibit pure ALS phenotypes (“CHCHD10 Variants in Amyotrophic Lateral Sclerosis,” 2018).

### **1.4.3 Bulk RNAseq Analysis Frameworks used in ALS**

#### **1.4.3.1 Differential Expression Analysis**

The most common use of RNAseq data is to quantify and compare the levels of gene expression between people with ALS and controls, by performing differential expression analysis. The number of reads which map to each gene are acquired via alignment to a reference genome or transcriptome, before aggregating the counts of each transcript to produce gene counts. These are then normalised for factors such as gene transcript length, average number of reads per sample and sequencing protocol and platform specific batch effects (Conesa et al., 2016). Popular packages used to perform expression analysis include edgeR (Robinson et al., 2010) and DESeq2 (Love et al., 2014). They take normalised gene count matrices and phenotypic information containing covariates to adjust for any potential factors which may affect the accuracy of expression estimates, such as sex, age, and site of onset. Further preprocessing may be conducted, such as the removal of genes with low read counts across samples, and algorithm-specific normalisation. Both of these packages perform parametric analysis as they assume a negative binomial distribution of the data; edgeR introduces sources of bias into the design to perform normalisation and differential expression, whereas DESeq2 normalises based on size factors, which is the median ratio or geometric mean of all samples for each gene (Conesa et al., 2016). Once the list of differentially expressed genes (DEGs) are obtained, downstream analysis can be performed to elucidate the biological processes that the DEGs are involved in. Typical methods include gene enrichment, pathway and network analysis.

#### **1.4.3.2 Molecular Subtyping**

Molecular subtyping involves applying various machine learning techniques to expression data to cluster individuals into biologically homogeneous groups, which is

the main method implemented in precision medicine frameworks. Unsupervised machine learning approaches, which do not require labelled data such as ALS-control status, are typically used to identify molecular phenotypes which can be used for stratification, as they can find unknown clusters of genes with similar expression profiles which would otherwise be hidden.

There have been several recent studies which have performed molecular subtyping using post-mortem brain expression data of people with SALS and controls. The earliest study, performed in 2015, used hierarchical clustering to analyse the motor cortex transcriptome of 31 people with SALS and 10 controls. They identified three clusters; one represented a control-specific signature, with two being unique to SALS. The first group, termed SALS 1, was occupied by 16 patients and exhibited increased expression of genes involved in antigen processing, glycolysis and mitochondrial energy homeostasis, whereas the remainder of people with ALS, assigned to SALS 2, displayed downregulation in expression of these pathways. In fact, the SALS 2 expression signature was enriched for several biologically relevant pathways, with the upregulation of genes involved in extrinsic apoptotic signalling, caspase activation and cytokine signalling, and the downregulation of antigen processing genes, vascular endothelial growth factors, alongside differential expression of cell adhesion genes (Aronica et al., 2015). A subsequent follow-up study focusing on the expression of 203 causal and susceptibility-linked ALS genes was performed in the same dataset using the same clustering approach, which again, identified two subgroups of SALS and a control-specific cluster. A total of 118 genes were differentially expressed between SALS and controls, with 75 of them residing in SALS 2. Functional analysis revealed that SALS1 was enriched for intracellular signal transduction, regulation of cellular communication and chemotaxis, whereas SALS2 showed enrichment for oxidative stress responses, cytoskeleton organisation and cellular localisation, confirming that these subtypes confer diverging processes of ALS pathogenesis in specific subgroups of patients (Morello et al., 2017).

Other molecular stratification studies have been able to separate people with ALS based on their dominant pathology, with hierarchical clustering analysis of 148 frontal and motor cortex transcriptomes of people with SALS revealing that samples can be assigned to one of three distinct molecular subtypes; oxidative and endoplasmic reticulum stress (61%), TDP-43 mediated transposable element activation and

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increased cytoplasmic aggregate formation (20%), and glial activation (19%). Further analysis also confirmed that three transposable elements were significantly upregulated in motor cortex tissue in those assigned to the transposable element subtype - long interspersed nuclear element (LINE) L1HS, and the small interspersed nuclear repeat family classes AluYk12 and AluYa5 (Tam et al., 2019). Finally, 451 samples from 208 people with ALS from a publicly available ALS RNAseq dataset (Prudencio et al., 2020) were analysed using the same approach, which yielded three subtypes: glial activation with reduced transposable element expression, oxidative stress and synaptic signalling, and dysregulation of transcription. These strengthen the support for the previous defined molecular phenotypes. Interestingly, people with ALS assigned to the glial subtype demonstrated the fastest disease progression, with a median survival of 28 months (Eshima et al., 2023).

## Chapter 2. Summary of Thesis Objectives

In this thesis, I demonstrate how exploiting the potentialities of large-scale NGS data by using several bioinformatics and machine learning approaches can help us to decipher the genomic heterogeneity of ALS, in relation to the missing heritability incurred by GWAS and microarray-based technologies. These are explored in depth using two cohorts which have predominantly recruited people with SALS: Project MinE and TargetALS.

Chapter 4 explores how WGS can advance our understanding of the genetic basis of ALS, in particular through the lens of structural variation. I develop an upgraded version of a previously developed end-to-end bioinformatics pipeline, DNAscan2, through the addition of tools frequently used for WGS studies of complex neurodegenerative diseases.

Chapter 5 examines how genetic variation in the neurofilament heavy chain gene (*NEFH*) influences ALS susceptibility in a combined cohort of 11,130 people with ALS and 7,416 controls from a literature search and the Project MinE cohort. I firstly analysed the contribution of previously identified SNVs to ALS risk by performing a literature-based meta-analysis of genetic association studies which employ traditional sequencing and NGS approaches. Comprehensive screening of SNVs and SVs in the Project MinE cohort was then performed, followed by assessment of their contributions to ALS risk via logistic regression and rare variant burden analysis.

In Chapters 6 and 7, I utilise bulk RNAseq expression data of the motor cortex from TargetALS and a subset of Project MinE (KCL BrainBank), which when combined, represents the largest motor cortex expression cohort to date. Chapter 6 assesses the molecular landscape of ALS by performing independent case-control differential expression analyses of both cohorts. Differentially expressed genes underwent gene and pathway enrichment analysis, with genes common to both datasets reviewed in regard to their involvement in known mechanisms of ALS pathogenesis. Correlation analysis of genes implicated in commonly enriched pathways was also performed against clinical outcomes; namely age of onset and survival. Cell type deconvolution was performed to assess if gene enrichment results were a product of the differential contribution of cell types in both datasets. In Chapter 7, I try to test the hypothesis that molecular subgroups of people with ALS are defined by a predominant molecular

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mechanism of pathogenesis that reflect differences in onset, progression and survival measures. I do this by performing unsupervised hierarchical clustering of KCL BrainBank cases to generate the molecular subtypes, before determining their molecular architectures via gene enrichment, network and cell composition analysis. Subtype validation was achieved by applying linear discriminant models to the cases from TargetALS, as well as Italian and Dutch blood expression datasets. I also determine the ALS and regional specificity of the expression signatures of each subtype using KCL BrainBank, TargetALS and Dutch controls, and occipital cortex and cerebellum samples from TargetALS before constructing case-control and motor cortex-other region logistic regression classifier models. Phenotype analysis was also performed to assess subtype-specific clinical outcomes.



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## Chapter 3. Materials and Methods

### 3.1 Data Preparation

This section outlines the data preparation protocol of datasets that were used for analysis in multiple chapters. The Project MinE WGS dataset was used for Chapters 4, 5 and 7. The KCL BrainBank and Target ALS RNAseq data were used for Chapters 6 and 7.

#### 3.1.1 Project MinE WGS Dataset

Genomic DNA from venous blood drawn from patients and controls was isolated using standard methods before DNA integrity was assessed using gel electrophoresis. Samples were sequenced using Illumina's FastTrack Services (San Diego, CA), using PCR-free library preparation on the Illumina HiSeq2000 platform (for Chapters 4, 5 and 7) and HiSeqX platforms (for Chapter 5) to ~35× coverage with 100 bp reads and ~25× coverage with 150 bp reads, respectively.

##### 3.1.1.1 Development of a next-generation sequencing bioinformatics analysis pipeline

Sequenced samples were aligned to the hg38 genome using BWA-mem and were provided to us in compressed reference-oriented alignment map (CRAM) format to be inputted into DNAscan and DNAscan2.

##### 3.1.1.2 Investigating the role of *NEFH* as an ALS risk gene

Sequencing data alignment to GRCh37 (with the Isaac aligner) and variant calling (SNVs and indels with Strelka; SVs with Manta) were performed using the Illumina Isaac pipeline.

##### 3.1.1.3 Utilising hierarchical clustering to identify molecular subtypes of ALS

Sequenced data was aligned to GRCh37 using BWA-mem and binary sequence alignment/map (BAM) format files were generated for each individual.

### **3.1.2 RNAseq Protocol**

#### **3.1.2.1 MRC London Neurodegenerative Diseases Brain Bank (KCL BrainBank)**

##### **3.1.2.1.1 Purification, isolation, and quality control**

For all individuals, postmortem delay (PMD), defined as the time between death and tissue being frozen in hours, was collected, before the 100mg frozen tissue blocks were divided; one for RNA purification and the other for DNA. The 30mg tissue block for RNA was homogenised using a Qiagen PowerLyzer 24 Homogenizer. Total RNA was purified from the homogenate using the standard protocol of the RNeasy Lipid Tissue Mini Kit (Qiagen), with on-column DNase digestion. RNA integrity was estimated using Agilent Bioanalyzer 2100's RNA 6000 Nano assays. RNA quantification was performed using a NanoDrop.

##### **3.1.2.1.2 Library preparation and RNA sequencing**

Library preparation was performed using the standard Illumina TruSeq Stranded Total RNA Sample Preparation Guide with Ribo-Zero Human/Mouse/Rat (October 2013 Rev E.). Fragmentation steps were tailored to degrees of degraded RNA samples using Agilent Bioanalyzer 2100's Nano assay results from the previous section. Libraries were validated using an Agilent Bioanalyzer 2100 to assess fragment size distribution. Library concentrations were estimated using a Qubit RNA High Sensitivity Assay Kit. Nanomolar (nM) concentrations were estimated using  $nM = ng/ul \times (1500/Average\ bp)$ . Libraries were sequenced using Illumina HiSeq 4000 flow cells with 150bp paired-end reads with a target depth of 30 million clusters (60 million reads per sample).

##### **3.1.2.2 TargetALS**

Information for the library preparation and RNA extraction of the TargetALS dataset is available at <http://www.targetals.org/wp-content/uploads/2020/11/README-1.zip>.

### **3.1.3 RNAseq Data Processing Pipeline**

Paired FASTQ files from KCL BrainBank and TargetALS datasets (used in Chapters 6 and 7), and the Zucca PBMC case-only dataset (used in Chapter 7) were transformed to raw transcript counts using a standard bioinformatics processing pipeline (available at [https://github.com/rkabiljo/RNASeq\\_Genes\\_ERVs](https://github.com/rkabiljo/RNASeq_Genes_ERVs)). Paired reads were interleaved using BMap reformat (v38.18.0) under default options before adapters were right-clipped and low-quality reads were removed using BMap bbdup (v38.18.0), as part

of the BBTools suite (Bushnell, 2014). The interleaved reads were aligned to hg38 using STAR (v2.7.10a) under default settings (Dobin et al., 2013), using the Homo\_sapiens.GRCH38.104.gtf reference assembly. Raw transcript counts for each gene were then quantified using HTSeq (Anders et al., 2015) on a sample-wide basis before merging into dataset-specific matrices.

## **3.2 Development of a next-generation sequencing bioinformatics analysis pipeline**

The information presented below was restricted to the Supplementary Methods in the publication due to journal formatting constraints.

### **3.2.1 Datasets**

To compare the SNV and indel calling performance of Freebayes, Strelka2 and GATK Haplotype Caller, we used the paired-end Illumina HiSeq4000 WES of NA12878 (NCBI SRA Accession: ERR1905890) and Illumina HiSeqX PCR-free WGS of HG002 (NCBI SRA Accession: SRR14724544). Samples were aligned to the hg19 genome using the `-alignment` flag of DNAscan in both fast and normal mode prior to SNV and indel calling. Alignment is performed by HISAT2 in fast and normal mode, with BWA-mem introduced in the latter for realignment of soft clipped and unaligned reads to improve the detection of small indels and structural variants in downstream calling steps. Structural variant calling performance of Manta and Delly was evaluated using the aligned HG002 reads in addition to simulated paired-end Illumina WGS reads containing the positions of haplotype-resolved deletion and inversion calls of NA12878 (Sudmant et al., 2015), generated and aligned to the hg38 genome using the VISOR package (Bolognini et al., 2020). For comparing the variant calling and computational power of the new and previous implementations of DNAscan, we utilised 10 UK control WGS samples sequenced as part of the Project MinE amyotrophic lateral sclerosis sequencing consortium (Project MinE ALS Sequencing Consortium, 2018). Sequencing information is provided in Chapters 3.1.1 and 3.1.1.1.

### **3.2.2 Benchmarking of variant callers for DNAscan2**

It was not necessary for callers associated with every additional functionality to undergo benchmarking as they either demonstrate beneficial value for identifying novel disease relevant loci i.e., ExpansionHunter Denovo (Fazal et al., 2020; Rafehi

et al., 2019), or consistently show high performance in benchmarking studies i.e., MELT for mobile element insertion detection (Kosugi et al., 2019; Vendrell-Mir et al., 2019).

### 3.2.2.1 SNVs and Indels

The calling performance of Freebayes and GATK HaplotypeCaller was assessed by running DNAscan with the `-variantcalling` flag in fast, normal and intensive modes for the NA12878 WES and HG002 WGS samples. Fast and normal mode uses Freebayes to call SNVs and indels from a coordinate sorted BAM file. Intensive mode employs GATK HaplotypeCaller to call indels from genomic positions (identified from HISAT2 and BWA-mem alignment) that contain at least one read that potentially harbours a deletion or insertion variant. A similar approach was adopted for Strelka2; both SNVs and indels were called from aligned reads generated by fast and normal mode of DNAscan, with the BED file of probable indel variant positions being used to separate output into SNV and indel variant files with the VCFtools `--exclude-bed` and `--bed` flags, analogous to DNAscan intensive mode. For NA12878, Strelka2 was run with the `--exome` flag. Benchmarking of variant calling performance was performed using hap.py v0.3.14 (*Haplotype Comparison Tools*, 2015/2021) with the RTG vcfeval engine. An example command is shown below, where the baseline VCF and confident regions BED file correspond to the appropriate true positive callsets used to evaluate the SNV and indel calls:

```
hap.py --false-positives {confident_regions.bed} --reference hg19.fa --
report-prefix {outdir} --engine=vcfeval --threads {4} {baseline.vcf}
{comparison.vcf}
```

The NA12878 WES calls were evaluated against the National Institute of Science and Technology (NIST) with Platinum Genomes phase transfer small variant truth set (v3.3.2). Confident call regions were defined as the hg19 exome probe locations from the Agilent SureSelect Human All Exon v5 kit (ELID:S04380110). HG002 calls were evaluated with both the truth variants and confident regions of the NIST small variant benchmarking (v4.2.1) and Genome In A Bottle Challenging Medically-Relevant Genes (GIAB CMRG v1.00) datasets.

### 3.2.2.2 Structural Variants

The structural variant detection power of Manta and Delly was assessed in a similar fashion to that of SNV and indel callers. The HISAT2 and/or BWA-mem aligned BAM files of HG002 and NA12878 WGS samples were processed by Manta as per the old DNAscan implementation, with the same approach adopted for Delly as to obtain a comparable dataset. Calls were then evaluated using Truvari v2.2.1 (*Spiralgenetics/Truvari*, 2018/2021) using the following command:

```
truvari bench -b {baseline.vcf} -c {comparison.vcf} -f {reference.fasta} -o {outdir} --includebed {confident_regions.bed}
```

For HG002, the performance of Delly and Manta on detecting deletions was evaluated using the variant calls and confident regions of the GIAB CMRG deletion SV truth set (v0.6). Deletion and inversion calls of NA12878 were evaluated using calls from the 1000 Genomes structural variant map (Sudmant et al., 2015) as the comparison VCF. To further compare the obtained structural variant calls, the `--sizemin` and `--sizemax` flags were supplied to Truvari. Parameters were defined as 50-100, 101-1000, 1001-10000 and 10000-50000bp (the default `--sizemax` parameter of Truvari).

## 3.2.3 Comparison between DNAscan and DNAscan2

### 3.2.3.1 Variant Calling Performance

Both SNV/indel and structural variant calls were evaluated using precision, recall and F-measure metrics calculated by hap.py and Truvari, where precision is

$$\frac{\text{True Positives}}{(\text{True Positives} + \text{False Positives})}, \text{ recall is } \frac{\text{True Positives}}{(\text{True Positives} + \text{False Negatives})} \text{ and F1 score is } \frac{\text{True Positives}}{\text{True Positives} + \frac{1}{2}(\text{False Positives} + \text{False Negatives})}.$$

Where possible, calling performance of DNAscan and DNAscan2 was assessed by averaging the number of SNV/indel, SV, repeat expansion and MEI calls and STR loci obtained for all Project MinE samples. SV and MEI calls were also separated into their respective subclasses i.e., deletions, insertions, inversions, duplications, Alu, SVA, LINE1. Additionally, the number and percentage of filtered synonymous and non-synonymous SNV variants was acquired from the classification given by refGene annotation.

### 3.2.3.2 Computational Performance

Computational efficiency of the SNV/indel and structural variant callers was assessed by obtaining the wall and CPU time (in hh:mm:ss format) and RAM usage (maximum resident set size in gigabytes) for HG002 and NA12878 samples from the SLURM `sacct` command `--format "Elapsed,CPUTime,MaxRSS"`. The same approach was applied for the comparison of DNAscan and DNAscan2, albeit with time and memory usage being averaged across the 10 samples, and estimated disk read and write usage obtained with addition of `"MaxDiskRead,MaxDiskWrite"` to the above `sacct` command.

### 3.2.4 Hardware

All tests were performed on an Intel Xeon E5-2670 2.6GHz processor with 4 CPUs and 16Gb RAM (in line with the standard computational requirements of DNAscan), except for processes which involved Freebayes, which ran with 4 CPUs and 64Gb RAM.

### 3.2.5 Data Availability

The variant call file containing haplotype-resolved deletion and inversion calls of NA12878 is available at:

[http://ftp.1000genomes.ebi.ac.uk/vol1/ftp/phase3/integrated\\_sv\\_map/supporting/GRCh38\\_positions/ALL.wgs.integrated\\_sv\\_map\\_v1\\_GRCh38.20130502.svs.genotypes.vcf.gz](http://ftp.1000genomes.ebi.ac.uk/vol1/ftp/phase3/integrated_sv_map/supporting/GRCh38_positions/ALL.wgs.integrated_sv_map_v1_GRCh38.20130502.svs.genotypes.vcf.gz)

The NA12878 NIST with Platinum Genomes phase transfer small variant callset (v3.3.2) is available at:

[https://ftp-trace.ncbi.nlm.nih.gov/giab/ftp/release/NA12878\\_HG001/latest/GRCh37/HG001\\_GRCh37\\_GIAB\\_highconf\\_CG-IIIFB-IIIGATKHC-Ion-10X-SOLID\\_CHROM1-X\\_v.3.3.2\\_highconf\\_PGandRTGphasetransfer.vcf.gz](https://ftp-trace.ncbi.nlm.nih.gov/giab/ftp/release/NA12878_HG001/latest/GRCh37/HG001_GRCh37_GIAB_highconf_CG-IIIFB-IIIGATKHC-Ion-10X-SOLID_CHROM1-X_v.3.3.2_highconf_PGandRTGphasetransfer.vcf.gz)

[Probe regions used for the whole exome sequencing of NA12878 are available from the Agilent SureDesign Dashboard \(https://earray.chem.agilent.com/suredesign/\).](https://earray.chem.agilent.com/suredesign/)  
[Account registration and sign-in is required to access the regions file from the Agilent catalogue \(S04380110\\_Regions.bed\).](#)

The HG002 NIST small variant benchmarking callset containing variant calls and confident regions files (v4.2.1) are available at the following directory:

[https://ftp-trace.ncbi.nlm.nih.gov/giab/ftp/release/AshkenazimTrio/HG002\\_NA24385\\_son/NIST\\_v4.2.1/GRCh37/](https://ftp-trace.ncbi.nlm.nih.gov/giab/ftp/release/AshkenazimTrio/HG002_NA24385_son/NIST_v4.2.1/GRCh37/)

The HG002 GIAB CMRG small variant calls and confident regions files (v1.00) are available at the following directory:

[https://ftp-trace.ncbi.nlm.nih.gov/ReferenceSamples/giab/release/AshkenazimTrio/HG002\\_NA24385\\_son/CMRG\\_v1.00/GRCh37/SmallVariant/](https://ftp-trace.ncbi.nlm.nih.gov/ReferenceSamples/giab/release/AshkenazimTrio/HG002_NA24385_son/CMRG_v1.00/GRCh37/SmallVariant/)

### **3.3 Investigating the role of *NEFH* as an ALS risk gene**

#### **3.3.1 Quality Control of Project MinE**

After sequencing data was processed (see Chapters 3.1.1 and 3.1.1.2), sites with a genotype quality <10 and variants with low quality scores (<20 for single nucleotide variants and <30 for indels) were removed. Samples with a transition-transversion ratio, total number of single nucleotide variants, indels and singletons outside the interval mean  $\pm$  6 SD from the full distribution of samples were removed. Variants with missingness >2% across all samples were excluded. Genetically inferred sex, based on the number of X and Y chromosomes, was compared to the sex reported in the phenotypic data. The full dataset consisted of 9,050 individuals: 6,603 ALS cases and 2,447 age and sex-matched controls. We then removed duplicates and individuals who did not have available matching clinical or variant information.

### **3.4 Differential gene expression analysis of two large ALS sequencing consortia**

#### **3.4.1 TargetALS Sample Selection**

In this study, we included 234 samples from 132 subjects from the TargetALS dataset (information about sequencing available in Chapter 3.1.2.2). The region distribution is as follows: 112 samples in the medial motor cortex, 112 in the lateral motor cortex and a further 10 samples in unspecified motor cortex. Of these, 30 subjects contributed a

single sample, while 102 subjects contributed two samples from two different regions of the motor cortex. Figure 3-1A shows the principal component analysis of the 234 samples, coloured by the motor cortex region, which showed that the motor cortex regions do not form distinct groups. Instead, there appears to be a strong sex effect in this cohort (Figure 3-1B). To assess if merging the three motor cortex regions was suitable, we performed separate case-control differential expression analysis of the medial and lateral motor cortices and compared the results to an analysis which pools all motor cortex regions together. We did not perform differential expression analysis for the unspecified motor cortex as there was only 10 samples available. In the medial motor cortex (93 ALS cases and 19 controls), 42 genes crossed genome wide significance (corrected  $p$ -value $<0.05$ ), with 39 of these genes (93%) also being significant in the merged dataset. In the lateral motor cortex (96 ALS cases and 16 controls), 8 genes crossed genome wide significance (corrected  $p$ -value $<0.05$ ). All these genes are significant in the merged dataset. Therefore, the merged dataset was used as it gives us more statistical power and still detects the vast majority of differentially expressed genes in the two regional subsets.

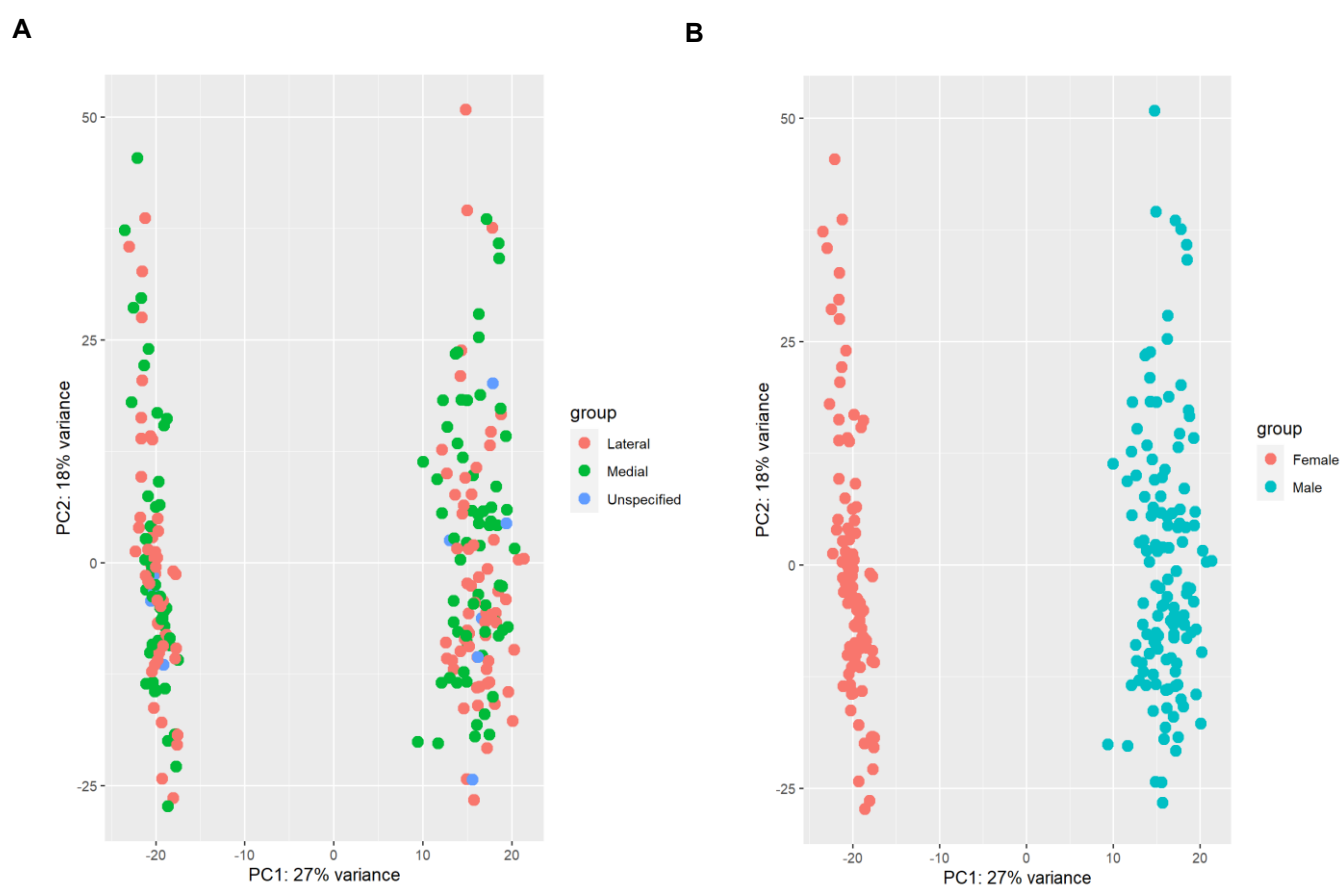


Figure 3-1. Principal component analysis of 234 samples (cases and controls) from a total of 132 individuals in the TargetALS dataset. Samples were coloured by A) motor cortex region and B) sex.



### **3.4.2 Gene Expression Explorer Webserver**

The backend and frontend code for the webserver is publicly available at (<https://github.com/guypwhunt/alsgeexplorer>) and requires R v4.1.2 ≤.

## **3.5 Utilising hierarchical clustering to identify molecular subtypes of ALS**

### **3.5.1 RNAseq Dataset Preparation**

Information about the preparation of the KCL BrainBank and TargetALS datasets are available in Chapters 3.1.2.1 and 3.1.2.2. The library preparation and RNA extraction of the Zucca PBMC dataset is available at (Zucca et al., 2019) and the RNA sequencing and microarray normalisation protocol for the van Rheenen PBMC dataset is available at (van Rheenen et al., 2018). The Zucca dataset (RNA-seq) is available at GEO: GSE106443, GSE115259. The van Rheenen dataset (microarray) is available at GEO: GSE112681.

### **3.5.2 KCL BrainBank Methylation Microarray Preparation**

DNA methylation was analysed using Illumina Infinium EPIC array following the standard Infinium HD array methylation protocol (Illumina).

## Chapter 4. Development of a next-generation sequencing bioinformatics analysis pipeline

### 4.1 Publication

The work described in this chapter was published in *Bioinformatics* (Marriott, Kabiljo, Al Khleifat, et al., 2023):

#### **DNAscan2: a versatile, scalable, and user-friendly analysis pipeline for human next-generation sequencing data**

Heather Marriott<sup>1,2</sup>, Renata Kabiljo<sup>1,2</sup>, Ahmad Al Khleifat<sup>1</sup>, Richard J Dobson<sup>2,3,4</sup>,  
Ammar Al-Chalabi<sup>1,5</sup> and Alfredo Iacoangeli<sup>1,2,3\*</sup>

<sup>1</sup>Department of Basic and Clinical Neuroscience, King's College London, London, United Kingdom; <sup>2</sup>Department of Biostatistics and Health Informatics, King's College London, London, United Kingdom; <sup>3</sup>NIHR BRC SLAM NHS Foundation Trust, London, United Kingdom; <sup>4</sup>Institute of Health Informatics and NIHR BRC at University College London Hospitals NHS Foundation Trust, London, United Kingdom; <sup>5</sup>King's College Hospital, London, United Kingdom

\*Correspondence should be addressed to [alfredo.iacoangeli@kcl.ac.uk](mailto:alfredo.iacoangeli@kcl.ac.uk)

### 4.2 Abstract

#### *Summary*

The current widespread adoption of next-generation sequencing (NGS) in all branches of basic research and clinical genetics fields means that users with highly variable informatics skills, computing facilities and application purposes need to process, analyse, and interpret NGS data. In this landscape, versatility, scalability, and user-friendliness are key characteristics for an NGS analysis software. We developed DNAscan2, a highly flexible, end-to-end pipeline for the analysis of NGS data, which (i) can be used for the detection of multiple variant types, including SNVs, small indels, transposable elements, short tandem repeats, and other large structural variants; (ii) covers all standard steps of NGS analysis, from quality control of raw data and genome

alignment to variant calling, annotation, and generation of reports for the interpretation and prioritization of results; (iii) is highly adaptable as it can be deployed and run via either a graphic user interface for non-bioinformaticians and a command line tool for personal computer usage; (iv) is scalable as it can be executed in parallel as a Snakemake workflow, and; (v) is computationally efficient by minimizing RAM and CPU time requirements.

#### *Availability and implementation*

DNAscan2 is implemented in Python3 and is available at <https://github.com/KHP-Informatics/DNAscanv2>.

### **4.3 Background**

Thanks to its growing accessibility and affordability, next-generation sequencing (NGS) is now being adopted in all fields of clinical and biomedical genetics. As a consequence, a broad audience of users require flexible and easy-to-use bioinformatics software able to adapt to their informatics proficiency, computing infrastructure, and study objectives. Current publicly available NGS pipelines normally focus on the analysis of specific types of genetic variants, e.g., only SNVs and small indels, or only structural variants, do not cover the whole analysis process (i.e., they are not end-to-end), and are not suitable for users with limited informatics skill (Chiang et al., 2015; Collins et al., 2020; DePristo et al., 2011; Zarate et al., 2020). Although tools that focus on solving some of these factors exist, e.g., being end-to-end (Causey et al., 2018) or user-friendly (Blankenberg et al., 2010), to our knowledge, only commercial bioinformatics solutions which are not accessible to the majority of NGS users, cover all of these aspects (Miller et al., 2015). On such a basis, we developed DNAscan2.

### **4.4 Results and Interpretation**

DNAscan2 is written in Python3 and is an open-source software tool available to download from GitHub (<https://github.com/KHPInformatics/DNAscanv2>). The installation of its software and database dependencies (Table A1) can be performed manually, with a bash helper script or via a GUI. An Anaconda (Anaconda Software

Distribution. (2022), n.d.) environment file of available binary dependencies is also provided for those who want to install software without package conflicts. The full list of dependencies with their installation specifics are shown in Table A2.

#### **4.4.1 New and upgraded features**

DNAscan2 presents substantial improvements with respect to DNAscan (Iacoangeli, Al Khleifat, Sproviero, Shatunov, Jones, Morgan, et al., 2019) in all phases of the analysis (see sections below). Unlike in DNAscan, where users could select one of three modes (fast, normal, and intensive) to tailor the computational requirements to their availability, DNAscan2 implements a single protocol that automatically tailors itself according to the type of variants the user is interested in by default (see Figure A1A and Table A2), and it allows the selection of a fast mode which does not perform computationally intensive steps for users with limited RAM and/or CPU time constraints. It also demonstrates improved calling power for several variant classes (Table A3). Descriptions of the benchmarking procedure is available in Chapter 3.2, and detailed results are available in Appendices I. Chapter 4 and II. Chapter 4.

##### **4.4.1.1 SNV and indel calling**

The Strelka2 small variant caller (S. Kim et al., 2018) has replaced Freebayes (Garrison & Marth, 2012) and GATK Haplotype Caller (Poplin et al., 2018) for both SNV and indel calling (Figure A1A), as it has a similar performance for SNVs and consistently demonstrates a higher precision and F-measure for indel detection on both NA12878 WES and HG002 WGS samples for both standard calls (Figures A2 and A3A) and medically relevant genetic variants in challenging regions (Figure A3B).

##### **4.4.1.2 Structural variant calling**

An enhanced structural variant calling protocol was developed via the addition of Delly (Rausch et al., 2012) to call inversion and deletion variants as well as tandem duplications and translocation events. Delly exhibits a 28–35% higher F-measure for small (50–1000 bp) and medium (1001–10 000 bp) deletions (Figure A4A) on BWA-mem and HISAT2 aligned HG002 WGS reads generated with DNAscan, in addition to a 35% increase in precision for small (101–1000 bp) haplotype-resolved inversion calls (Sudmant et al., 2015) on simulated NA12878 WGS reads (Figure A5A). Furthermore, almost all true positive deletion and inversion calls for both datasets are exclusive to Delly or shared by both Manta and Delly (Figures A4B and A5B). This

improved calling comes at the expense of increased runtime, with DNAscan2 taking 24- 30hours longer to run (Table A4). Structural variant calling with Delly is not performed in fast mode.

#### **4.4.1.3 Transposable element and short tandem repeat discovery**

The protocol for the detection of mobile element insertions (Alu, SVA and LINE1) and tandem repeats has been substantially improved with the addition of new state-of-the-art tools. Mobile elements can now be discovered and genotyped via MELT (Gardner et al., 2017) and a genome-wide non-reference short tandem repeat loci profile with details of the motif composition and estimated repeat size of each identified repeat can be generated using ExpansionHunter Denovo (Dolzhenko et al., 2020). Users also have the option to convert the repeat loci into a catalog format compatible with ExpansionHunter (using a conversion script available at <https://github.com/francescalucas/ehdn-to-eh>) to undergo repeat size estimation and genotyping (Figure A1A). Short tandem repeat genotyping is not performed in fast mode.

#### **4.4.1.4 Variant annotation and report generation**

The spectrum of variants that can now be annotated has been extended to include structural and transposable elements (Figure A1A) with the incorporation of AnnotSV (Geoffroy et al., 2018), in addition to known and novel repeat expansions using user-defined ANNOVAR databases. Additionally, an HTML report of variants annotated with AnnotSV produced with the knotAnnotSV program (Geoffroy et al., 2021), and a generalized annotation report giving type, genomic location, overlapping genes and population variant frequency of all identified variants are created for the user's convenience (Figure A6).

#### **4.4.2 Snakemake and GUI accessibility**

To expand the accessibility of DNAscan2, both a graphical user interface (Figures A1B–D) and a Snakemake workflow (available at [https://github.com/KHP-Informatics/DNAscanv2\\_snakemake](https://github.com/KHP-Informatics/DNAscanv2_snakemake)) have been developed. This renders DNAscan2 available as both an easy-to-use, end-to-end program via its GUI and as a highly scalable command line tool which can be executed on high-performance computing facilities.

#### **4.4.3 Computational performance**

DNAscan2 is optimized to minimize the computational resources necessary for its use. The average memory usage in the SNV and indel calling stage for WGS is approximately 1 Gb (Table A4, Figure A7); an improvement of 97% compared with DNAscan. DNAscan2 can complete the full protocol, including alignment, full SV calling and annotation, on WGS data in 50 hours using 4 CPUs and 15 Gb RAM (Table A4, Figures A7 and A8), which is reduced to 20 h when fast mode is implemented, generally within the hardware specifications of a midrange personal computer.

#### **4.5 Conclusions**

DNAscan2 adapts to the heterogenic needs of a wide audience that uses NGS data nowadays. It shows potential to be of great value for a broad range of users and applications, e.g., clinical geneticists focusing on disease diagnostics ((Iacoangeli, Al Khleifat, Sproviero, Shatunov, Jones, Opie-Martin, et al., 2019); Figure A9, Table A5), as well as biomedical researchers working on large-scale genomic studies.

## Chapter 5. Investigating the role of *NEFH* as an ALS risk gene

### 5.1 Abstract

#### *Background*

Neurofilament heavy chain gene (*NEFH*) variants are associated with multiple neurodegenerative diseases, however, their relationship with ALS susceptibility has not been robustly explored. Still, *NEFH* is commonly included in genetic screening panels worldwide. We aimed to determine if genetic variants in *NEFH* modify ALS risk.

#### *Methods*

Genetic data of 11,130 ALS patients and 7,416 controls from both the literature and Project MinE, were analysed. We performed fixed and random effects model meta-analysis of published case-control studies reporting *NEFH* variants, and rare variant analysis of *NEFH* variation in the Project MinE whole-genome sequencing data.

#### *Results*

Fixed effects meta-analysis found that rare (MAF<1%) missense variants in the tail domain of *NEFH* increase ALS risk (OR 4.55, 95% CI 2.13-9.71,  $p<0.0001$ ). In Project MinE *NEFH* ultra-rare variants increased ALS risk (OR 1.37 95% CI 1.14-1.63,  $p=0.0007$ ). When stratifying variants by functional effect and gene domain, we showed that ultra-rare variants, mostly intronic, in the rod domain appeared to drive the association (OR 1.45 95% CI 1.18-1.77, Madsen-Browning  $p=0.0007$ , SKAT-O  $p=0.003$ ). Also, ultra-rare (MAF<0.1%) pathogenic missense variants in the tail domain were associated with ALS (OR 1.94, 95% CI 0.86-4.37, Madsen-Browning  $p=0.039$ ). High-frequency rare (MAF 0.1-1%) tail in-frame deletions were also found to confer disease susceptibility (OR 1.18, 95% CI 0.67-2.07, SKAT-O  $p=0.03$ ).

#### *Conclusions*

This study shows that *NEFH* tail missense and in-frame deletion variants and intronic rod variants are a risk factor for ALS. However, they are not variants of large effect, and their functional impact needs to be assessed in further experimental studies before determining whether they should be included in routine genetic screening panels.

## 5.2 Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease resulting from upper and lower motor neuron loss. Around 40 genes have been implicated in ALS and are involved in cellular processes such as autophagy, DNA damage repair, protein degradation, mitochondrial function and cellular/axonal transport (Mejzini et al., 2019). The neurofilament heavy chain gene (*NEFH*), encodes the neurofilament heavy subunit protein (NF-H), which regulates several of these activities to maintain neuronal homeostasis.

Neurofilament protein subunits preserve neuronal architecture by using their side-arms to construct cross-bridges with cytoskeletal components such as microtubules and actin filaments, forming a stable filament-centred matrix that allows intracellular signalling, mitochondrial localisation and ER transport to occur (Yuan et al., 2017). This is predominantly orchestrated by the phosphorylation of the head and tail domains of neurofilament genes. For instance, phosphorylation of the head domain acts as a primer for matrix formation, controlling polymerisation of the NF-H subunit in the cell body before the subunits move to the axon, where the lysine-serine-proline (KSP) repeat of the tail domain is phosphorylated to construct the matrix structure and stabilise the neurofilament side arms (Didonna & Opal, 2019). As a result, *NEFH* disruption could influence selective motor neuron degeneration in the brain and spinal cord of affected individuals with ALS via dysregulation of neuronal function (Theunissen, West, et al., 2021).

Frameshift and missense mutations in *NEFH* have been convincingly linked to various neurological diseases, including Charcot-Marie-Tooth disease type 2CC (Ikenberg et al., 2019; Pipis et al., 2022), spinal muscular atrophy (Ando et al., 2022) and Alzheimer's disease (Yemni et al., 2019).

Several lines of evidence suggest hyperphosphorylation of the KSP repeat causes axonal aggregation of phosphorylated NF-H (pNF-H), thereby compromising neuronal integrity and increasing circulating pNF-H levels in the serum and CSF (Didonna & Opal, 2019). Raised pNF-H levels have already been established as a biomarker for ALS progression, survival (Puentes et al., 2021; Z. Xu et al., 2016), patterns of motor neuron involvement, and can clinically distinguish ALS from mimics such as hereditary spastic paraplegia, spinal muscular atrophy and myasthenia gravis (Poesen et al.,



2017). While pNF-H demonstrates prognostic value, there have not been robust studies examining the relationship between *NEFH* mutations and ALS susceptibility. The association between small insertions and deletions (indels) in the KSP repeat and ALS risk has been suggestively reported in a number of studies (Al-Chalabi et al., 1999; Figlewicz et al., 1994; Tomkins et al., 1998), however, it has not been widely reproduced nor does solid statistical evidence exist. Still, *NEFH* is commonly included in genetic testing panels worldwide (Dilliot et al., 2023). This study aims to fill this gap by first performing a meta-analysis of published ALS case-control studies that reported *NEFH* variants and second conducting a large-scale investigation of *NEFH* variation using genetic data from the Project MinE international ALS whole-genome sequencing consortium.

## **5.3 Methods**

### **5.3.1 Systematic Review**

This study was performed in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). Registration and study protocol of the review aspect of this study was not performed.

#### **5.3.1.1 Eligibility Criteria**

Primary research articles published in the English language between January 1993 and October 2021 were included if they reported individual *NEFH* variant frequencies in ALS patients via a candidate or panel gene approach (targeted panel resequencing, variant screening), whole genome sequencing, whole-exome sequencing, microarray, or PCR-based approaches. Studies were excluded if they were clinical, functional, or epidemiological, if *NEFH* variants were not identified, were identified in non-ALS cases only, or if individual frequencies of all variants were not reported.

#### **5.3.1.2 Information Sources, Search Strategy and Screening Process**

Relevant studies were identified by searching PubMed, Embase and Medline databases with the search terms “amyotrophic lateral sclerosis” OR “ALS” in combination with “neurofilament heavy chain gene”, “NEFH”, “NFH” OR “NF-H”. After removing duplicate records, title and abstract screening was performed against the eligibility criteria, which were formatted into a table checklist. Studies which advanced to full text screening were subject to backward citation screening using Web of Science

to identify any articles which may have been missed. Full text screening of database and citation identified records was then performed. The search strategy was independently performed, and the results were crosschecked by two members of the team.

### 5.3.1.3 Data Collection Process and Data Synthesis

The following characteristics were extracted from the eligible records: author, publication year, study design, screening method and genetic technology used to detect *NEFH* variants, population (country of origin), study groups, sex and age of ALS groups and diagnostic criteria. For each variant, the following information was obtained: HGVS nomenclature, mutation type, *NEFH* domain location, rsID, and pathogenicity according to SIFT and PolyPhen. Study-specific variant information i.e., frequency in cases and controls, odds ratios (ORs) and 95% confidence intervals with p-values and other ALS-associated gene variants carried in *NEFH*-positive individuals, were also extracted. Population-specific *NEFH* variant frequencies were added to each variant record using the gnomADv2.1.1 non-neuro database (Karczewski et al., 2020). If the rsID was not supplied, dbSNP (Sherry et al., 2001) and gnomAD were searched. For variants without pathogenicity predictions, gnomAD and the Variant Effect Predictor (VEP) (McLaren et al., 2016) were used to obtain variant consequence status. All of this information was tabulated into separate study-specific and variant-specific characteristics tables.

### 5.3.2 Meta-Analysis

Individual missense and exonic indel variants found in two or more case-control studies were eligible for variant-level meta-analysis. Subgroup meta-analysis was also performed according to combinations of population-specific gnomAD non-neuro frequency (ultra-rare: <0.1%, high-frequency rare: 0.1-1%, rare: <1%, or common: >1%), domain (head, rod, or tail) and variant type. Studies that identified variants absent from gnomAD but present in more than one control were classified as common for the stratified analysis. Synonymous variants were excluded from the analysis. Inverse-variance weighted meta-analyses were conducted with both fixed-effect (Cochran-Mantel-Haenszel) and random-effect (DerSimonian-Laird) models. Crude ORs were calculated from the extracted data. Between-study heterogeneity was assessed using the combination of the  $I^2$  test and Cochran-Q statistic, with significant heterogeneity indicated when  $I^2 > 50\%$  and  $Q < 0.10$ . In this case, the result from the

random-effect model is the result that we report and use. Publication bias was assessed with both Egger's and Harbord's test, with p-values <0.05 classed as displaying significant outcome heterogeneity and selective reporting. All statistical analyses were performed using the *metabin* and *metabias* functions of the meta R package (v6.5.0; (Balduzzi et al., 2019)).

### 5.3.3 Genetic Screening

Whole-genome sequencing samples collected as part of the Project MinE ALS sequencing consortium (Project MinE ALS Sequencing Consortium, 2018) were used to investigate *NEFH* variants in ALS and for replicating the literature based meta-analysis results. Information about recruitment and data collection is available in the Project MinE paper. After standard data preparation (see Chapter 3.3.1), the dataset comprised of 6,469 ALS cases and 2,434 controls from 13 countries (breakdown available in Table A6) for which SNV and small indel data were available. Structural variants (SVs) generated with Manta (X. Chen et al., 2016) were available for approximately two thirds of samples (4,686 ALS cases and 1,859 controls). Variants were annotated with VEP for both functional consequence/type (e.g., UTR, intronic, missense, indel, synonymous) and impact classification (high, moderate, low, modifier) before a union SV dataset was created. SVs greater than 100,000bp were excluded to reduce false positives. The remaining SVs were annotated with AnnotSV (Geoffroy et al., 2018) and CADD-SV (Kleinert & Kircher, 2022) to assess their potential pathogenicity. All results files were converted into a matrix to calculate case-control frequencies. For the review-identified variants and SVs present in Project MinE, Firth logistic regression was performed using RVTtests (Zhan et al., 2016) with default settings, to assess potential associations between variants and ALS susceptibility. Results were corrected for sex and the first 10 principal components. All data was aligned to hg19.

### 5.3.4 Rare Variant Burden Analysis

Burden analysis of all *NEFH* variants identified in Project MinE was performed with RVTtests, using Madsen-Browning and SKAT-O methods with default settings. Results were corrected for sex and the first 10 principal components. Variants were initially grouped by frequency (ultra-rare: <0.1%, high-frequency rare: 0.1-1%, rare: <1%), according to the highest value in control databases (gnomAD non-neuro non-Finnish European and Project MinE controls), before being grouped by functional domain

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(whole gene, head, rod, tail) with the *ensembldb* R package (v2.22.0; (Rainer et al., 2019)). For each functional domain, variant burden was calculated for several variant types (missense, synonymous, insertion, deletion, 3'UTR, 5'UTR, intronic) and VEP impact classes (high, moderate, low, modifier). Also, the burden of missense variants predicted pathogenic by SIFT and/or PolyPhen was assessed.

### **5.3.5 Controlling for Multiplicity of Testing**

In both meta-analysis and burden analyses, we report p-values <0.05 as indicators of nominal significance in addition to estimate of effects and 95% confidence intervals. In our initial discovery phase, we took multiple testing into account (Bonferroni correction) testing the association between variants and ALS risk based on four *NEFH* variant frequencies (MAF <0.1%, MAF 0.1–1%, MAF <1%, and MAF >1%), that is, corrected p-values <0.0125. Any additional subgroup analyses aiming to explain which types of frequency-grouped variants contributed to the already discovered associations were considered significant if p-values <0.05 and the direction of effect was concordant with the initial association.

## 5.4 Results

### 5.4.1 Systematic Review

#### 5.4.1.1 Study Selection

The systematic literature review process flowchart is presented in Figure 5-1. The initial search identified 29 articles which were eligible for title and abstract screening, of which 16 were the wrong study type, disease, or instances where genetic screening did not include *NEFH* or identify *NEFH* variants even if *NEFH* was present in the targeted sequencing panel. Backward citation searching of the remaining 13 articles found an additional 251 records for screening. Manual full text inspection removed a further 242 records (2 from database search and 240 from citation search) as the inclusion criteria were not met. In total, 22 studies involving a total of 10,959 individuals (6,090 ALS cases and 4,869 controls) from 14 countries were included in the present study.

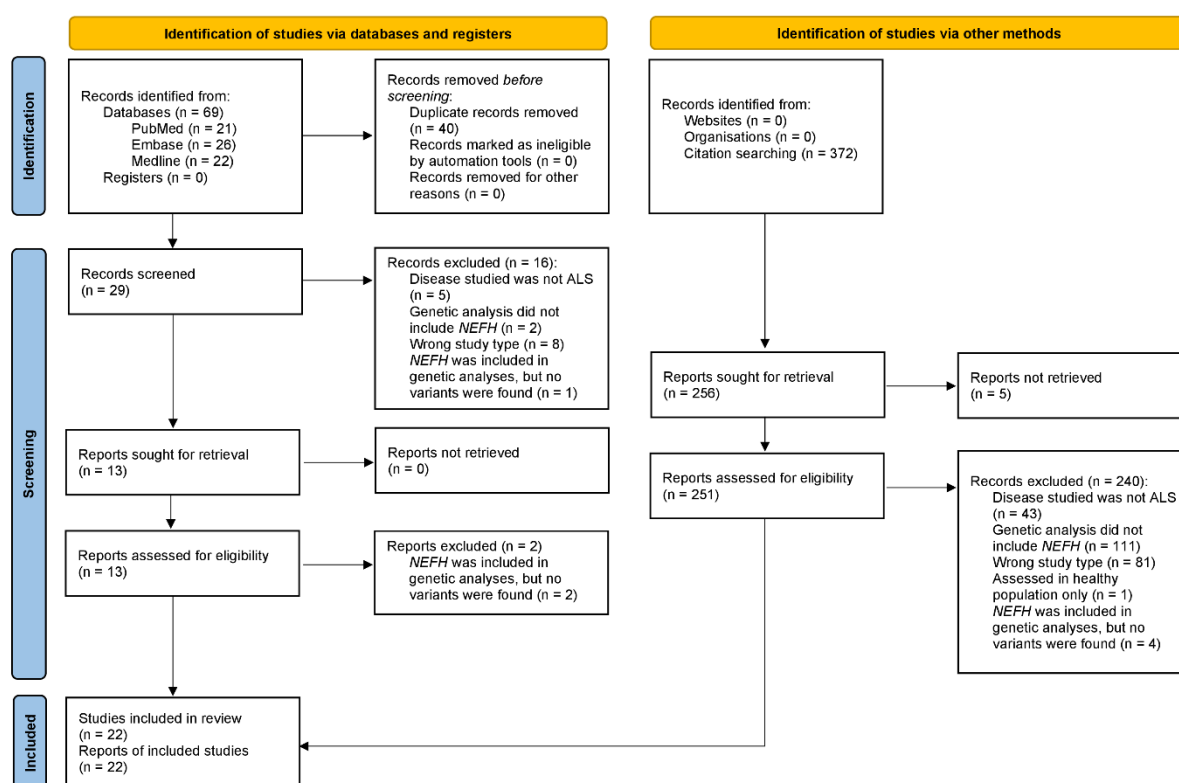


Figure 5-1. PRISMA flowchart of the systematic review process for identification of *NEFH* variants from the literature. The left of the figure outlines screening for articles identified via PubMed, Embase and Medline databases, whilst the right outlines the process for articles found via backwards citation screening of articles undergoing full-text screening.

#### 5.4.1.2 Study Characteristics

An overview of the characteristics of all included studies is given in Table A7. European (N Studies = 9) and Asian (N Studies = 7) populations were the most represented, with family disease history reported in 77% of studies. Diagnostic criteria were applied to support inclusion in 15 studies (68%), with varying definitions of El Escorial criteria employed in 93% of those. A combination of El Escorial and Awaji-Shima criteria was used in one study. The average age of recruitment of the ALS patients ranged from 30.7 to 62.1 (median 58.1), with a male: female ratio ranging between 0.60 and 1.78 (median 1.38) across studies. When separating by country, Asian populations had a younger median age at recruitment and a higher median male: female ratio than European populations (Asian: age 52.01, sex ratio 1.52; European: age 60.1, sex ratio 1.22). A case-control design was adopted in 12 studies (55%), with 6 investigating *NEFH* variation in ALS via candidate gene-based methods. Gene panels including *NEFH* were used in 13 studies, with a further 2 opting for custom variant panel screening. The most popular genetic technology was whole-exome sequencing (N Studies = 6) and a combination of whole-exome sequencing with validation approaches such as PCR and Sanger sequencing (N Studies = 6).

#### 5.4.1.3 Variant Characteristics

We extracted information for 59 *NEFH* variants from the included studies. The full synthesised variant information is represented in Table A8, with the genomic coordinates and base-pair substitutions available in Table A9. Missense variants were the most represented (67.8%), followed by inframe deletions (13.6%), synonymous variants (13.6%), inframe insertions (1.7%), frameshift deletions (1.7%) and stop-gained SNVs (1.7%). Indels ranged from 3bp to 48bp in length and exclusively occupied the tail, whilst only two missense variants were found in the head domain (Figure 5-2). Only 18 variants (30.5%) were reported in more than one study. Eleven people with *NEFH* variants also harboured variants in other ALS-associated genes, including *SOD1*, *FUS*, *OPTN*, *SETX*, *ALS2* and *CHMP2B* (Table A8). When looking at the functional impact of these variants in the gnomAD database, both *OPTN* variants (M98K and R545Q) and the *ALS2* T293I variant are predicted to be tolerated and benign according to SIFT and PolyPhen, whilst the *FUS* c.37 C>T variant is predicted as benign with CADD and SpliceAI. The remaining variants have conflicting

pathogenicity results, therefore their influence on ALS risk in individuals harbouring these variants are uncertain.

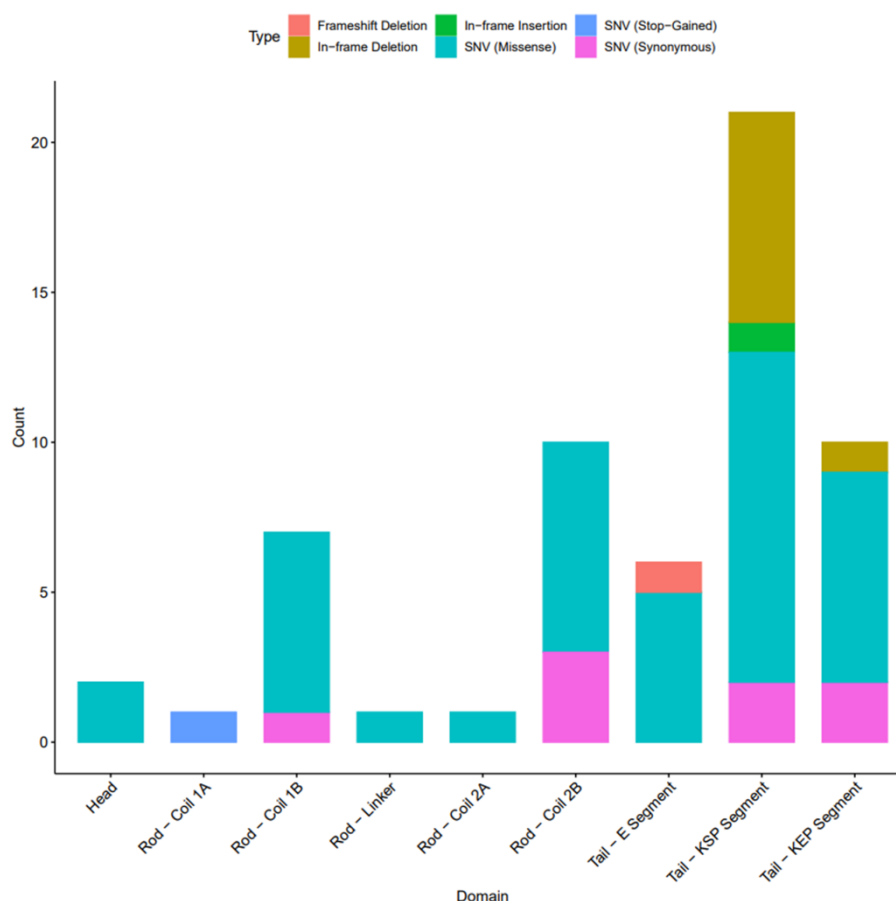


Figure 5-2. *NEFH* domain distribution of the 59 SNV and indel variants identified from the systematic review. Colours characterise the different variant types. KEP = lysine-glutamic acid-proline; KSP = lysine-serine-proline.

### 5.4.2 Meta-Analysis

The twelve case-control studies were selected for meta-analysis. In total, 34 deletion, insertion and missense variants were reported across them (top panel of Figure 5-3A) in 9,496 individuals (4,527 cases; 4,969 controls). Of these, 9 variants (3 in-frame deletions and 6 missense) were identified in two or more case-control studies and were included in the variant-level meta-analysis. No singular variant was shown to significantly alter risk for ALS (Table A10), with K790del displaying high between-study heterogeneity (Cochran's  $Q = 3.03$ ,  $p\text{-value} = 0.08$ ;  $I^2 = 67\%$ ).

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We then performed meta-analyses of *NEFH* variants based on the aggregation of variants stratified by frequency, domain, and variant type. We found that both rare missense and rare tail variants were associated with an increased risk of ALS (Table 5-1). We determined that the rare missense tail variants were driving this result as they were more significant, with a higher OR (OR 4.55, 95% CI 2.13-9.71,  $p_{\text{fixed-effect}} < 0.0001$ , Figure 5-4), and removing them from the rare missense and rare tail meta-analyses caused these associations to be lost. There was no evidence of inter-study heterogeneity (Cochran's  $Q = 2.30$ ,  $p = 0.51$ ;  $I^2 = 0\%$ ) or publication bias (Egger  $t = 2.07$ ,  $p = 0.17$ ; Harbord  $t = 1.82$ ,  $p = 0.21$ ). By further stratifying *NEFH* variants into high-frequency rare and ultra-rare categories, we identified a similar but albeit weaker significant association for the high-frequency rare missense tail variants (OR 3.91, 95% CI 1.77-8.64,  $p_{\text{fixed-effect}} = 0.0007$ ), with ultra-rare missense tail variants approaching significance for increasing ALS risk (OR 5.05, 95% CI 0.84-30.22;  $p_{\text{fixed-effect}} = 0.08$ ). Across all categories, tail deletions did not significantly increase or reduce susceptibility for ALS (Table 5-1). High between-study heterogeneity was reported for common missense and tail missense variants, and all tail missense variants, with tail ultra-rare variants displaying publication/reporting bias (Table 5-1).





| MAF Category                 | Subgroup      | No. Studies | N Cases | N Controls | Fixed OR (95% CI; p-value)        | Random OR (95% CI; p-value)     | Heterogeneity (Q statistic; p-value) | Heterogeneity (I-squared) | Publication Bias (Egger t statistic; p-value) | Publication Bias (Harbord t statistic; p-value) |
|------------------------------|---------------|-------------|---------|------------|-----------------------------------|---------------------------------|--------------------------------------|---------------------------|---|---|
| Ultra-Rare (<0.1%)           | All           | 10          | 2729    | 2483       | 2.64 (1.22-5.68; <b>0.01</b> )    | 2.27 (0.99-5.18; 0.05)          | 5.12 (0.82)                          | 0%                        | 2.17; 0.06                                    | 1.13; 0.29                                      |
|                              | Tail          | 7           | 1918    | 2063       | 2.01 (0.80-5.05; 0.14)            | 1.82 (0.68-4.87; 0.24)          | 3.06 (0.80)                          | 0%                        | 4.38; <b>7.2E-03</b>                          | 3.01; <b>0.03</b>                               |
|                              | Missense      | 6           | 1679    | 1521       | 4.35 (1.39-13.64; <b>0.01</b> )   | 4.14 (1.30-13.18; <b>0.02</b> ) | 1.17 (0.95)                          | 0%                        | -0.29; 0.78                                   | 0.40; 0.71                                      |
|                              | Head Missense | 2           | 285     | 290        | 1.70 (0.22-12.95; 0.61)           | 1.63 (0.20-13.35; 0.65)         | 0.25 (0.62)                          | 0%                        | N/A   | N/A   |
|                              | Rod Missense  | 5           | 1368    | 1321       | 3.28 (0.82-13.15; 0.09)           | 3.17 (0.78-12.90; 0.11)         | 0.77 (0.94)                          | 0%                        | -0.92; 0.43                                   | -0.76; 0.50                                     |
|                              | Tail Missense | 3           | 868     | 1101       | 5.05 (0.84-30.22; 0.08)           | 5.10 (0.87-29.98; 0.07)         | 0.01 (0.99)                          | 0%                        | 3.88; 0.16                                    | 15.36; <b>0.04</b>                              |
|                              | Tail Deletion | 3           | 886     | 753        | 0.97 (0.28-3.40; 0.97)            | 0.94 (0.26-3.38; 0.93)          | 0.52 (0.77)                          | 0%                        | 2.25; 0.27                                    | 2.45; 0.25                                      |
| High-Frequency Rare (0.1-1%) | All           | 7           | 2764    | 3106       | 2.11 (1.23-3.62; <b>6.5E-03</b> ) | 2.16 (0.77-6.10; 0.15)          | 9.92 (0.13)                          | 40%                       | 0.55; 0.61                                    | 0.45; 0.67                                      |
|                              | Missense      | 5           | 1282    | 2187       | 2.23 (1.25-3.97; <b>6.7E-03</b> ) | 2.53 (0.82-7.85; 0.11)          | 6.49 (0.17)                          | 38%                       | 0.80; 0.48                                    | 0.79; 0.49                                      |
|                              | Tail          | 5           | 2464    | 2906       | 3.14 (1.56-6.31; <b>1.3E-03</b> ) | 3.26 (0.99-10.74; 0.05)         | 6.64 (0.16)                          | 40%                       | 0.30; 0.79                                    | 0.17; 0.88                                      |
| High-Frequency Rare (0.1-1%) | Rod Missense  | 4           | 982     | 1111       | 1.01 (0.42-2.44; 0.98)            | 0.95 (0.38-2.39; 0.91)          | 1.58 (0.66)                          | 0%                        | 1.30; 0.32                                    | 1.39; 0.30                                      |
|                              | Tail Missense | 3           | 982     | 1987       | 3.91 (1.77-8.64; <b>7.0E-04</b> ) | 4.44 (1.41-13.96; <b>0.01</b> ) | 2.16 (0.34)                          | 7%                        | 1.81; 0.32                                    | 1.93; 0.30                                      |

|             |                         |    |      |      |  |                                       |              |     |            |             |
|-------------|-------------------------|----|------|------|--|---------------------------------------|--------------|-----|------------|-------------|
|             | All                     | 13 | 4355 | 4272 | 2.54 (1.59-4.06; <<br><b>1.0E-04</b> ) | 2.28 (1.38-3.77;<br><b>1.3E-03</b> )  | 12.08 (0.44) | 1%  | 0.23; 0.82 | 0.12; 0.90  |
|             | Tail                    | 9  | 3344 | 3752 | 2.83 (1.59-5.04;<br><b>4.0E-04</b> )   | 2.57 (1.10-5.98;<br><b>0.03</b> )     | 10.80 (0.21) | 26% | 0.30; 0.78 | 0.03; 0.98  |
| Rare (< 1%) | Tail (exc.<br>Missense) | 5  | 2176 | 1575 | 1.37 (0.54-3.43;<br>0.51)              | 1.05 (0.37-3.01;<br>0.93)             | 4.32 (0.36)  | 7%  | 1.22; 0.31 | 0.16; 0.88  |
|             | Missense                | 8  | 2179 | 2697 | 2.78 (1.64-4.71; <<br><b>1.0E-04</b> ) | 2.60 (1.34-5.10;<br><b>4.8E-03</b> )  | 7.52 (0.38)  | 7%  | 0.93; 0.39 | 0.89; 0.41  |
|             | Missense<br>(exc. Tail) | 7  | 1879 | 1621 | 1.57 (0.77-3.21;<br>0.22)              | 1.44 (0.68-3.05;<br>0.34)             | 2.71 (0.84)  | 0%  | 1.22; 0.28 | 1.44; 0.21  |
|             | Rod<br>Missense         | 7  | 1879 | 1621 | 1.51 (0.72-3.15;<br>0.28)              | 1.41 (0.67-3.04;<br>0.38)             | 2.37 (0.89)  | 0%  | 1.33; 0.24 | 1.97; 0.11  |
|             | Tail<br>Missense        | 4  | 1168 | 2177 | 4.55 (2.13-9.71; <<br><b>1.0E-04</b> ) | 4.65 (1.79-12.11;<br><b>1.6E-03</b> ) | 2.30 (0.51)  | 0%  | 2.07; 0.17 | 1.82; 0.21  |
| Rare (< 1%) | Tail<br>Deletion        | 4  | 2012 | 1366 | 1.22 (0.46-3.22;<br>0.68)              | 0.90 (0.30-2.74;<br>0.85)             | 3.62 (0.31)  | 17% | 0.75; 0.53 | -0.50; 0.66 |
|             | All                     | 6  | 2025 | 2442 | 1.11 (0.94-1.30;<br>0.21)              | 1.20 (0.87-1.65;<br>0.26)             | 9.30 (0.10)  | 46% | 0.99; 0.38 | 1.13; 0.32  |
|             | Tail                    | 6  | 2025 | 2442 | 1.11 (0.95-1.31;<br>0.19)              | 1.20 (0.88-1.63;<br>0.25)             | 8.95 (0.11)  | 44% | 1.00; 0.37 | 1.14; 0.32  |

|               |               |   |      |      |                                |                        |                       |            |            |            |
|---------------|---------------|---|------|------|--------------------------------|------------------------|-----------------------|------------|------------|------------|
| Common (> 1%) | Missense      | 5 | 1818 | 2223 | 1.12 (0.94-1.34; 0.20)         | 1.18 (0.79-1.78; 0.42) | 10.12 ( <b>0.04</b> ) | <b>61%</b> | 0.32; 0.77 | 0.34; 0.76 |
|               | Tail Missense | 5 | 1818 | 2223 | 1.13 (0.95-1.36; 0.17)         | 1.19 (0.79-1.77; 0.40) | 9.62 ( <b>0.05</b> )  | <b>58%</b> | 0.30; 0.78 | 0.32; 0.77 |
|               | Tail Deletion | 2 | 578  | 930  | 1.03 (0.78-1.35; 0.85)         | 1.03 (0.78-1.35; 0.86) | 0.48 (0.49)           | 0%         | N/A        | N/A        |
| All           | Rod Missense  | 7 | 1879 | 1721 | 1.26 (0.67-2.37; 0.48)         | 1.18 (0.61-2.29; 0.62) | 2.69 (0.85)           | 0%         | 1.82; 0.13 | 2.42; 0.06 |
|               | Tail Missense | 8 | 2615 | 3689 | 1.24 (1.04-1.48; <b>0.02</b> ) | 1.45 (0.96-2.19; 0.08) | 14.58 ( <b>0.04</b> ) | <b>52%</b> | 2.20; 0.07 | 2.41; 0.05 |
|               | Tail Deletion | 5 | 2383 | 2077 | 1.04 (0.80-1.35; 0.77)         | 1.02 (0.78-1.33; 0.89) | 4.02 (0.40)           | 1%         | 0.29; 0.79 | 0.35; 0.75 |

Table 5-1. Results of the subgroup meta-analysis of variants identified from the systematic review that were supported by two or more case-control studies. N/A values represent instances where publication bias could not be calculated as the minimum number of studies required for calculation was not reached.

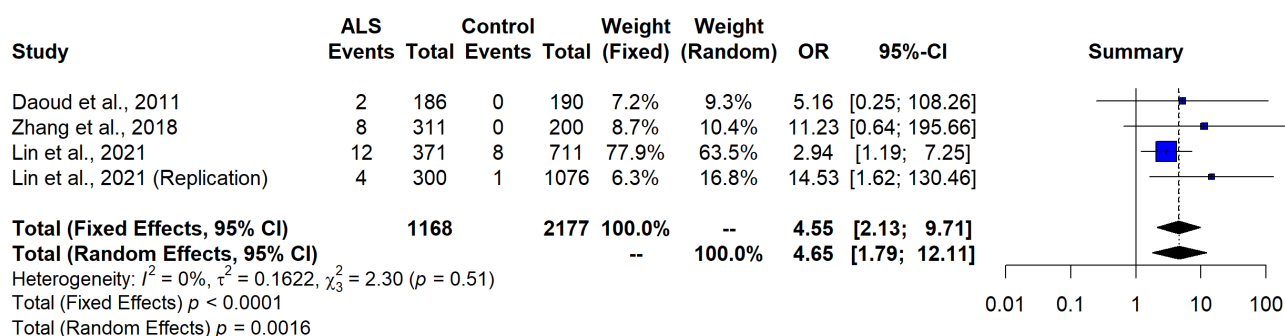


Figure 5-4. Forest plot demonstrating that rare ( $MAF < 1\%$ ) missense variants in the tail domain increase the risk of ALS. Breakdown of heterogeneity values are as follows:  $I^2 = I^2$  statistic,  $\tau^2 = \tau^2$  Tau-squared (estimate of between-study variance in random-effects models),  $\chi^2_3 = \chi^2_3$  Cochran's Q (chi-squared distribution).

### 5.4.3 Genetic Screening in Project MinE

#### 5.4.3.1 SNVs and Indels

We screened the whole *NEFH* gene in the Project MinE dataset (6,469 ALS cases and 2,434 controls). A total of 591 SNVs and indels were identified (Figure 5-5A and Table A11). Interestingly, intronic regions contained 65% of all variants found in the cohort, with 220 (57.29%) being singletons (Figure 5-5B). 462 (78.17%) were identified only in Project MinE and not in the review or gnomAD non-neuro non-Finnish database (Figure 5-5C) and are therefore classified as 'novel' in this study.

Sixteen (27.1%) of the *NEFH* variants identified from the systematic review were found in Project MinE (Figure 5-5C). Examination of case-control frequencies of review-identified variants present in Project MinE (Table 5-2) suggested that K790del could be protective against ALS (0.14% cases, 0.37% controls; OR = 0.38, 95% 0.15-0.95). Using Project MinE as an additional study for meta-analysis of individual review-identified variants did not offer any additional insight into their role in ALS risk (Figure 5-6; Table A12).

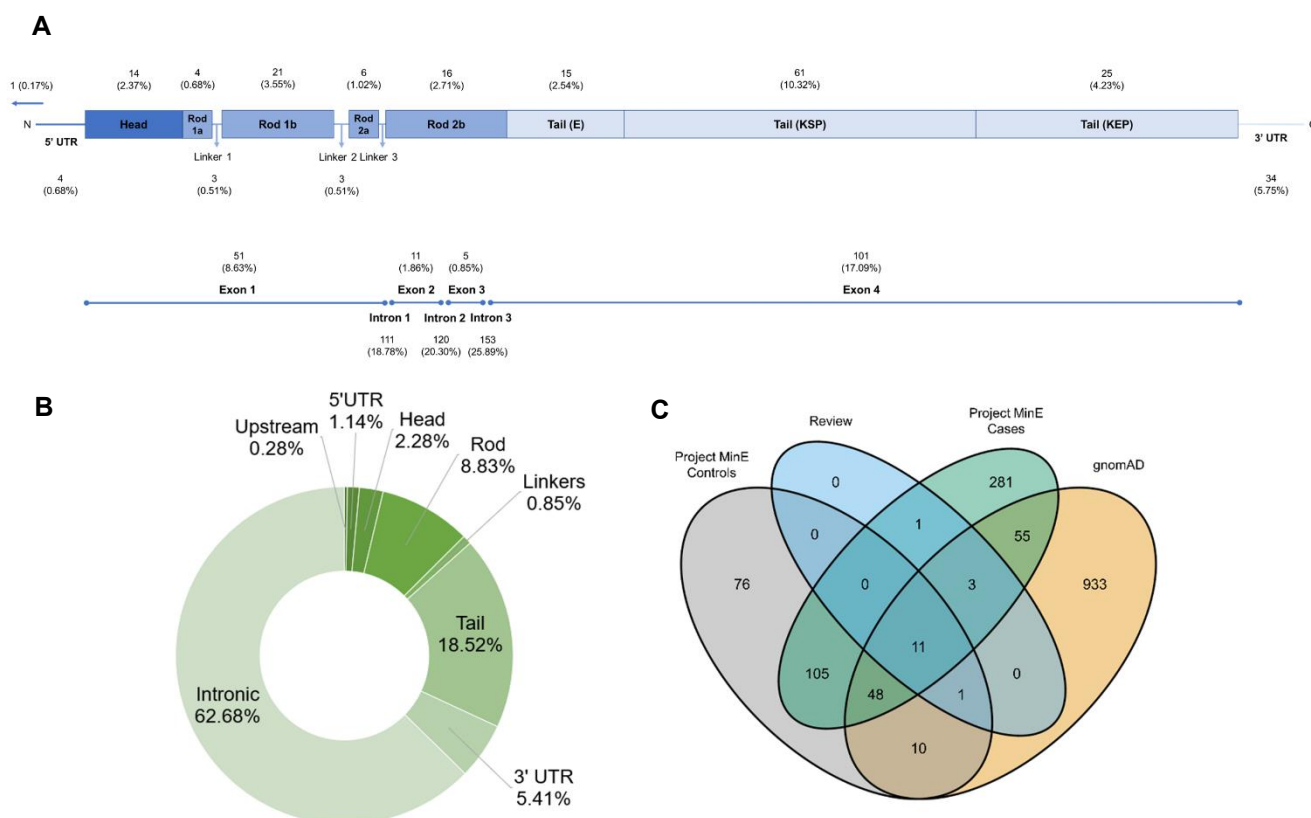


Figure 5-5. Results of the SNV/indel screening analysis in the Project MinE cohort. Additional information on all 591 variants identified are available in Table A11. a) Proportion of variants found in various gene domains and untranslated regions (top), and in exons and introns (bottom). b) Breakdown of the 351 *NEFH* singletons by domain. c) A Venn diagram illustrating the overlap of the *NEFH* variants in Project MinE cases and controls, the systematic review and the gnomAD v2.1.1 database. The value for variants that are only in gnomAD (933) refers to the remaining *NEFH* variants in the catalogue after accounting for variants shared with Project MinE or the review.

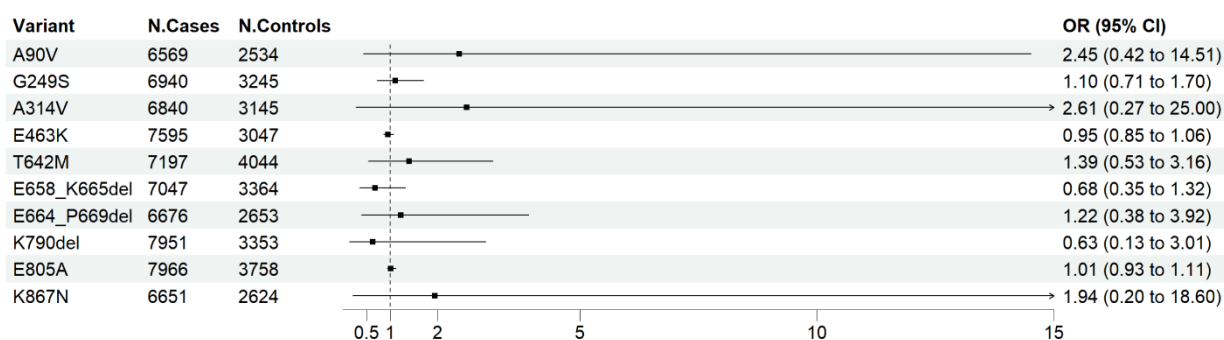


Figure 5-6. Summary forest plot demonstrating that offering Project MinE as an additional study for meta-analysis of systematic-review identified variants does not appear to reveal any further insights into their modulation on ALS risk. The full results are available in Table A12. N. Cases and N. Controls refers to the sample sizes used to evaluate each variant.

### 5.4.3.2 Structural Variants

Only 4 SVs were identified in Project MinE (Table 5-2). All were in the KSP and KEP segments of the tail domain, and none were pathogenic according to CADD-SV. When comparing case-control frequencies of the SVs, the 113bp KEP segment deletion was found to be strongly protective against ALS (17.95% cases vs 23.91% controls; OR 0.72, 95% CI 0.64-0.81).

| Variant      | Position          | Type           | Pathogenicity Prediction      | CADD-SV Score | Total Carriers (Case/Control) | Beta (SE)      | OR (95% CI)        | P Value     |
|--------------|-------------------|----------------|-------------------------------|---------------|-------------------------------|----------------|--------------------|-------------|
| A90V         | 29876520          | Missense       | Tolerated/Benign              | N/A           | 7 (6/1)                       | 0.49 (0.95)    | 2.26 (0.27-18.77)  | 0.61        |
| G249S        | 29876996          | Missense       | Tolerated/Benign              | N/A           | 92 (69/23)                    | 0.03 (0.23)    | 1.13 (0.70-1.82)   | 0.91        |
| A314V        | 29879421          | Missense       | Deleterious/Probably Damaging | N/A           | 1 (1/0)                       | 0.22 (2.11)    | 1.13 (0.05-27.73)  | 0.92        |
| E463K        | 29885016          | Missense       | Deleterious/Probably Damaging | N/A           | 1527 (1103/424)               | -0.0065 (0.06) | 0.97 (0.86-1.10)   | 0.91        |
| T642M        | 29885554          | Missense       | Tolerated/Benign              | N/A           | 1 (0/1)                       | -2.47 (2.11)   | 0.13 (0.005-3.08)  | 0.24        |
| K647N        | 29885570          | Missense       | Deleterious/Possibly Damaging | N/A           | 1 (1/0)                       | 0.40 (2.12)    | 1.13 (0.05-27.73)  | 0.85        |
| P777L        | 29885959          | Missense       | Deleterious/Probably Damaging | N/A           | 1 (1/0)                       | 0.14 (2.12)    | 1.13 (0.05-27.73)  | 0.95        |
| E805A        | 29886043          | Missense       | Deleterious/Possibly Damaging | N/A           | 2578 (1873/705)               | -0.028 (0.05)  | 1.00 (0.90-1.11)   | 0.54        |
| K867N        | 29886230          | Missense       | Deleterious/Possibly Damaging | N/A           | 1 (1/0)                       | 0.40 (2.12)    | 1.13 (0.05-27.73)  | 0.85        |
| A400A        | 29881828          | Synonymous     | N/A                           | N/A           | 2569 (1867/702)               | 0.03 (0.05)    | 1.00 (0.90-1.11)   | 0.57        |
| S580S        | 29885369          | Synonymous     | N/A                           | N/A           | 199 (147/52)                  | 0.10 (0.16)    | 1.07 (0.77-1.47)   | 0.56        |
| D919D        | 29886386          | Synonymous     | N/A                           | N/A           | 148 (105/43)                  | -0.05 (0.18)   | 0.92 (0.64-1.31)   | 0.77        |
| V928V        | 29886413          | Synonymous     | N/A                           | N/A           | 8492 (6198/2324)              | -0.007 (0.04)  | 1.08 (0.86-1.36)   | 0.85        |
| K790del      | 29885996          | Small Deletion | N/A                           | N/A           | 18 (9/9)                      | -1.03 (0.47)   | 0.38 (0.15-0.95)   | <b>0.03</b> |
| E658_K665del | 29885604          | Small Deletion | N/A                           | N/A           | 29 (18/11)                    | 0.02 (0.64)    | 0.61 (0.29-1.30)   | 0.98        |
| E664_P669del | 29885622          | Small Deletion | N/A                           | N/A           | 13 (10/3)                     | -2.20 (2.11)   | 1.25 (0.35-4.56)   | 0.30        |
| INS_61       | 29877834-29877895 | Large Deletion | N/A                           | 14.27         | 1 (1/0)                       | 0.47 (2.11)    | 1.19 (0.049-29.24) | 0.82        |

|          |                   |                |                   |      |                 |               |                    |                 |
|----------|-------------------|----------------|-------------------|------|-----------------|---------------|--------------------|-----------------|
| INS_56   | 29879816-29879872 | Large Deletion | N/A               | 0.75 | 1 (0/1)         | -2.38 (2.11)  | 0.13 (0.0054-3.25) | 0.26            |
| DEL_1169 | 29880841-29882010 | Large Deletion | Likely Pathogenic | 9.83 | 1 (1/0)         | 0.65 (2.11)   | 1.19 (0.049-29.24) | 0.76            |
| DEL_113  | 29885279-29885870 | Large Deletion | VUS               | 4.85 | 1743 (1161/582) | -0.34 (0.061) | 0.72 (0.64-0.81)   | <b>2.60E-08</b> |

*Table 5-2 Case-control frequencies and results of logistic regression association analysis of the 16 SNV/indel variants found in the systematic review and Project MinE, and the 4 structural variants identified in a subset of Project MinE. Results were corrected for sex and 10 principal components. N/A refers to a pathogenicity prediction that could not be reached as the variant type was inappropriate for the tool (SIFT/PolyPhen for SNVs and indels; ACMG and CADD-SV for SVs).*

#### 5.4.4 Rare Variant Burden Analysis in Project MinE

All the SNV/indel variants from Project MinE were subject to burden analysis stratified by frequency and domain (Tables 5-3, 5-4, and 5-5). We found that ultra-rare variants in *NEFH* increase ALS risk (OR 1.37 95% CI 1.14-1.63, Madsen-Browning  $p=0.0007$ , SKAT-O  $p=0.0033$ ). When stratifying by domain and functional effect, ultra-rare variants, mostly intronic, in the rod domain appeared to drive the association (OR 1.45 95% CI 1.18-1.77, Madsen-Browning  $p=0.0007$ , SKAT-O  $p=0.003$ ). However, ultra-rare pathogenic missense tail variants were also associated with an increased risk of ALS (OR 1.94, 95% CI 0.86-4.37; Madsen-Browning  $p=0.039$ ), which supported the result of the meta-analysis to a high degree, despite high-frequency rare pathogenic missense tail variants in this cohort not appearing to confer ALS risk (Table 5-4). Stratifying this by subdomain revealed that the KEP repeat drove this result (OR 5.65, 95% CI 0.75-42.83, Madsen-Browning  $p=0.02$ ), and that other sub-domains showed consistent, although not significant, effects (OR  $>1$ ) (Table 5-3). In line with previous reports, ultra-rare tail domain in-frame deletions had a large impact on ALS risk, but this finding was at the border of the significance testing threshold (OR 3.01, 95% CI 0.69-13.12, Madsen-Browning  $p=0.052$ ). A similar but significant effect was observed for high-frequency rare in-frame deletions (Table 5-4), with an OR of 1.18 (95% CI 0.67-2.07, SKAT-O  $p=0.03$ ). Ultra-rare pathogenic missense variants and high-frequency rare in-frame deletions identified and assessed in these burden analyses are detailed in Figure 5-3A (bottom panel) and Table A13. The case-control distribution of all missense and in-frame deletion variants are displayed in Figure 5-3B,C,D.



| Frequency (<0.1%)               | No. of Variants | Madsen Browning p-value | SKAT-O p-value | Cases | Controls | Odds Ratio (95% CI) |
|---------------------------------|-----------------|-------------------------|----------------|-------|----------|---------------------|
| <i>All (29876207-29887379)</i>  | 512             | <b>7.0E-04</b>          | <b>3.3E-03</b> | 595   | 168      | 1.37 (1.14-1.63)    |
| Synonymous                      | 37              | 0.12                    | 0.43           | 47    | 12       | 1.48 (0.78-2.79)    |
| Missense                        | 80              | 0.11                    | 0.25           | 85    | 24       | 1.34 (0.85-2.11)    |
| All pathogenic missense         | 51              | 0.11                    | 0.37           | 51    | 13       | 1.48 (0.80-2.73)    |
| Inframe Deletion                | 11              | 0.051                   | 0.35           | 16    | 2        | 3.01 (0.69-13.12)   |
| Inframe Insertion               | 11              | 0.38                    | 0.75           | 12    | 3        | 1.51 (0.42-5.34)    |
| Intronic                        | 332             | <b>4.3E-03</b>          | <b>0.01</b>    | 419   | 115      | 1.40 (1.13-1.73)    |
| 3' UTR                          | 30              | 0.29                    | 0.72           | 39    | 12       | 1.22 (0.64-2.34)    |
| 5' UTR                          | 4               | <b>4.0E-03</b>          | <b>0.037</b>   | 1     | 3        | 0.13 (0.01-1.21)    |
| VEP High                        | 6               | 0.13                    | 0.11           | 3     | 4        | 0.28 (0.06-1.26)    |
| VEP Low                         | 37              | 0.12                    | 0.43           | 47    | 12       | 1.48 (0.78-2.79)    |
| VEP Moderate                    | 102             | <b>0.032</b>            | 0.16           | 113   | 29       | 1.47 (0.98-2.22)    |
| VEP Modifier                    | 367             | <b>4.5E-03</b>          | <b>0.012</b>   | 458   | 130      | 1.35 (1.10-1.65)    |
| <i>Head (29876252-29876554)</i> | 13              | 0.76                    | 0.26           | 15    | 9        | 0.63 (0.27-1.43)    |
| Synonymous                      | 7               | 0.49                    | 0.24           | 8     | 3        | 1.00 (0.27-3.79)    |
| Missense                        | 6               | 0.091                   | 0.17           | 7     | 6        | 0.44 (0.15-1.31)    |
| Pathogenic missense             | 1               | N/A                     | 0.069          | 1     | 0        | 1.13 (0.05-27.73)   |
| VEP Low                         | 7               | 0.49                    | 0.24           | 8     | 3        | 1.00 (0.27-3.79)    |
| VEP Moderate                    | 6               | 0.091                   | 0.17           | 7     | 6        | 0.44 (0.15-1.31)    |
| <i>Rod (29876555-29884868)</i>  | 379             | <b>7.0E-04</b>          | <b>3.0E-03</b> | 473   | 126      | 1.45 (1.18-1.77)    |
| Synonymous                      | 20              | 0.08                    | 0.25           | 28    | 5        | 2.11 (0.81-5.48)    |
| Missense                        | 23              | 0.065                   | 0.25           | 29    | 6        | 1.82 (0.76-4.39)    |
| Pathogenic missense             | 14              | 0.48                    | 0.73           | 15    | 5        | 1.13 (0.41-3.11)    |
| Inframe Insertion               | 1               | 0.26                    | 0.53           | 1     | 0        | 1.13 (0.041-27.73)  |
| Intronic                        | 332             | <b>4.0E-03</b>          | <b>0.01</b>    | 419   | 115      | 1.40 (1.13-1.73)    |
| VEP High                        | 3               | 0.18                    | 0.20           | 1     | 2        | 0.19 (0.02-2.07)    |
| VEP Low                         | 20              | 0.08                    | 0.25           | 28    | 5        | 2.11 (0.81-5.48)    |
| VEP Moderate                    | 24              | 0.052                   | 0.22           | 30    | 6        | 1.89 (0.78-4.54)    |
| VEP Modifier                    | 332             | <b>0.004</b>            | <b>0.01</b>    | 419   | 115      | 1.40 (1.13-1.73)    |
| <i>Tail (29884869-29886689)</i> | 85              | <b>0.057</b>            | 0.30           | 89    | 23       | 1.46 (0.92-2.32)    |
| Synonymous                      | 10              | 0.65                    | 0.71           | 11    | 4        | 1.03 (0.33-3.25)    |
| Missense                        | 51              | 0.084                   | 0.21           | 49    | 12       | 1.54 (0.82-2.90)    |
| Pathogenic Missense             | 36              | <b>0.039</b>            | 0.19           | 36    | 7        | 1.94 (0.86-4.37)    |
| E Segment                       | 8               | 0.48                    | 0.68           | 6     | 2        | 1.19 (0.23-5.60)    |
| KSP Segment                     | 17              | 0.34                    | 0.73           | 16    | 4        | 1.51 (0.50-4.51)    |
| KEP Segment                     | 11              | <b>0.02</b>             | 0.11           | 15    | 1        | 5.65 (0.75-42.83)   |
| Inframe Deletion                | 11              | 0.052                   | 0.35           | 16    | 2        | 3.01 (0.69-13.12)   |
| Inframe Insertion               | 10              | 0.43                    | 0.84           | 11    | 3        | 1.38 (0.38-4.95)    |
| VEP High                        | 3               | 0.36                    | 0.35           | 2     | 2        | 0.38 (0.05-2.67)    |

|  |     |                |                |     |     |                  |
|--|-----|----------------|----------------|-----|-----|------------------|
| VEP Low                                | 10  | 0.65           | 0.71           | 11  | 4   | 1.03 (0.33-3.25) |
| VEP Moderate                           | 72  | <b>0.024</b>   | 0.15           | 76  | 17  | 1.69 (1.00-2.87) |
| All excluding tail (29876207-29884868) | 392 | <b>3.0E-03</b> | <b>7.5E-03</b> | 478 | 133 | 1.38 (1.13-1.68) |

Table 5-3. Results of the ultra-rare ( $MAF < 0.1\%$ ) *NEFH* variant burden analysis. Significant results are denoted by bold *p*-values. All results are corrected for sex and the first 10 principal components.

| Frequency (0.1-1%)                            | No. Variants | Madsen Browning p-value | SKAT-O p-value | Cases | Controls | Odds Ratio (95% CI) |
|---|--------------|-------------------------|----------------|-------|----------|---------------------|
| <i>All (29876207-29887379)</i>                | 45           | 0.78                    | 0.61           | 735   | 285      | 0.97 (0.84-1.12)    |
| Synonymous                                    | 4            | 0.97                    | 1.00           | 38    | 13       | 1.10 (0.59-2.07)    |
| Missense                                      | 7            | 0.26                    | 0.58           | 91    | 34       | 1.01 (0.68-1.50)    |
| All pathogenic missense                       | 5            | 0.27                    | 0.39           | 18    | 9        | 0.75 (0.34-1.68)    |
| Inframe Deletion                              | 3            | 0.44                    | <b>0.03</b>    | 50    | 16       | 1.18 (0.67-2.07)    |
| Intronic                                      | 29           | 0.82                    | 0.64           | 625   | 240      | 0.98 (0.84-1.14)    |
| 3' UTR  | 2            | 0.82                    | 0.80           | 21    | 9        | 0.88 (0.40-1.92)    |
| VEP Low                                       | 4            | 0.97                    | 1.00           | 38    | 13       | 1.10 (0.59-2.07)    |
| VEP Moderate                                  | 10           | 0.69                    | 0.27           | 141   | 50       | 1.06 (0.77-1.47)    |
| VEP Modifier                                  | 31           | 0.82                    | 0.64           | 644   | 248      | 0.97 (0.84-1.14)    |
| <i>Head (29876252-29876554)</i>               | -            | -                       | -              | -     | -        | -                   |
| <i>Rod (29876555-29884868)</i>                | 34           | 0.60                    | 0.56           | 641   | 252      | 0.95 (0.82-1.11)    |
| Missense                                      | 5            | 0.11                    | 0.52           | 81    | 32       | 0.95 (0.63-1.44)    |
| Intronic                                      | 29           | 0.82                    | 0.64           | 625   | 240      | 0.98 (0.84-1.14)    |
| VEP Moderate                                  | 5            | 0.11                    | 0.52           | 81    | 32       | 0.95 (0.63-1.44)    |
| VEP Modifier                                  | 29           | 0.82                    | 0.64           | 625   | 240      | 0.98 (0.84-1.14)    |
| <i>Tail (29884869-29886689)</i>               | 9            | 0.71                    | 0.22           | 95    | 33       | 1.08 (0.73-1.62)    |
| Synonymous                                    | 4            | 0.96                    | 1.00           | 38    | 13       | 1.10 (0.59-2.07)    |
| Missense                                      | 2            | 0.91                    | 0.73           | 16    | 6        | 1.00 (0.39-2.57)    |
| Inframe Deletion                              | 3            | 0.45                    | <b>0.03</b>    | 50    | 16       | 1.18 (0.67-2.07)    |
| VEP Low                                       | 4            | 0.96                    | 1.00           | 38    | 13       | 1.10 (0.59-2.07)    |
| VEP Moderate                                  | 5            | 0.58                    | <b>0.04</b>    | 66    | 22       | 1.13 (0.70-1.84)    |
| <i>All excluding tail (29876207-29884868)</i> | 34           | 0.60                    | 0.56           | 641   | 252      | 0.95 (0.82-1.11)    |

Table 5-4. Results of the high-frequency rare (MAF 0.1-1%) *NEFH* variant burden analysis. Significant results are denoted by bold p-values. All results are corrected for sex and the first 10 principal components.

| Frequency (<1%)                 | No. Variants | Madsen Browning p-value | SKAT-O p-value | Cases | Controls | Odds Ratio (95% CI) |
|---------------------------------|--------------|-------------------------|----------------|-------|----------|---------------------|
| <i>All (29876207-29887379)</i>  | 557          | <b>0.03</b>             | 0.38           | 1269  | 438      | 1.11 (0.99-1.25)    |
| Synonymous                      | 41           | 0.11                    | 0.32           | 47    | 12       | 1.48 (0.78-2.79)    |
| Missense                        | 87           | 0.11                    | 0.56           | 85    | 24       | 1.34 (0.85-2.11)    |
| All pathogenic missense         | 56           | 0.36                    | 0.8            | 69    | 22       | 1.18 (0.73-1.91)    |
| Inframe Deletion                | 15           | <b>0.05</b>             | 0.42           | 16    | 2        | 3.01 (0.69-13.12)   |
| Inframe Insertion               | 11           | 0.38                    | 0.75           | 12    | 3        | 1.51 (0.42-5.34)    |
| Intronic                        | 361          | <b>4.0E-03</b>          | <b>0.034</b>   | 419   | 115      | 1.40 (1.13-1.73)    |
| 3' UTR                          | 31           | 0.22                    | 0.66           | 39    | 11       | 1.34 (0.68-2.61)    |
| 5' UTR                          | 4            | <b>4.0E-03</b>          | <b>0.037</b>   | 1     | 3        | 0.13 (0.01-1.21)    |
| VEP High                        | 6            | 0.13                    | 0.11           | 3     | 4        | 0.28 (0.06-1.26)    |
| VEP Low                         | 41           | 0.11                    | 0.32           | 47    | 12       | 1.48 (0.78-2.79)    |
| VEP Moderate                    | 113          | <b>0.029</b>            | 0.18           | 113   | 29       | 1.47 (0.98-2.22)    |
| VEP Modifier                    | 397          | <b>3.1E-03</b>          | <b>0.034</b>   | 460   | 127      | 1.39 (1.14-1.70)    |
| <i>Head (29876252-29876554)</i> | 13           | 0.76                    | 0.26           | 15    | 9        | 0.63 (0.27-1.43)    |
| Synonymous                      | 7            | 0.49                    | 0.24           | 8     | 3        | 1.00 (0.27-3.79)    |
| Missense                        | 6            | 0.091                   | 0.17           | 7     | 6        | 0.44 (0.15-1.31)    |
| Pathogenic missense             | 1            | N/A                     | 0.069          | 1     | 0        | 1.13 (0.05-27.73)   |
| VEP Low                         | 7            | 0.49                    | 0.24           | 8     | 3        | 1.00 (0.27-3.79)    |
| VEP Moderate                    | 6            | 0.091                   | 0.17           | 7     | 6        | 0.44 (0.15-1.31)    |
| <i>Rod (29876555-29884868)</i>  | 413          | <b>0.03</b>             | 0.32           | 1062  | 363      | 1.12 (0.98-1.28)    |
| Synonymous                      | 20           | 0.08                    | 0.25           | 28    | 5        | 2.11 (0.81-5.48)    |
| Missense                        | 28           | 0.07                    | 0.55           | 29    | 6        | 1.82 (0.76-4.39)    |
| Pathogenic missense             | 17           | 0.85                    | 0.46           | 23    | 12       | 0.72 (0.36-1.45)    |
| Inframe Insertion               | 1            | 0.26                    | 0.53           | 1     | 0        | 1.13 (0.041-27.73)  |
| Intronic                        | 361          | <b>4.0E-03</b>          | <b>0.034</b>   | 419   | 115      | 1.40 (1.13-1.73)    |
| VEP High                        | 3            | 0.18                    | 0.2            | 1     | 2        | 0.19 (0.02-2.07)    |
| VEP Low                         | 20           | 0.08                    | 0.25           | 28    | 5        | 2.11 (0.81-5.48)    |
| VEP Moderate                    | 29           | <b>0.05</b>             | 0.48           | 30    | 6        | 1.89 (0.78-4.54)    |
| VEP Modifier                    | 397          | <b>3.1E-03</b>          | <b>0.034</b>   | 460   | 127      | 1.39 (1.14-1.70)    |
| <i>Tail (29884869-29886689)</i> | 95           | 0.18                    | 0.21           | 193   | 63       | 1.15 (0.86-1.54)    |
| Synonymous                      | 14           | 0.65                    | 0.89           | 10    | 4        | 0.94 (0.29-3.00)    |
| Missense                        | 53           | 0.08                    | 0.41           | 49    | 12       | 1.54 (0.82-2.90)    |
| Pathogenic Missense             | 38           | 0.09                    | 0.36           | 52    | 13       | 1.51 (0.82-2.78)    |
| Inframe Deletion                | 15           | <b>0.05</b>             | 0.42           | 16    | 2        | 3.01 (0.69-13.12)   |
| Inframe Insertion               | 10           | 0.43                    | 0.84           | 11    | 3        | 1.38 (0.38-4.95)    |
| VEP High                        | 3            | 0.36                    | 0.35           | 2     | 2        | 0.38 (0.05-2.67)    |
| VEP Low                         | 14           | 0.65                    | 0.89           | 10    | 4        | 0.94 (0.29-3.00)    |
| VEP Moderate                    | 78           | <b>0.024</b>            | 0.28           | 76    | 17       | 1.69 (1.00-2.87)    |

|  |     |      |      |      |     |                  |
|--|-----|------|------|------|-----|------------------|
| All excluding tail (29876207-29884868) | 431 | 0.06 | 0.43 | 1068 | 372 | 1.10 (0.96-1.25) |
|--|-----|------|------|------|-----|------------------|

Table 5-5. Results of the rare ( $MAF < 1\%$ ) *NEFH* variant burden analysis. Significant results are denoted by bold *p*-values. All results are corrected for sex and the first 10 principal components.

## 5.5 Discussion

Leveraging genetic data from 11,130 ALS patients and 7,416 controls from both the literature and Project MinE, we found that rare variants ( $MAF < 1\%$ ) in the *NEFH* gene increase the risk of ALS (meta-analysis  $p < 0.0001$  and Project MinE burden analysis  $p = 0.0007$  when taking multiple testing into account). We report that this association may be primarily driven by missense variants in the tail domain and intronic variants in the rod domain. Our meta-analysis reported that rare missense tail *NEFH* variants in a total of 1164 ALS patients and 2177 controls yielded an OR of 4.55 ( $p < 0.0001$ ). This was replicated to some extent, although with a lower OR and nominal association, when performing ultra-rare variant burden analysis of pathogenic missense tail variants in the Project MinE dataset (OR 1.94, Madsen-Browning  $p = 0.039$ ). The difference between effect sizes is likely due to the discrepancy in sample size between the two cohorts, with smaller sample sizes often reporting a larger effect size for significant relationships in either direction (L. Lin, 2018), or also the ‘winner’s curse’ effect commonly observed in genetic association discovery studies (Xiao & Boehnke, 2009). Furthermore, as the aforementioned Project MinE association is nominal, but there was no association with rare missense variants as a whole due to the nature of how we dealt with multiple testing, we could deliberate as to whether these effects are consistent. However, as most missense variants in the meta-analysis are deleterious and possibly/probably damaging according to SIFT and PolyPhen, which are the same criteria used in the Project MinE burden analyses, we can attest that the effects we are seeing do share some consistency.

The effect of missense tail variants on *NEFH* is not clear (Theunissen, West, et al., 2021), but it is plausible to hypothesise that they could modify the effects of phosphorylation in the KSP repeat, thereby changing the conformation of the NF-H subunit in such a way that simultaneously increases the propensity of pNF-H aggregate formation in the axon and disrupts energy metabolism and protein transport. We also found that rare small in-frame deletions in the tail domain confer susceptibility to ALS within Project MinE, which agrees with previous findings in the literature (Al-

Chalabi et al., 1999; Figlewicz et al., 1994), but not in the meta-analysis. This discrepancy could again be due to the relatively small sample sizes used in the meta-analysis compared to Project MinE, or that there may be subdomain-specific effects occurring in the tail that the meta-analysis design could not account for. For instance, we identified that deletions in the KSP repeat were associated with an increased risk for ALS, and we also found a novel protective common (MAF > 1%) 113bp deletion in the KEP segment, which despite having discordance in direction of effect with the non-significant ultra-rare KEP repeat in-frame deletions from the burden analysis, is still suggestive of the fact that there is a complex genetic architecture in this domain with different classes and frequencies of variants playing different roles. This is plausible in other domains as well given that recent studies identified other protective variants in the gene (Grassano et al., 2021; Theunissen et al., 2022) and that we found ultra-rare (MAF<0.1%) intronic rod SNVs and indels were the main drivers of the association between *NEFH* variants and ALS, despite a recent study reporting a common non-coding repeat polymorphism in the same domain as being protective against ALS (Theunissen et al., 2022). Therefore, future studies should incorporate genetic evidence of missense tail mutations and the characterisation of both small and large deletions with proteomic and transcriptomic data to determine if there is an aberrant stoichiometry of NF-H that is due solely to the action of these mutations or is a product of a more complex interaction between microRNA and protein targets.

In conclusion, we demonstrate that missense variants and in-frame deletions in the tail domain, and intronic variants in the rod domain of *NEFH* are associated with an increased risk of ALS. However, they are not variants of large effect, and their functional impact needs to be assessed in further experimental studies before determining whether they should be included in routine genetic screening panels. In recent years several studies have shown that non-coding variants have a major role in ALS: for example, enhancer variants in *CAV1* and *CAV2* (Adey et al., 2023; Cooper-Knock et al., 2021) and intronic variants in *UNC13A* (A.-L. Brown et al., 2022; Ma et al., 2022). Our findings expand this by also implicating *NEFH* non-coding variants in ALS. However, understanding the functional effect of variants in non-coding regions is challenging and further research is needed to understand how non-coding neurofilament variants contribute to ALS risk.

## Chapter 6. Differential gene expression analysis of two large ALS sequencing consortia

### 6.1 Abstract

#### *Background*

Amyotrophic lateral sclerosis (ALS) is a fatal heterogeneous neurodegenerative disease that typically leads to death from respiratory failure within two to five years. Despite the identification of several genetic risk factors, the biological processes involved in ALS pathogenesis remain poorly understood. The motor cortex is an ideal region to study dysregulated pathological processes in ALS as it is affected from the earliest stages of the disease. In this study, we investigated motor cortex gene expression of cases and controls to gain new insight into the molecular footprint of ALS.

#### *Methods*

We performed a large case-control differential expression analysis of two independent post-mortem motor cortex bulk RNAseq datasets from the King's College London BrainBank (N = 171) and TargetALS (N = 132). Differentially expressed genes from both datasets were subjected to gene and pathway enrichment analysis. Genes common to both datasets were also reviewed for their involvement with known mechanisms of ALS pathogenesis to identify potential candidate genes. Finally, we performed a correlation analysis of genes implicated in pathways enriched in both datasets with clinical outcomes such as age of onset and survival. Cell type deconvolution was performed to assess if gene enrichment results were a product of the differential contribution of cell types in both datasets.

#### *Results*

Differential expression analysis identified 2,290 and 402 differentially expressed genes in KCL BrainBank and TargetALS cases, respectively. There were 45 differentially expressed genes which were common to both datasets, which represented previously recognised mechanisms of ALS pathogenesis, such as lipid metabolism, mitochondrial energy homeostasis and neurovascular unit dysfunction. Differentially expressed genes in both datasets were significantly enriched for the neuropeptide signalling

pathway. By looking at the relationship between the expression of neuropeptides and their receptors with clinical measures, we found that *TACR1* expression positively correlated with disease duration, and *NPBWR1* expression negatively correlated with age of onset in both datasets. We provide access to gene-level expression results to the broader research community through a publicly available web application (<https://alsgeexplorer.er.kcl.ac.uk>).

### *Conclusion*

This study identified motor-cortex specific genes and pathways altered in ALS patients, and a set of neuropeptides and receptors for further investigation as potential biomarkers of onset and progression.

## **6.2 Introduction**

Amyotrophic lateral sclerosis (ALS) is a devastating, heterogeneous neurodegenerative disease that leads to death from neuromuscular respiratory failure within two to five years. Despite the heritability of ALS being largely unknown, the discovery of several genetic risk factors has driven the identification of multiple biological processes involved in the disease aetiology (Julien, 2001; Rowland & Shneider, 2001). However, the pathogenic mechanisms of ALS remain poorly understood.

The motor cortex is affected from the earliest stages of the disease and is one of the brain regions majorly affected by ALS pathology. Consequently, its disease expression signatures have been investigated to gain insight into the disease aetiology. Recent studies have reported differential expression of genes related to transcription, neurotransmission, protein synthesis and oxidative stress processes (X.-S. Wang et al., 2006), with extensive RNA expression alterations of neuroinflammatory and synaptic-related pathways identified at both gene and isoform levels (Dols-Icardo et al., 2020). Nevertheless, studies of this critical region at the whole-transcriptome level usually involve relatively small sample sizes and do not replicate their results in independent datasets.

To study functional changes occurring in the motor cortex of ALS patients, we have utilised two large independent RNAseq datasets of ALS patients and controls from the



King's College London (KCL) BrainBank (171 subjects) and TargetALS (234 samples from 132 subjects). By analysing the two datasets, our goal was to obtain profiles of altered gene expression that would identify the underlying molecular footprint of ALS and use this information to propose novel hypotheses about disease mechanisms, potential drug targets and biomarkers.

## **6.3 Methods**

### **6.3.1 Datasets**

The KCL BrainBank RNAseq dataset (described previously in Iacoangeli et al., 2021; Jones et al., 2021) consists of post-mortem RNAseq samples from KCL and the Medical Research Council (MRC) London Neurodegenerative Diseases Brain Bank. Frozen human post-mortem tissue was taken from the primary motor cortex. The RNAseq protocol is outlined in Chapter 3.1.2.1. In total, 112 sporadic ALS cases and 59 controls were included in this analysis.

The TargetALS RNAseq dataset comes from The TargetALS Human Postmortem Tissue Core and the New York Genome Centre (NYGC). We obtained the TargetALS dataset from <https://www.targetals.org/>. Details about the RNAseq protocol is available in Chapter 3.1.2.2. A list of the sample IDs of 234 samples (from 132 subjects, 112 ALS cases and 20 controls) used in this study is available in Table A14. Frozen human post-mortem tissue was taken from the motor cortex (medial, lateral, and unspecified). Samples from different motor cortex regions for the same subjects were included, where available, for differential expression analysis (see Chapter 3.4.1 for more information on the inclusion of multiple samples per subject).

To determine whether the sample characteristics for cases and controls differed in each dataset, we performed unpaired t-tests for age at death, RIN number and post-mortem delay (PMD) and the chi-square test for sex assigned at birth for both datasets. Any continuous variables that were not normally distributed were assessed with the Wilcoxon-rank test. A p-value of  $< 0.05$  denotes significance.

### **6.3.2 Bioinformatics, data processing and expression analysis**

Both datasets were processed using the same transcript quantification pipeline, which is detailed in Chapter 3.1.3. Normalisation and differential expression was performed

using DESeq2 (Love et al., 2014). For normalisation we used the *estimateSizeFactors* function of DESeq2, before the Wald test was used for differential expression analysis, with the Benjamini-Hochberg method used for p-value adjustment. For both datasets, we included age, sex, RIN number, PMD and a surrogate variable obtained by SVA (Leek & Storey, 2007) as covariates in the DESeq2 design. The sequencing centre was also included as a covariate for the TargetALS dataset. We decided to include surrogate variables in our design as they can effectively eliminate the influence of naturally grouped variables which might unknowingly be affecting the differential expression results. For instance, principal component analysis of the TargetALS dataset reveals that there two distinct groups which are not influenced by motor cortex region (Figure 3-1), but this grouping was effectively eliminated with the application of the one surrogate variable identified during analysis (Figure A10).

The differential expression code is available at [https://github.com/rkabiljo/DifferentialExpression\\_Genes](https://github.com/rkabiljo/DifferentialExpression_Genes). For MA Plots, *apeglm* was used for LFC shrinkage (Zhu et al., 2019). Enrichment analysis was performed using MetaCore™ (available at <https://portal.genego.com>) for Gene Ontology (GO) Biological Processes, Pathway Maps, Process Networks and Disease by Biomarker enrichments, whilst *gProfiler2* (Kolberg et al., 2020) was used for Reactome (Gillespie et al., 2022) enrichment. Due to a non-one-to-one mapping of the MetaCore algorithm of uploaded gene lists to their proprietary concept of network objects, the resulting enrichment lists consisted of 1,004 objects for KCL BrainBank and 366 for TargetALS. For background genes, we used a list of 41,709 transcripts which had at least 10 counts in at least 5 subjects, which were subsequently mapped in MetaCore to 26,484 network objects.

To test whether the number of differentially expressed genes identified in our analysis was due to chance, we performed 1,000 random permutations of case/control labels and performed differential expression analysis on each permutation. For each permutation, we counted the number of genes with false discovery rate (FDR) adjusted p-value lower than our selected cut-off of 0.05. The random permutation scripts are available here <https://github.com/rkabiljo/ShufflingLabelsForDE>.

To assess if gene enrichment results were a product of the contribution of different cell types, we used the MuSiC2 R package (v1.0.0; (Fan et al., 2022)) to derive cell

proportions for the following cell types; astrocytes, endothelial cells, microglia, neurons, and oligodendrocytes. We performed deconvolution using the raw RNAseq count matrix of KCL BrainBank, TargetALS medial motor cortex, and TargetALS lateral motor cortex. The single-cell RNAseq reference dataset which was used to derive expression information for each cell type consisted of 8 adults and 4 embryonic samples (16-18 weeks gestational age) from the temporal lobe (Darmanis et al., 2015), which was downloaded via the scRNAseq R package (v2.14.0; (Risso D, Cole M, 2023)). Due to the relatively small sample sizes of each of our datasets, the detection of cell-type-specific differentially expressed genes and cell-type deconvolution was performed using the t-statistic approach of MuSiC2. Case-control differences in cell type proportions were assessed using one-way ANCOVA corrected for age of death and sex, with a p-value of  $< 0.05$  denoting significance.

To assess the relationship between neuropeptide receptors and ligands with age of onset and disease duration, we performed correlation analysis of RNAseq counts normalised via the variance-stabilising transformation algorithm in DESeq2 for ALS patients in the KCL BrainBank and TargetALS medial and lateral motor cortex datasets. We derived the neuropeptide-related genes from the Hugo Gene Nomenclature Committee (HGNC) Neuropeptides and Peptide Receptors lists (available at <https://www.genenames.org>) before the receptors and ligands which were expressed in each dataset (102 in KCL BrainBank, 105 in TargetALS medial motor cortex and 106 in TargetALS lateral motor cortex) were analysed. Correlation analysis was performed using the *cor.test* function in the stats R package (v4.2.3) Nominal p-values were identified from the output of these tests, with adjusted p-values calculated using the false-discovery rate method, whereby the p-values were multiplied by the number of neuropeptides tested in each dataset. A p-value of  $< 0.05$  denoted significance.

To share the results with the wider community, we developed a web application using the R “shiny” framework (v1.7.1) to allow quick visualisation of specific gene expression in ALS cases and controls, available at <https://alsgeexplorer.er.kcl.ac.uk>.

## 6.4 Results

### 6.4.1 Sample Characteristics

The summary characteristics of the two datasets are shown in Table 6-1. The KCL BrainBank dataset had significant differences between cases and controls in terms of age, RNA integrity number (RIN) and post-mortem delay (PMD). The TargetALS dataset showed no significant differences in age, sex, and RIN between cases and controls, but did display a significant difference in PMD ( $p$ -value = 0.0027). We accounted for these differences through our choice of covariates included in the differential expression analyses.

| Dataset       | Variables                    | ALS Cases               | Controls                | Statistic and p-value* |
|---------------|------------------------------|-------------------------|-------------------------|------------------------|
| KCL BrainBank | <b>Total (Individuals)</b>   | 112                     | 59                      |                        |
|               | Age (mean $\pm$ SD)          | 64.8 $\pm$ 12.7         | 76.2 $\pm$ 14.6         | 5.28; <b>3.9E-07</b>   |
|               | Male : Female (%)            | 65 (58%) : 47 (42%)     | 26 (44.1%) : 33 (55.9%) | 3.03; 0.08             |
|               | RIN Number (mean $\pm$ SD)** | 6.45 $\pm$ 1.26         | 5.33 $\pm$ 1.58         | 1847; <b>2.2E-06</b>   |
|               | PMD (mean $\pm$ SD)          | 26.0 $\pm$ 12.1         | 37.6 $\pm$ 19.3         | 4.17; <b>7.6E-05</b>   |
| TargetALS     | <b>Total (Individuals)</b>   | 112                     | 20                      |                        |
|               | Age (mean $\pm$ SD)          | 63.9 $\pm$ 10.6         | 62.6 $\pm$ 11.9         | -0.52; 0.61            |
|               | Male : Female (%)            | 64 (57.1%) : 48 (42.9%) | 9 (45%): 11 (55%)       | 1.01; 0.31             |
|               | <b>Total (Samples)</b>       | 198                     | 36                      |                        |
|               | RIN Number (mean $\pm$ SD)** | 6.21 $\pm$ 1.15         | 5.91 $\pm$ 1.25         | 3161; 0.28             |
|               | PMD (mean $\pm$ SD)**        | 10.5 $\pm$ 6.92         | 21.2 $\pm$ 22.8         | 4683; <b>2.7E-03</b>   |

Table 6-1. Sample characteristics of KCL BrainBank and TargetALS. Age: Age at death. PMD: Post-mortem delay. RIN: RNA integrity number. \*Statistic and p-value refers to the Chi-square test for categorical variables (Sex assigned at birth – Male: Female) and unpaired T-test for continuous variables (Age, RIN Number, PMD). \*\*Wilcoxon test was performed as data was not normally distributed.

## **6.4.2 Differential expression analysis**

### **6.4.2.1 KCL BrainBank**

A total of 2,290 genes were differentially expressed with an adjusted p-value of  $<0.05$ , in the KCL BrainBank dataset. Of these, 1,507 of the genes were upregulated and 783 were downregulated in cases (Figures 6-1A and 6-1B). None of the 1000 random permutations produced more differentially expressed genes than the actual differential expression analysis, thus confirming the significance of these results. In the vast majority of the permutations, there were no differentially expressed genes (with adjusted p-value  $<0.05$ ), with the number of significant genes across permutations averaging 4.5. Table A15 displays the full details of the 2,290 significant differentially expressed genes discovered using DESeq2.

### **6.4.2.2 TargetALS**

A total of 402 genes were differentially expressed, with an adjusted p-value of  $<0.05$ , in the TargetALS dataset. Of these, 250 of these genes were downregulated and 152 were upregulated in cases (Figures 6-1C and 6-1D). When performing random permutations, 9 (0.9%) produced as many or more differentially expressed genes as the actual differential expression analysis. In most of the permutations, there were no differentially expressed genes (with adjusted p-value  $<0.05$ ), with an average of 28 significantly expressed genes across permutations. Table A16 displays the full details of the 402 significant differentially expressed genes discovered using DESeq2.

### **6.4.2.3 Shared differentially expressed genes**

We found 45 genes significant in both datasets with an adjusted p-value of  $<0.05$ . Of these, 44 of these had a concordant direction of regulation in both datasets; 29 genes were downregulated and 15 were upregulated (Figure 6-1E). To estimate the significance of this intersection between differentially expressed genes in the two datasets, we performed a hypergeometric test, using 41,709 as the number of background genes. The p-value obtained was  $< 1.2E-05$ . Genes that were significant in both datasets are listed in Table 6-2.

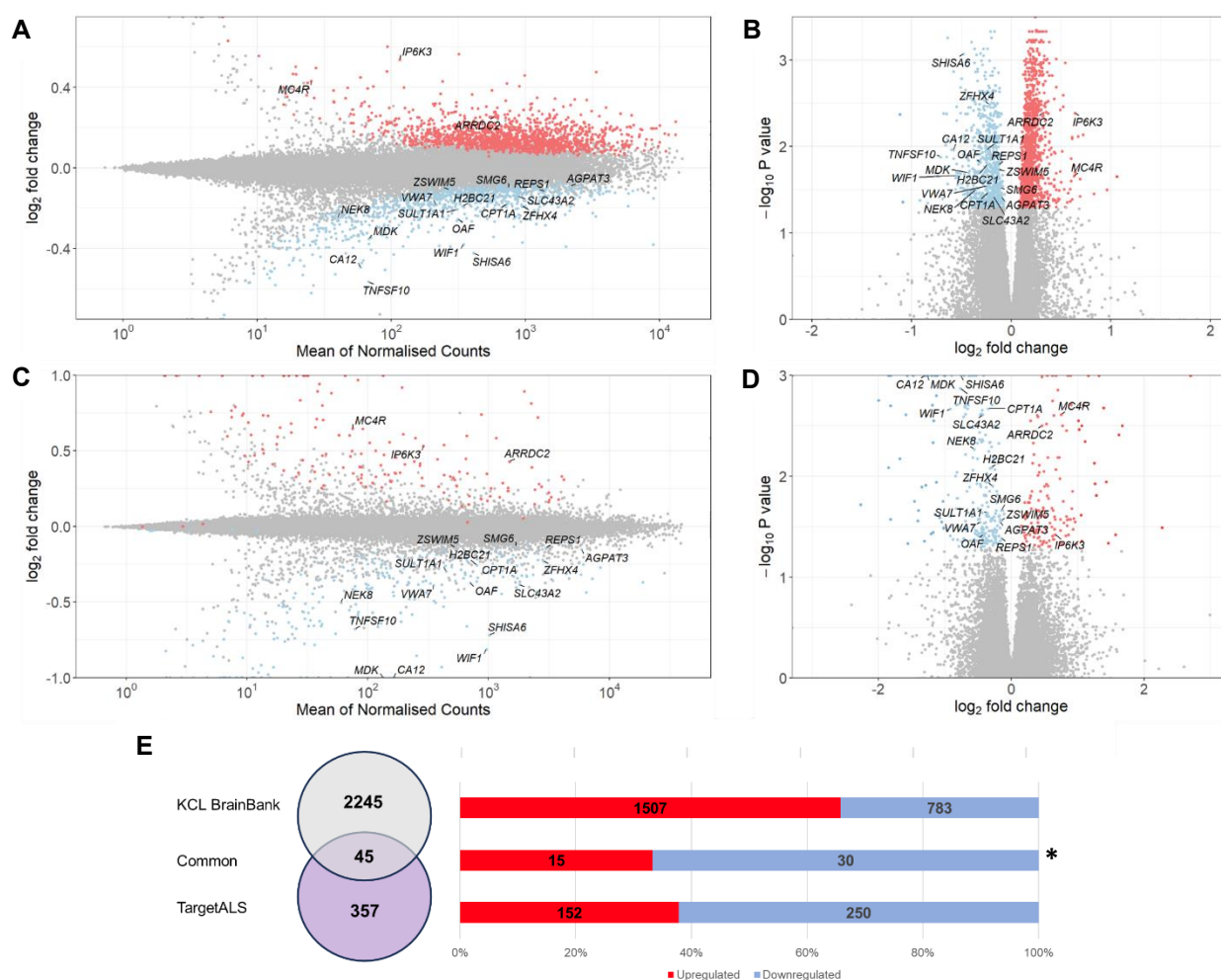


Figure 6-1. Visualisation of the distribution of differentially expressed genes in KCL BrainBank and TargetALS. A) KCL BrainBank and C) TargetALS MA plots representing the distribution of log<sub>2</sub> fold change (log<sub>2</sub>FC) across all expression levels; B) KCL BrainBank and D) TargetALS Volcano plots. In plots A - D, genes coloured red are significantly upregulated in ALS cases and genes coloured blue are significantly downregulated in ALS cases. E) Numbers of differentially expressed genes in the two datasets. Left: Number of unique and shared differentially expressed genes. Right: Breakdown of numbers of upregulated and downregulated genes in each dataset (Total KCL BrainBank: 2,290, TargetALS: 402, Common: 45). \* One gene is missing from this breakdown as it displayed a discordant direction of expression.

| Ensembl ID      | Gene Symbol         | KCL BrainBank |         |              | TargetALS |         |              | Biological Theme  |
|-----------------|---------------------|---------------|---------|--------------|-----------|---------|--------------|---|
|                 |                     | LogFC         | p-value | adj. p-value | LogFC     | p-value | adj. p-value |   |
| ENSG00000121858 | <i>TNFSF10</i>      | -0.71         | 3.4E-04 | 0.013        | -0.77     | 1.7E-06 | 1.3E-03      | UPS/Autophagy   |
| ENSG00000164309 | <i>CMYA5</i>        | -0.28         | 1.8E-04 | 5.8E-03      | -0.29     | 1.9E-04 | 0.027        | UPS/Autophagy   |
| ENSG00000074410 | <i>CA12</i>         | -0.58         | 2.0E-04 | 0.011        | -1.3      | 6.0E-15 | 5.2E-11      | NVU Dysfunction   |
| ENSG00000101439 | <i>CST3</i>         | -0.27         | 5.4E-03 | 0.042        | -0.41     | 4.2E-04 | 0.039        | NVU Dysfunction   |
| ENSG00000271447 | <i>MMP28</i>        | -0.33         | 3.1E-03 | 0.030        | -0.58     | 9.4E-06 | 3.3E-03      | Neuroinflammation   |
| ENSG00000110492 | <i>MDK</i>          | -0.43         | 5.5E-04 | 0.02         | -1.26     | 2.1E-18 | 6.3E-14      | Neuroinflammation, Neurogenesis                           |
| ENSG00000188803 | <i>SHISA6</i>       | -0.48         | 2.6E-06 | 8.4E-04      | -0.76     | 4.7E-10 | 1.6E-06      | Neuronal Signalling (AMPA/NMDA)                           |
| ENSG00000196502 | <i>SULT1A1</i>      | -0.25         | 5.8E-04 | 0.011        | -0.36     | 1.7E-04 | 0.023        | Metabolism, Neuronal Signalling (AMPA/NMDA)               |
| ENSG00000110090 | <i>CPT1A</i>        | -0.23         | 4.1E-03 | 0.034        | -0.35     | 4.2E-06 | 2.1E-03      | Metabolism (Fatty Acid)                                   |
| ENSG00000204396 | <i>VWA7</i>         | -0.24         | 2.4E-03 | 0.028        | -0.47     | 2.4E-04 | 0.028        | Extracellular Matrix                                      |
| ENSG00000156076 | <i>WIF1</i>         | -0.55         | 1.5E-03 | 0.022        | -0.92     | 3.8E-06 | 2.1E-03      | WNT/ $\beta$ -Catenin Signalling                          |
| ENSG00000160602 | <i>NEK8</i>         | -0.35         | 1.4E-03 | 0.031        | -0.56     | 1.9E-05 | 5.4E-03      | DNA Damage Response                                       |
| ENSG00000091656 | <i>ZFHX4</i>        | -0.22         | 6.5E-05 | 3.3E-03      | -0.28     | 6.2E-05 | 0.013        | Transcriptional Regulation                                |
| ENSG00000184678 | <i>H2BC21</i>       | -0.24         | 9.7E-04 | 0.016        | -0.30     | 3.2E-05 | 8.2E-03      | Nucleosome  |
| ENSG00000237686 | <i>SCIRT</i>        | -0.65         | 2.6E-05 | 4.2E-03      | -0.65     | 1.1E-05 | 4.7E-03      | NVU Dysfunction   |
| ENSG00000261888 | <i>Lnc-METRNL-1</i> | -0.64         | 7.5E-04 | 0.027        | -0.81     | 1.4E-06 | 1.9E-03      | Metabolism (Glucose)                                      |
| ENSG00000271646 | <i>IRF2-DT</i>      | -0.45         | 9.4E-05 | 6.5E-03      | -0.38     | 5.7E-04 | 0.046        | Neuroinflammation   |
| ENSG00000134042 | <i>MRO</i>          | -0.31         | 5.6E-03 | 0.041        | -0.47     | 4.5E-06 | 2.4E-03      | -   |
| ENSG00000184232 | <i>OAF</i>          | -0.31         | 8.9E-04 | 0.015        | -0.42     | 4.0E-04 | 0.038        | Molecular Chaperone                                       |
| ENSG00000267904 | <i>Lnc-MED26-2</i>  | -0.27         | 7.0E-04 | 0.020        | -0.21     | 4.4E-04 | 0.031        | Transcriptional Regulation                                |
| ENSG00000135597 | <i>REPS1</i>        | -0.13         | 1.1E-03 | 0.016        | -0.15     | 4.4E-04 | 0.041        | Neuronal Signalling (Vesicular Transport and Endocytosis) |
| ENSG00000162415 | <i>ZSWIM5</i>       | -0.13         | 1.3E-03 | 0.018        | -0.15     | 2.2E-04 | 0.028        | Metal Ion Binding   |
| ENSG00000070366 | <i>SMG6</i>         | -0.11         | 2.9E-03 | 0.030        | -0.15     | 1.6E-04 | 0.022        | Telomere Maintenance, Nonsense-Mediated Decay             |
| ENSG00000145476 | <i>CYP4V2</i>       | -0.20         | 3.0E-03 | 0.030        | -0.23     | 3.9E-04 | 0.036        | Metabolism (Fatty Acid)                                   |
| ENSG00000167703 | <i>SLC43A2</i>      | -0.18         | 4.3E-03 | 0.037        | -0.43     | 4.5E-06 | 2.4E-03      | Amino Acid and Ion Transport                              |
| ENSG00000160216 | <i>AGPAT3</i>       | -0.10         | 4.4E-03 | 0.038        | -0.17     | 2.5E-04 | 0.028        | Metabolism (Lipid)  |
| ENSG00000215154 | <i>LOC652276</i>    | -0.26         | 6.9E-04 | 0.019        | -0.28     | 1.1E-03 | 0.048        | -   |
| ENSG00000172270 | <i>BSG</i>          | -0.16         | 6.2E-04 | 0.044        | -0.30     | 3.5E-04 | 0.035        | Neuroinflammation   |

|                 |                       |       |         |         |       |         |         |                                     |
|-----------------|-----------------------|-------|---------|---------|-------|---------|---------|-------------------------------------|
| ENSG00000143819 | <i>EPHX1</i>          | -0.19 | 6.2E-03 | 0.046   | -0.37 | 2.9E-04 | 0.032   | Metabolism (Fatty Acid)             |
| ENSG00000166603 | <i>MC4R</i>           | 0.63  | 7.4E-04 | 0.022   | 0.75  | 8.2E-06 | 2.4E-03 | Neuropeptide Signalling, Metabolism |
| ENSG00000105643 | <i>ARRDC2</i>         | 0.32  | 9.5E-05 | 4.1E-03 | 0.46  | 8.4E-06 | 3.1E-03 | Metabolism, Neuronal Signalling     |
| ENSG00000161896 | <i>IP6K3</i>          | 0.64  | 1.0E-04 | 4.1E-03 | 0.66  | 4.1E-04 | 0.038   | Metabolism                          |
| ENSG00000183196 | <i>CHST6</i>          | 0.41  | 1.2E-05 | 1.5E-03 | 0.62  | 4.2E-07 | 4.9E-04 | Metabolism                          |
| ENSG00000176641 | <i>RNF152</i>         | 0.29  | 4.2E-04 | 8.5E-03 | 0.33  | 1.4E-05 | 4.7E-03 | UPS/Autophagy                       |
| ENSG00000156804 | <i>FBXO32</i>         | 0.21  | 8.2E-04 | 0.014   | 0.25  | 1.0E-04 | 0.018   | UPS/Autophagy                       |
| ENSG00000240583 | <i>AQP1</i>           | 0.63  | 1.1E-03 | 0.016   | 0.86  | 2.1E-04 | 0.027   | NVU Dysfunction                     |
| ENSG00000154188 | <i>ANGPT1</i>         | 0.42  | 2.3E-03 | 0.042   | 0.67  | 6.2E-07 | 4.0E-04 | NVU Dysfunction                     |
| ENSG00000134817 | <i>APLNR</i>          | 0.56  | 5.7E-03 | 0.044   | 0.90  | 2.8E-06 | 2.0E-03 | NVU Dysfunction, Apelin Signalling  |
| ENSG00000168386 | <i>FILIP1L</i>        | 0.30  | 5.1E-05 | 3.3E-03 | 0.25  | 2.6E-04 | 0.032   | WNT/ $\beta$ -Catenin Signalling    |
| ENSG00000286653 | NA (novel transcript) | 0.57  | 3.0E-04 | 0.034   | 0.61  | 1.4E-04 | 0.021   | -                                   |
| ENSG00000052795 | <i>FNIP2</i>          | 0.14  | 1.7E-03 | 0.020   | 0.20  | 1.1E-04 | 0.018   | Metabolism, Autophagy, Apoptosis    |
| ENSG00000171451 | <i>DSEL</i>           | 0.16  | 5.9E-03 | 0.045   | 0.30  | 1.3E-04 | 0.021   | -                                   |
| ENSG00000198740 | <i>ZNF652</i>         | 0.19  | 8.6E-04 | 0.013   | 0.34  | 2.3E-05 | 6.1E-03 | Transcriptional Regulation          |
| ENSG00000138798 | <i>EGF</i>            | 0.40  | 3.2E-04 | 0.012   | 0.42  | 3.9E-05 | 9.1E-03 | -                                   |
| ENSG00000272505 | <i>Lnc-PRSS55-1</i>   | -0.20 | 0.0011  | 0.018   | 0.21  | 1.9E-04 | 0.024   | -                                   |

Table 6-2. Significantly differentially expressed genes shared in both KCL BrainBank and TargetALS (adjusted  $p$ -value < 0.05). For each gene, the fold change,  $p$ -value and adjusted  $p$ -value is displayed for both datasets, along with their major biological function. Red: Upregulated; Blue: Downregulated. White: Discordant direction of expression. LogFC: Log2 of Fold Change.

### 6.4.3 Gene and Pathway Enrichment Analysis

To compensate for the different numbers of differentially expressed genes in the two datasets when using 0.05 as the corrected  $p$ -value threshold (2,290 genes in KCL BrainBank and 402 in TargetALS), we applied an additional threshold of  $\log_{2}FC > 0.2$  to the KCL BrainBank dataset. This yielded differential expression for 1,013 genes, which were uploaded to MetaCore for enrichment analysis along with the 402 differentially expressed genes in TargetALS. We performed analyses using MetaCore to obtain enrichments for Pathway Maps, Process Networks, Disease Networks and Gene Ontology (GO) Biological Processes, and gProfiler2 for Reactome enrichment. Tables A17-A26 list the top 100 results for each of the enrichment categories (50 for Process Networks), with their  $p$ -value, false discovery rate (FDR) adjusted  $p$ -value,



and the genes from each dataset contributing to each enrichment within each category.

#### **6.4.3.1 Process Networks**

Among the most significant processes in KCL BrainBank (Figure 6-2A; Table A17) were several neurophysiological processes, such as transmission of nerve impulse (adjusted p-value = 0.000047) and GABAergic neurotransmission (adjusted p-value = 0.017), as well as axonal guidance (adjusted p-value = 0.0037). A related process that approached significance after adjustment was cholecystokinin signalling (adjusted p-value = 0.057). In addition, there was one significant process broadly related to muscle contraction (adjusted p-value = 0.0037); nitric oxide signalling in cardiovascular system (adjusted p-value = 0.016). In TargetALS, the most enriched networks, albeit not significant, were several processes related to inflammation; interferon signalling and natural killer (NK) cell cytotoxicity (Figure 6-2A; Table A18). There were two commonly significantly enriched processes; neuropeptide signalling pathways (KCL BrainBank adjusted p-value = 0.0025; TargetALS adjusted p-value = 1.5E-14) and blood vessel morphogenesis (KCL BrainBank adjusted p-value = 0.016; TargetALS adjusted p-value = 0.037).

#### **6.4.3.2 Diseases by Biomarkers, GO Biological Processes and Reactome**

We found that the two datasets demonstrated divergent enrichments for Diseases by Biomarkers (Tables A19 and A20), GO Biological Processes (Tables A21 and A22) and Reactome pathways (Tables A23 and A24). For instance, KCL BrainBank showed clear enrichments for nervous-system related diseases (Table A19), such as movement disorders (adjusted p-value = 1.2E-21), dyskinesias (adjusted p-value = 1.2E-20), neurodegenerative (adjusted p-value = 1.3E-19) and neuromuscular (adjusted p-value = 3.6E-12) diseases, as well as schizophrenia (adjusted p-value = 4.1E-13). The significant GO processes echoed this (Table A21), with enrichments for nervous system development (adjusted p-value = 1.2E-19) and synaptic signalling (adjusted p-value = 2.5E-15) and ion transmembrane transport (adjusted p-value = 1.5E-16) alongside chemical synaptic transmission, which related to several significant enrichments in Reactome (Figure 6-2B; Table A23).

In contrast, TargetALS was enriched for immune-system related diseases and processes, which includes several diseases connected with response to various viral

infections (Table A20) including COVID-19 and pneumonia (adjusted p-value = 1.5E-22), GO processes related to immune response (Table A22), including innate immune response (adjusted p-value = 5.1E-09), negative regulation of cytokine production (adjusted p-value = 6.5E-08) and phagocytosis (adjusted p-value = 1.5E-07), and Reactome pathways pertaining to interferon signalling (Figure 6-2B).

### 6.4.3.3 Pathway Maps

Prominent themes in the KCL BrainBank enrichments were oxidative stress and signal transduction (Figure 6-2C; Table A25). The most significant pathways concerned *NRF2* regulation of oxidative stress (adjusted p-value = 0.0023) and excitability of cortical pyramidal neurons (adjusted p-value = 0.0025). Related neuronal excitability enrichments included activity-dependent AMPA receptor removal (adjusted p-value = 0.0074), GABA-A receptor life cycle (adjusted p-value = 0.0075), synaptic vesicle fusion and recycling at nerve terminals (adjusted p-value = 0.0075), the regulation of dopamine D1A receptor signalling by glutamic acid (adjusted p-value = 0.014) and NMDA receptor trafficking (adjusted p-value = 0.020). Other oxidative stress-specific enrichments included apoptosis signal-regulating kinase 1 (*ASK1*) function (adjusted p-value = 0.0043), BAD phosphorylation (adjusted p-value = 0.010) and activation of *NOX1*, *NOX5*, *DUOX1* and *DUOX2* (adjusted p-value = 0.010). In contrast, there were three significant TargetALS pathway maps; two related to pro-opiomelanocortin (POMC) processing and one to immune response (Figure 6-2C; Table A26). Interestingly, the most significant network in TargetALS (POMC processing in protein folding and maturation) includes several agonists of *MC4R* (Figure 6-3), a neuropeptide receptor which was found to be significantly upregulated in both datasets (see Chapter 6.4.2.3 and Table 6-2) and is present in the neuropeptide signalling process network which was significantly enriched in both datasets (see Chapter 6.4.3.1).

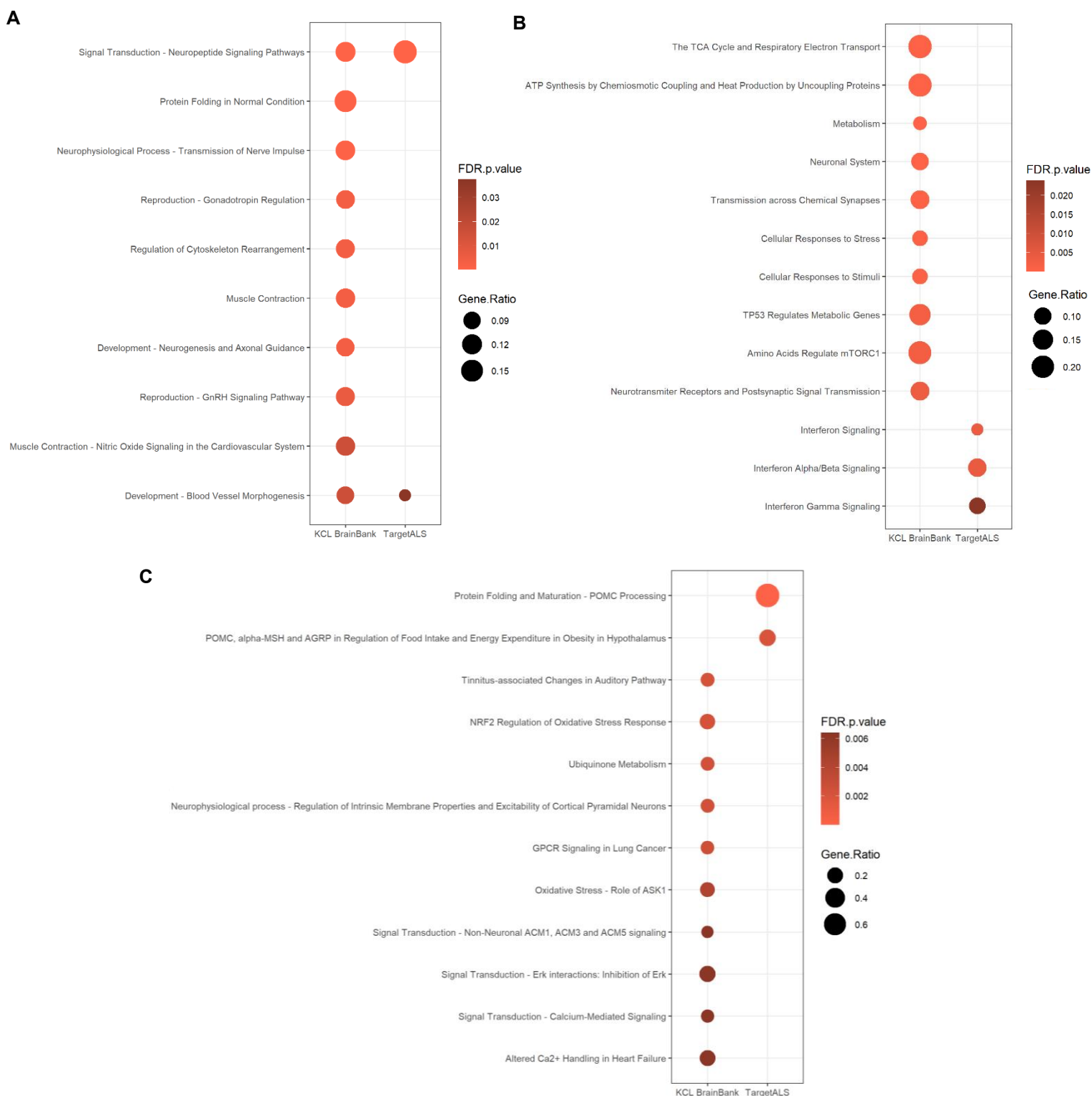


Figure 6-2. Gene and pathway enrichment results in KCL BrainBank and TargetALS for A) MetaCore Process Networks, B) Reactome and C) MetaCore Pathway Maps. The ten most significant enrichments, sorted by adjusted p-value (FDR.p.value) are shown, or fewer if less than ten were significant after multiple testing correction. Gene.Ratio refers to the number of differentially expressed genes identified in each dataset for that term, divided by the total number of genes which are included in the term definition.

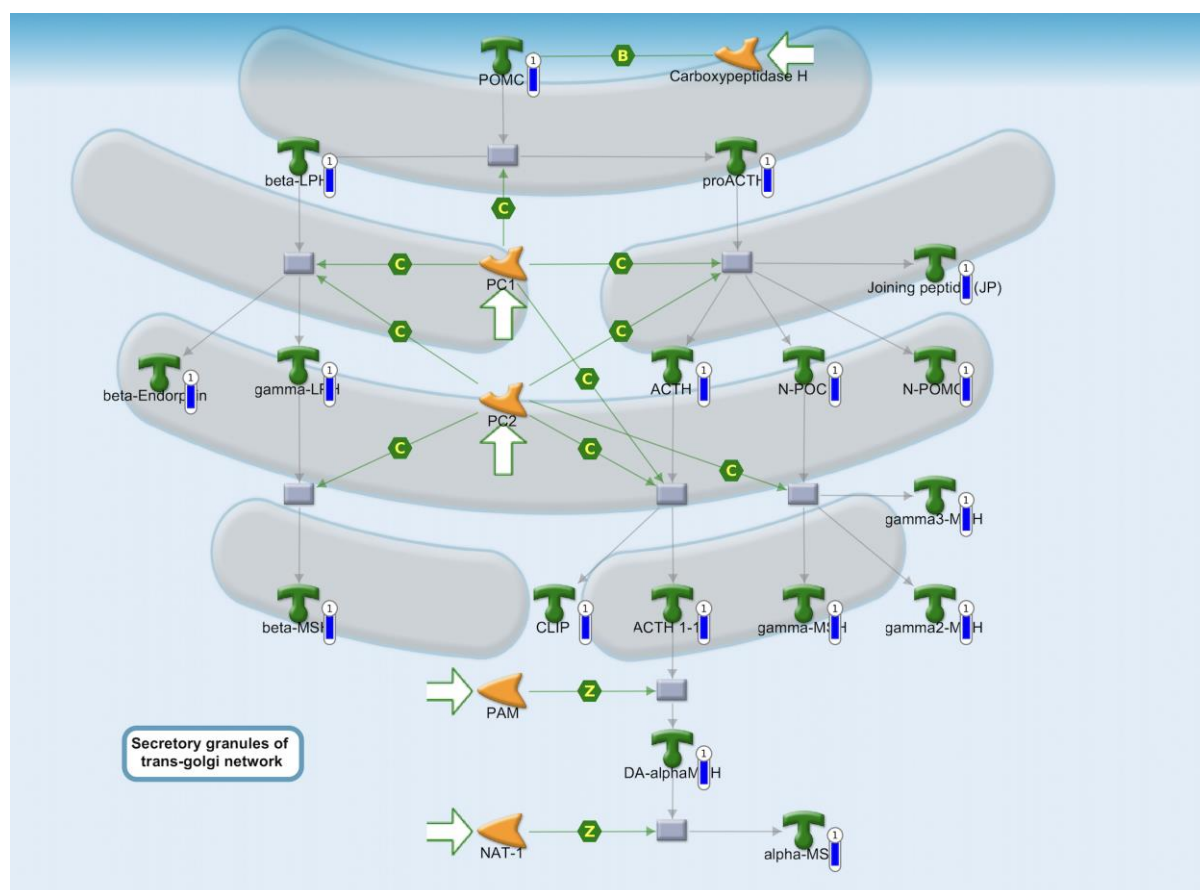


Figure 6-3. Protein folding and maturation POMC processing pathway map from MetaCore, where blue barometers represent downregulated genes from the TargetALS dataset. The descriptions of what the other symbols represent are available in Figure A11.

#### 6.4.4 Correlation analysis of neuropeptides and neuropeptide receptors with ALS clinical phenotype

As neuropeptide signalling was the only altered biological network in both datasets, and neuropeptides have been implicated with the ALS clinical phenotype (Ahmed et al., 2019; Clark et al., 2021; Zuccaro et al., 2021), we decided to test the correlation between the expression of neuropeptides and their receptors with age at onset and disease duration of the ALS patients in the KCL BrainBank ( $n = 112$ ), and the medial ( $n = 93$ ) and lateral ( $n = 96$ ) TargetALS motor cortex datasets. There were 102, 105 and 106 neuropeptide ligand and receptor genes in KCL BrainBank, TargetALS medial and TargetALS lateral datasets, respectively. We found that 18 neuropeptide-related genes were nominally correlated with disease duration in at least one dataset, although none of them maintained significance after multiple testing correction (Table 6-3). The only gene which was nominally significant in KCL BrainBank and at least one of the TargetALS datasets was *TACR1*, whose expression weakly positively

correlated with disease duration (KCL BrainBank:  $r = 0.211$ ,  $p\text{-value}=0.0370$ ; TargetALS lateral:  $r = 0.233$ ,  $p\text{-value}=0.0245$ ). Visualisation of *TACR1* expression against disease duration is available in Figures 6-4A (KCL BrainBank) and 6-4B (TargetALS lateral motor cortex). On the contrary, 32 genes nominally correlated with age of onset in at least one dataset, with *PTHLH* and *IGF1* surviving multiple correction in KCL BrainBank (*PTHLH*:  $r = -0.385$ , adjusted  $p\text{-value}=0.0111$ ; *IGF1*:  $r = -0.380$ , adjusted  $p\text{-value}=0.0136$ ), and *TRH* surviving multiple correction in TargetALS lateral motor cortex ( $r = -0.467$ , adjusted  $p\text{-value}=0.000371$ ). As with disease duration, the expression of only one gene, *NPBWR1*, was found to be nominally negatively correlated with age of onset in KCL BrainBank ( $r = -0.346$ ,  $p\text{-value}=0.000565$ ) and the TargetALS lateral motor cortex ( $r = -0.336$ ,  $p\text{-value}=0.000991$ ). Visualisation of *NPBWR1* expression against age of onset is available in Figure 6-4C (KCL BrainBank) and 6-4D (TargetALS lateral motor cortex). Complete correlation results can be found in Table A27.

#### 6.4.5 Cell Type Composition Analysis

The cell type composition analysis is shown in Figure 6-5. Compared to controls, KCL BrainBank cases (shown in Figure 6-5A) contained a significantly smaller proportion of astrocytes (median  $\pm$  IQR:  $0.191 \pm 0.0748$  vs  $0.279 \pm 0.106$ ,  $F = 18.192$ ,  $p\text{-value} = 3.34\text{E-}05$ ), whilst neuronal content was significantly higher (median  $\pm$  IQR:  $0.662 \pm 0.118$  vs  $0.578 \pm 0.179$ ,  $F = 15.295$ ,  $p\text{-value} = 1.34\text{E-}04$ ). There were no differences in the proportion of cell types between cases and controls in both the medial and lateral TargetALS datasets (Figure 6-5B and 5C). The full breakdown is available in Table A28.

#### 6.4.6 ALS Gene Expression Explorer

The ALS Gene Expression Explorer web application (<https://alsgeexplorer.er.kcl.ac.uk>) enables users to explore and compare the expression levels for specific genes in ALS cases and controls in the two datasets.

| Clinical Phenotype        | Ensembl ID      | Gene Symbol   | KCL BrainBank   |                 |               | TargetALS (medial) |                 |               | TargetALS (lateral) |                 |               |
|---------------------------|-----------------|---------------|-----------------|-----------------|---------------|--------------------|-----------------|---------------|---------------------|-----------------|---------------|
|                           |                 |               | Pearson's r     | p-value         | p-value (adj) | Pearson's r        | p-value         | p-value (adj) | Pearson's r         | p-value         | p-value (adj) |
| Disease Duration (months) | ENSG00000126895 | <i>AVPR2</i>  | -0.323          | <b>1.17E-03</b> | 0.119         | 0.0397             | 0.710           | 1.0           | -0.0608             | 0.563           | 1.0           |
|                           | ENSG00000144891 | <i>AGTR1</i>  | -0.237          | <b>0.0187</b>   | 1.0           | -0.0541            | 0.613           | 1.0           | -0.130              | 0.214           | 1.0           |
|                           | ENSG00000115353 | <i>TACR1</i>  | 0.211           | <b>0.0370</b>   | 1.0           | 0.114              | 0.285           | 1.0           | 0.233               | <b>0.0245</b>   | 1.0           |
|                           | ENSG00000157005 | <i>SST</i>    | 0.206           | <b>0.0418</b>   | 1.0           | 0.139              | 0.193           | 1.0           | 0.129               | 0.217           | 1.0           |
|                           | ENSG00000101188 | <i>NTSR1</i>  | 0.0691          | 0.499           | 1.0           | 0.286              | <b>6.37E-03</b> | 0.669         | 0.0337              | 0.749           | 1.0           |
|                           | ENSG00000171596 | <i>NMUR1</i>  | -0.079          | 0.440           | 1.0           | 0.266              | <b>0.0112</b>   | 1.0           | 0.221               | <b>0.0329</b>   | 1.0           |
|                           | ENSG00000147437 | <i>GNRH1</i>  | -0.189          | 0.0622          | 1.0           | -0.257             | <b>0.0147</b>   | 1.0           | -0.214              | <b>0.0400</b>   | 1.0           |
|                           | ENSG00000110680 | <i>CALCA</i>  | -0.0377         | 0.713           | 1.0           | 0.251              | <b>0.0169</b>   | 1.0           | -0.0568             | 0.589           | 1.0           |
|                           | ENSG00000135744 | <i>AGT</i>    | 0.0847          | 0.407           | 1.0           | 0.220              | <b>0.0374</b>   | 1.0           | 0.0880              | 0.401           | 1.0           |
|                           | ENSG00000166148 | <i>AVPR1A</i> | -0.0991         | 0.332           | 1.0           | 0.218              | <b>0.0393</b>   | 1.0           | 0.0951              | 0.365           | 1.0           |
|                           | ENSG00000162009 | <i>SSTR5</i>  | NA              | NA              | NA            | 0.216              | <b>0.0408</b>   | 1.0           | 0.143               | 0.171           | 1.0           |
|                           | ENSG00000121764 | <i>HCRTR1</i> | -0.0368         | 0.719           | 1.0           | 0.0450             | 0.674           | 1.0           | 0.241               | <b>0.0200</b>   | 1.0           |
|                           | ENSG00000288611 | <i>NPBWR1</i> | 0.0556          | 0.587           | 1.0           | 0.0200             | 0.852           | 1.0           | 0.239               | <b>0.0208</b>   | 1.0           |
|                           | ENSG00000170498 | <i>KISS1</i>  | NA              | NA              | NA            | NA                 | NA              | NA            | 0.220               | <b>0.0342</b>   | 1.0           |
|                           | ENSG00000163394 | <i>CCKAR</i>  | 0.0179          | 0.861           | 1.0           | 0.0286             | 0.789           | 1.0           | -0.216              | <b>0.0380</b>   | 1.0           |
|                           | ENSG00000166863 | <i>TAC3</i>   | 0.120           | 0.241           | 1.0           | 0.0782             | 0.464           | 1.0           | 0.212               | <b>0.0409</b>   | 1.0           |
|                           | ENSG00000119973 | <i>PRLHR</i>  | 0.140           | 0.169           | 1.0           | 0.0857             | 0.422           | 1.0           | 0.208               | <b>0.0450</b>   | 1.0           |
| ENSG00000017427           | <i>IGF1</i>     | 0.0900        | 0.378           | 1.0             | 0.0388        | 0.717              | 1.0             | 0.208         | <b>0.0456</b>       | 1.0             |               |
| Age of Onset              | ENSG00000087494 | <i>PTHLH</i>  | -0.385          | <b>1.09E-04</b> | <b>0.0111</b> | 0.0196             | 0.855           | 1.0           | -0.0614             | 0.559           | 1.0           |
|                           | ENSG00000017427 | <i>IGF1</i>   | -0.380          | <b>1.33E-04</b> | <b>0.0136</b> | -0.0720            | 0.500           | 1.0           | -0.204              | <b>0.0495</b>   | 1.0           |
|                           | ENSG00000288611 | <i>NPBWR1</i> | -0.346          | <b>5.65E-04</b> | 0.0576        | -0.112             | 0.293           | 1.0           | -0.336              | <b>9.91E-04</b> | 0.105         |
|                           | ENSG00000168081 | <i>PNOC</i>   | -0.344          | <b>6.07E-04</b> | 0.0619        | -0.143             | 0.179           | 1.0           | -0.111              | 0.289           | 1.0           |
|                           | ENSG00000146469 | <i>VIP</i>    | -0.317          | <b>1.64E-03</b> | 0.167         | -0.0154            | 0.886           | 1.0           | -0.174              | 0.0959          | 1.0           |
|                           | ENSG00000139874 | <i>SSTR1</i>  | -0.305          | <b>2.56E-03</b> | 0.261         | -0.146             | 0.170           | 1.0           | -0.146              | 0.164           | 1.0           |
|                           | ENSG00000175206 | <i>NPPA</i>   | -0.304          | <b>2.56E-03</b> | 0.262         | 0.0873             | 0.413           | 1.0           | 0.0266              | 0.800           | 1.0           |
|                           | ENSG00000171388 | <i>APLN</i>   | 0.291           | <b>3.99E-03</b> | 0.407         | -0.0612            | 0.567           | 1.0           | -0.0290             | 0.783           | 1.0           |
|                           | ENSG00000157005 | <i>SST</i>    | -0.287          | <b>4.51E-03</b> | 0.460         | -0.0494            | 0.644           | 1.0           | -0.0444             | 0.672           | 1.0           |
|                           | ENSG00000148926 | <i>ADM</i>    | 0.284           | <b>5.02E-03</b> | 0.512         | -0.149             | 0.160           | 1.0           | -0.106              | 0.314           | 1.0           |
|                           | ENSG00000134443 | <i>GRP</i>    | -0.282          | <b>5.45E-03</b> | 0.555         | 0.113              | 0.291           | 1.0           | 0.0530              | 0.614           | 1.0           |
|                           | ENSG00000166863 | <i>TAC3</i>   | -0.282          | <b>5.45E-03</b> | 0.556         | -0.021             | 0.847           | 1.0           | -0.175              | 0.0941          | 1.0           |
|                           | ENSG00000152034 | <i>MCHR2</i>  | -0.279          | <b>5.84E-03</b> | 0.595         | 0.0456             | 0.669           | 1.0           | -0.144              | 0.167           | 1.0           |
| ENSG00000166573           | <i>GALR1</i>    | -0.266        | <b>8.79E-03</b> | 0.897           | -0.130        | 0.221              | 1.0             | -0.108        | 0.301               | 1.0             |               |

|  |                 |               |         |               |     |         |                 |                 |          |               |     |
|--|-----------------|---------------|---------|---------------|-----|---------|-----------------|-----------------|----------|---------------|-----|
|  | ENSG0000049247  | <i>UTS2</i>   | 0.253   | <b>0.0129</b> | 1.0 | 0.0690  | 0.518           | 1.0             | 0.0833   | 0.427         | 1.0 |
|  | ENSG00000147571 | <i>CRH</i>    | -0.250  | <b>0.0140</b> | 1.0 | -0.129  | 0.226           | 1.0             | -0.999   | 0.341         | 1.0 |
|  | ENSG00000180616 | <i>SSTR2</i>  | -0.246  | <b>0.0157</b> | 1.0 | -0.0379 | 0.723           | 1.0             | -0.0605  | 0.565         | 1.0 |
|  | ENSG00000119973 | <i>PRLHR</i>  | -0.246  | <b>0.0157</b> | 1.0 | 0.0165  | 0.877           | 1.0             | -0.0385  | 0.714         | 1.0 |
|  | ENSG00000132911 | <i>NMUR2</i>  | 0.228   | <b>0.0257</b> | 1.0 | -0.0404 | 0.706           | 1.0             | -0.0762  | 0.468         | 1.0 |
|  | ENSG00000147437 | <i>GNRH1</i>  | 0.225   | <b>0.0275</b> | 1.0 | 0.109   | 0.306           | 1.0             | 0.0614   | 0.559         | 1.0 |
|  | ENSG00000181408 | <i>UTS2R</i>  | 0.223   | <b>0.0291</b> | 1.0 | 0.0880  | 0.409           | 1.0             | -0.00624 | 0.953         | 1.0 |
|  | ENSG00000132671 | <i>SSTR4</i>  | -0.211  | <b>0.0394</b> | 1.0 | -0.0826 | 0.439           | 1.0             | -0.0776  | 0.460         | 1.0 |
|  | ENSG00000139574 | <i>NPFF</i>   | 0.207   | <b>0.0426</b> | 1.0 | 0.0377  | 0.724           | 1.0             | -0.0171  | 0.871         | 1.0 |
|  | ENSG00000181195 | <i>PENK</i>   | -0.204  | <b>0.0461</b> | 1.0 | -0.0747 | 0.484           | 1.0             | -0.152   | 0.145         | 1.0 |
|  | ENSG00000163794 | <i>UCN</i>    | 0.204   | <b>0.0462</b> | 1.0 | 0.0709  | 0.506           | 1.0             | 0.0290   | 0.782         | 1.0 |
|  | ENSG00000078401 | <i>EDN1</i>   | 0.204   | <b>0.0462</b> | 1.0 | -0.133  | 0.212           | 1.0             | 0.00845  | 0.936         | 1.0 |
|  | ENSG00000109255 | <i>NMU</i>    | -0.202  | <b>0.0483</b> | 1.0 | -0.0547 | 0.609           | 1.0             | -0.0979  | 0.350         | 1.0 |
|  | ENSG00000170893 | <i>TRH</i>    | -0.0334 | 0.747         | 1.0 | -0.467  | <b>3.53E-06</b> | <b>3.71E-04</b> | -0.200   | 0.0546        | 1.0 |
|  | ENSG00000166148 | <i>AVPR1A</i> | -0.115  | 0.266         | 1.0 | -0.319  | <b>2.18E-03</b> | 0.229           | -0.181   | 0.0818        | 1.0 |
|  | ENSG00000145040 | <i>UCN2</i>   | -0.151  | 0.141         | 1.0 | 0.302   | <b>3.77E-03</b> | 0.396           | 0.141    | 0.178         | 1.0 |
|  | ENSG00000112038 | <i>OPRM1</i>  | 0.0760  | 0.461         | 1.0 | 0.221   | <b>0.0367</b>   | 1.0             | 0.0478   | 0.649         | 1.0 |
|  | ENSG00000121764 | <i>HCRTR1</i> | -0.136  | 0.186         | 1.0 | -0.0805 | 0.451           | 1.0             | -0.233   | <b>0.0247</b> | 1.0 |

Table 6-3. Neuropeptide receptors and ligands whose gene expression is significantly correlated with either disease duration or age of onset in people with ALS from either KCL BrainBank or medial and lateral samples from TargetALS. Adjusted *p*-values reflect the number of neuropeptide-related genes tested in each dataset (102 in KCL BrainBank, 105 in TargetALS medial and 106 in TargetALS lateral motor cortex). A *p*-value of < 0.05 denotes significance.

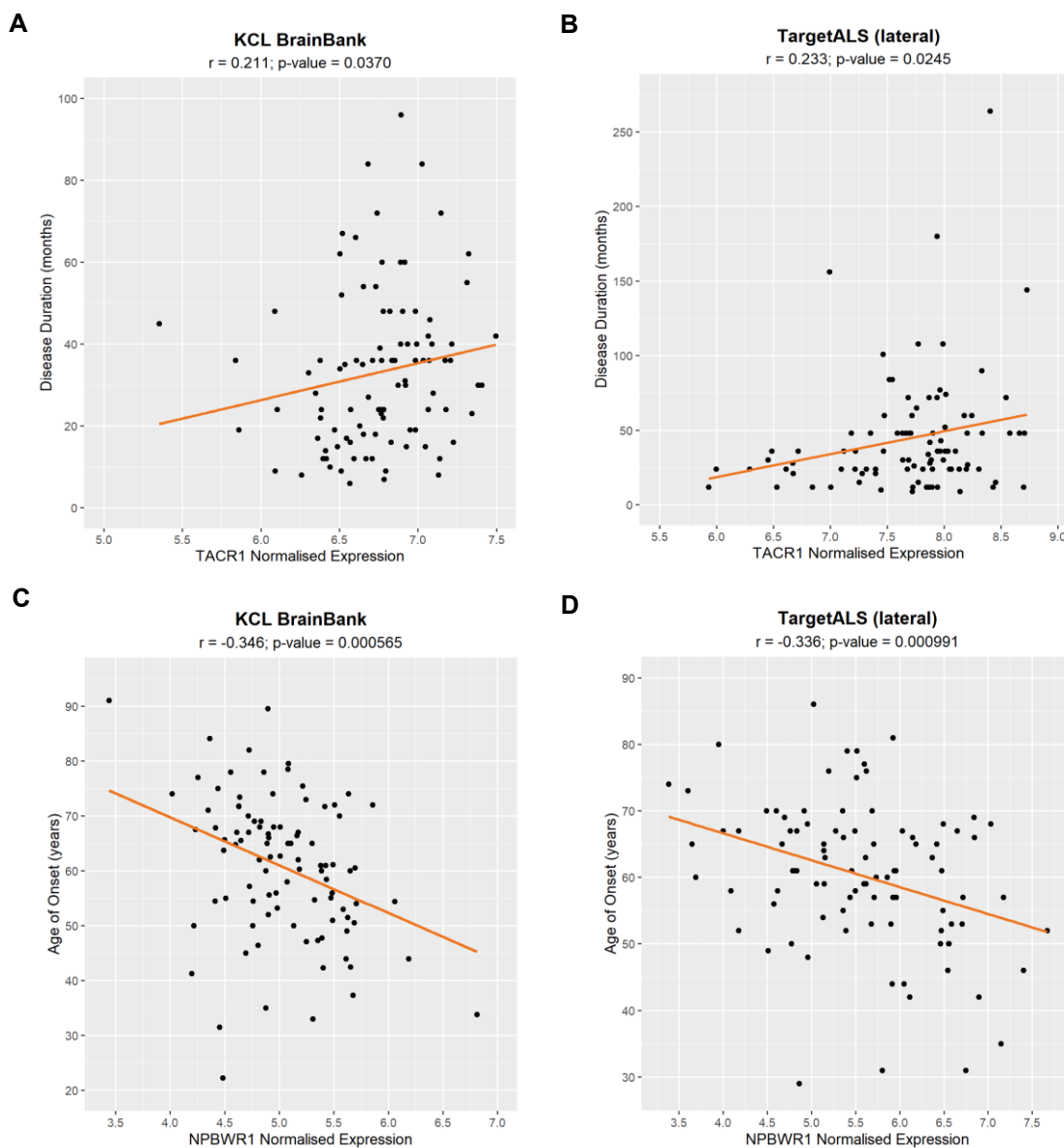


Figure 6-4. Scatterplots visualising the relationship between TACR1 and NPBWR1 normalised gene expression and clinical phenotype of ALS in both KCL BrainBank and TargetALS samples from the lateral motor cortex. A) and B) represent the absolute values for TACR1 normalised gene expression and disease duration in months. C) and D) represent the absolute values for NPBWR1 normalised gene expression and age of onset in years. Correlations with the clinical phenotype are represented visually with the orange line and numerically with the Pearson's correlation coefficient ( $r$ ) and  $p$ -value.



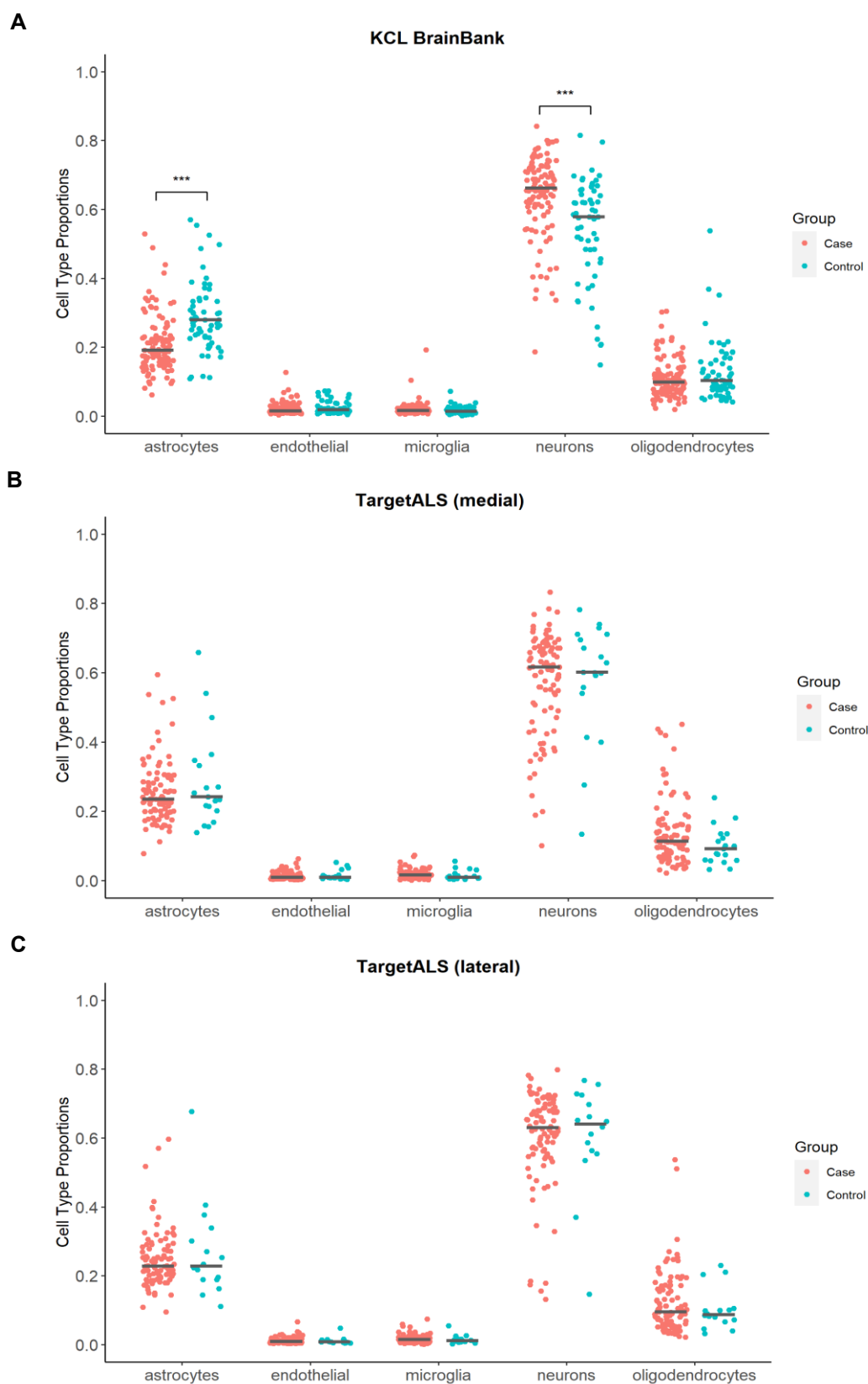


Figure 6-5. Case-control cell deconvolution analysis in KCL BrainBank (top panel) and TargetALS (medial: middle panel, lateral: bottom panel), using MuSiC2. Significance was assessed using one-way ANCOVA corrected for age of death and sex. Case-control comparisons with asterisks denote significance in cell type proportions. \*\*\* corresponds to a  $p$ -value of  $< 0.001$ .

## 6.5 Discussion

By leveraging motor cortex expression data from two independent large datasets (KCL BrainBank and TargetALS; 224 ALS cases and 79 controls) to obtain and compare ALS gene expression profiles, we identify alterations in the neuropeptide signalling pathway that indicate that this may be a key feature of ALS pathogenesis, whilst also reporting shared differentially expressed genes that represent previously recognised biological processes dysregulated in ALS.

There were several lines of evidence in this study to support the role of neuropeptide signalling in ALS pathogenesis. We found that differentially expressed genes involved in the neuropeptide signalling pathway were significantly overrepresented in both datasets via gene pathway enrichment, and whilst both datasets exhibited unique and shared differential expression of several neuropeptide ligands and receptors, the melanocortin receptor 4 gene (*MC4R*) was significantly upregulated across datasets. The role of the melanocortin system in ALS has largely been overlooked, despite *MC4R* activation inducing hypermetabolism, increased energy expenditure and cachexia; three processes associated with increased lower motor neuron weakness and poor prognosis in ALS patients (Holm et al., 2013; Jésus et al., 2018; Kasarskis et al., 2014; Kurihara et al., 2021; Steyn et al., 2018). Furthermore, *MC4R*-mediated signalling in the motor cortex also enhances the activity of sympathetic preganglionic neurons in the spinal cord, which modulates skeletal muscle contraction (Sohn et al., 2013; Ye et al., 2014), and rare (MAF < 1%) disruptive and damaging missense variants in *MC4R* might increase the risk of ALS (Beta = 2.15 SE = 1.52, p-value = 0.037, <http://databrowser.projectmine.com>). Therefore, we suggest further investigation on *MC4R* as a potential candidate target gene for future biomarker and screening studies.

To further investigate how neuropeptide signalling affects the ALS clinical phenotype, we also performed correlation analyses of neuropeptide-related genes (102 in KCL BrainBank, 105 in TargetALS medial and 106 in TargetALS lateral motor cortex) with age of onset and disease duration. We found that the expression levels of two genes in both KCL BrainBank and TargetALS datasets were found to nominally associate with the ALS phenotype; *TACR1* with disease duration, and *NPBWR1* with age of onset. Interestingly, both genes activate other biological processes that have been linked to ALS. For instance, one function of *TACR1* is to stimulate the production and

release of arachidonic acid (Naor & Catt, 1981; Steinhoff et al., 2014), a polyunsaturated fatty acid whose levels can distinguish ALS patients from mimics and controls and positively correlates with disease progression (Lawton et al., 2014), with higher levels also found in spinal cord motor neuron cultures (H. Lee et al., 2021). Furthermore, *NPBWR1* is expressed by GABAergic interneurons and when activated, can dampen their inhibitory effects (Chottova Dvorakova, 2018) and potentially modulate their excitability patterns in the motor cortex, which has been proposed as a possible trigger for the spread of ALS pathology (Eisen et al., 2017; Scekcic-Zahirovic et al., 2021). Therefore, the role of the neuropeptide signalling system on both lipid metabolism and cortical signalling in ALS and also its full impact on clinical phenotype is warranted, especially as our correlation results do not fully support and are only suggestive of a potential link between expression and modulation of phenotype.

We also linked many of the 45 differentially expressed genes common to both datasets with integral themes of ALS pathogenesis. These include carbohydrate/lipid metabolism, mitochondrial energy homeostasis (*SULT1A1*, *IP6K3*, *CPT1A*) (Dato et al., 2021; Sidharthan et al., 2013; Trabjerg et al., 2021), and neurovascular unit dysfunction (*AQP1*, *APLNR*, *CA12*, *AGPT1*, *CST3*) (Benndorf, 2018; Bonomini & Rezzani, 2010; Hosford et al., 2022; Hu et al., 2021; Siddiqui et al., 2015). Further investigations of these genes are needed to determine if they are the drivers of alterations in these pathways in ALS.

Despite the agreement in gene expression profiles, there was discrepancy between the number of differentially expressed genes; 2,290 and 402 in KCL BrainBank and TargetALS respectively. Moreover, synapse-related processes, such as GABAergic neurotransmission, calcium-mediated signalling and postsynaptic signalling were significantly enriched in KCL BrainBank, whilst TargetALS carried an immune-system related signature, with strong enrichments for interferon signalling and a related enrichment for natural killer cell neurotoxicity. While these enrichment profiles do reflect previously hypothesised mechanisms of ALS pathogenesis and so could be a product of the molecular heterogeneity which exists within each dataset, the inconsistency in pathway enrichment is most likely due to the fact that there were 5.7 times more differentially expressed genes found in the KCL BrainBank cohort. Although this might be linked to the larger number of controls in the KCL datasets (~3 times more than in TargetALS), there could also be several external factors influencing

these datasets, such as the methods of library preparation and RNA extraction, and populational variability in gene expression. Another important aspect which may have affected the lack of reproducibility of results were the demographic differences that existed between cases and controls across datasets. For example, there was a strong gender effect in the TargetALS cohort (Figure 3-1B) which we cannot be certain was removed with the generation of surrogate variables. Furthermore, whilst the ages of the cases in both datasets were similar, and the ages of TargetALS control samples were not statistically different to cases, the KCL BrainBank controls were 11.4 years older than cases, and 13.6 years older than the TargetALS controls. This could explain why there was a significantly lower proportion of neurons in KCL BrainBank controls, as you would expect to see this phenomenon as a consequence of aging. Gene expression levels can also be affected by RIN number, which is a measure of RNA sample quality, and post-mortem delay, which is the time from death to sample collection; both measures were significantly different between cases and controls, with lower RIN numbers and a longer post-mortem delay in controls. The average RIN numbers for cases and controls across both datasets were sub-optimal and indicative of moderate RNA degradation, which would affect the measurement of gene expression levels, although controlling for these effects in the differential expression framework can correct almost completely for this. As for the influence of post-mortem delay, longer intervals between death and sample collection could reduce the magnitude of gene expression changes, which could have also contributed to discrepancies in the number of statistically differentially expressed genes between datasets. Our study also has some limitations which are primarily linked to the fact that we identified gene expression signatures in post-mortem tissue. Firstly, as the cells we derive expression for have survived the neurodegenerative processes of ALS, we cannot infer if the changes we are observing are causing or are a consequence of the ALS phenotype. We do not have information on the staging of ALS in these patients so cannot attribute the expression profiles to a certain point of ALS progression.

In summary, we identified shared differentially expressed genes which represent several previously reported biological themes of ALS pathogenesis as well as identifying genes in the neuropeptide signalling pathway that warrant further investigation as potential biomarkers of onset and progression.

## Chapter 7. Utilising hierarchical clustering to identify molecular subtypes of ALS

### 7.1 Publication

The majority of the work described in this chapter was published in *Acta Neuropathologica Communications* (Marriott, Kabiljo, Hunt, et al., 2023):

#### **Unsupervised machine learning identifies distinct ALS molecular subtypes in post-mortem motor cortex and blood expression data**

Heather Marriott<sup>1,2</sup>, Renata Kabiljo<sup>2</sup>, Guy P Hunt<sup>1,2,3,4</sup>, Ahmad Al Khleifat<sup>1</sup>, Ashley Jones<sup>1</sup>, Claire Troakes<sup>1,5</sup>, Project MinE ALS Sequencing Consortium, TargetALS Sequencing Consortium, Abigail L Pfaff<sup>3,4</sup>, John P Quinn<sup>6</sup>, Sulev Koks<sup>3,4</sup>, Richard J Dobson<sup>2,7,8,9</sup>, Patrick Schwab<sup>10</sup>, Ammar Al-Chalabi<sup>1, 11</sup> and Alfredo Iacoangeli<sup>1,2,7\*</sup>

<sup>1</sup>Department of Basic and Clinical Neuroscience, Maurice Wohl Clinical Neuroscience Institute, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 9NU, UK; <sup>2</sup>Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; <sup>3</sup>Perron Institute for Neurological and Translational Science, Nedlands, WA, 6009, Australia; <sup>4</sup>Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Murdoch, WA, 6150, Australia; <sup>5</sup>MRC London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; <sup>6</sup>Department of Pharmacology and Therapeutics, Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, L69 3BX, UK; <sup>7</sup>NIHR Maudsley Biomedical Research Centre (BRC), South London and Maudsley NHS Foundation Trust and King's College London, London, UK; <sup>8</sup>Institute of Health Informatics, University College London, London, UK; <sup>9</sup>NIHR Biomedical Research Centre, University College London Hospitals NHS Foundation Trust, London, UK; <sup>10</sup>GlaxoSmithKline, Artificial Intelligence and Machine Learning, Durham, NC, USA; <sup>11</sup>King's College Hospital, London, SE5 9RS, UK

\*Correspondence should be addressed to [alfredo.iacoangeli@kcl.ac.uk](mailto:alfredo.iacoangeli@kcl.ac.uk)

## 7.2 Abstract

### *Background*

Amyotrophic lateral sclerosis (ALS) displays considerable clinical and genetic heterogeneity. Machine learning approaches have previously been utilised for patient stratification in ALS as they can disentangle complex disease landscapes. However, lack of independent validation in different populations and tissue samples have greatly limited their use in clinical and research settings.

### *Methods*

Hierarchical clustering was performed on the 5000 most variably expressed autosomal genes from motor cortex expression data of people with sporadic ALS from the KCL BrainBank (N=112). The molecular architectures of each cluster were established from gene enrichment, network and cell composition analysis. Cluster validation was achieved by applying linear discriminant analysis models trained on KCL BrainBank to cases from TargetALS US motor cortex (N=168), as well as Italian (N=15) and Dutch (N=397) blood expression datasets. The ALS and regional specificity of the expression signatures were tested by mapping KCL BrainBank (N=59), TargetALS (N=34) and Dutch (N=645) controls, and occipital cortex (N=45) and cerebellum (N=123) samples from TargetALS to each cluster, before constructing case-control and motor cortex-other region logistic regression classifiers. Cluster stability was assessed in all datasets using bootstrapping to derive uncertainty metrics for class assignment, and dominance analysis was performed in the case datasets to identify genes which drove assignment to one cluster over the others. Cell type composition analysis was performed in KCL BrainBank and TargetALS datasets to aid in the biological interpretation of the clusters. Phenotype analysis was also performed to assess cluster-specific differences in clinical- and omics-based outcomes.

### *Results*

Three clusters were identified: synaptic and neuropeptide signalling, oxidative stress and apoptosis, and neuroinflammation. These molecular phenotypes were validated across both motor cortex and blood independent datasets as samples were assigned to each with a high average assignment probability (80-90%), with these sample assignments being relatively stable. There was also considerable overlap in the top

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15 key drivers of cluster assignment in case datasets, further demonstrating the robustness of each molecular phenotype. We found that the expression signatures of each molecular phenotype not only demonstrated were not only able to distinguish people with ALS from controls with good-to-excellent discriminative ability (ROC AUC 0.7-1.0), but also reflect the motor cortex-based disease process, as there was near perfect discrimination between motor cortex and the other brain regions. Analysis of the top 30 case-control status predictors by cluster revealed 19 genes that were shared in at least two datasets, with the schizophrenia-linked gene *CTXN3* present in all. Cell types known to be involved in the biological processes of each molecular phenotype were found in higher proportions, reinforcing their biological interpretation. Phenotype analysis revealed distinct cluster-related outcomes in both motor cortex datasets, relating to disease onset and progression related measures.

### *Conclusion*

Our results support the hypothesis that different mechanisms underpin ALS pathogenesis in subgroups of patients and demonstrates potential for patient stratification and the development of personalised treatment approaches. Further work needs to be carried out to determine with certainty whether expression of specific genes within each molecular phenotype can accurately distinguish between people with ALS and controls. Our method is available for the scientific and clinical community at <https://alsgeclustering.er.kcl.ac.uk>.

### 7.3 Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease which displays considerable genetic heterogeneity. In approximately 90% of people with ALS, the disease is labelled as sporadic, without an apparent family history of the disease, with the remainder classed as familial (R. H. Brown & Al-Chalabi, 2017). Mutations in approximately 40 genes are known to be linked with ALS and can explain the majority of familial cases and approximately 20% of sporadic cases (SALS) (Mehta et al., 2022). However, a further 130 genes have been proposed to contribute to its risk or act as disease modifiers (Abel et al., 2012; Mejzini et al., 2019). ALS is also phenotypically variable, with differences in age and site of onset (spinal-innervated muscles vs bulbar), the balance of upper and lower motor neuron involvement, rate of disease progression, and the presence of cognitive or non-motor symptoms (Couratier et al., 2021). Furthermore, a multitude of molecular processes have been implicated in its pathogenesis, in part due to the vast number of causative and modifier genes associated with ALS that code for diverse cellular functions (Morgan & Orrell, 2016). It is therefore plausible that there is no universal approach to the treatment of people with ALS, especially given that many therapeutic strategies target specific molecular pathways. For example, the protective action of Riluzole on motor neurons is proposed to be the result of a reduction in glutamate-mediated excitotoxicity (Doble, 1996).

Machine learning approaches can be used to help us to understand the genetic and molecular complexity and heterogeneity of ALS, for example, by finding patterns in biological and clinical data that distinguish some groups of patients from the others. These subgroups can aid in identifying the best candidates for therapeutics which target specific biological processes. Machine learning methods have previously been applied to brain expression data to stratify people with SALS into molecular subgroups (Aronica et al., 2015; La Cognata et al., 2020; Morello et al., 2017; Tam et al., 2019), and has led to valuable insights into the genomic heterogeneity of ALS. However, some of these studies integrated samples from different brain regions to generate clusters and characterise their molecular architectures (Eshima et al., 2023; La Cognata et al., 2020; Tam et al., 2019). This design might present limitations in reflecting motor neuron-related ALS pathogenesis. Other studies adopted a case-control framework (Aronica et al., 2015; La Cognata et al., 2020; Morello et al., 2017), which could lead to reduced power given the potential decoupling between



mechanisms underlying risk and phenotype variability (Kalia et al., 2022; Opie-Martin et al., 2022; van Rheenen et al., 2021). Furthermore, previous work has not been validated in independent datasets or in different populations and did not investigate whether molecular subtypes identified in post-mortem brains are reflected in other tissues available pre-mortem. Such factors have greatly limited the applicability and impact of these results. We therefore aimed to identify and validate molecular and phenotypic patterns across multiple independent datasets, tissue types and populations, to generate gene expression derived molecular subtypes of ALS that can be utilised for stratification in the design and interpretation of future research and clinical studies.

## **7.4 Methods**

### **7.4.1 Study Cohorts**

We obtained raw post-mortem motor cortex bulk RNA sequencing data in FASTQ format from two datasets. The first, which was used to generate the clusters, consisted of 112 people from the UK with SALS from King's College London and the MRC London Neurodegenerative Diseases Brain Bank (KCL BrainBank), which has been previously described in (Iacoangeli et al., 2021). We additionally obtained matching whole-genome sequencing (WGS), methylation data and clinical data for the KCL BrainBank samples from Project MinE (Project MinE ALS Sequencing Consortium, 2018) to perform subgroup clinical and omics-based phenotype analysis. Additional information for WGS is available in Chapters 3.1.1 and 3.1.1.3, with the methylation protocol available in Chapter 3.5.2. For validation of KCL BrainBank-derived cluster expression signatures, 168 US samples from 93 people with SALS of North European ancestry, present in the Target ALS Human Post-mortem Tissue Core (TargetALS) were used. For further validation of KCL BrainBank-derived clusters, we also processed two peripheral blood mononuclear cell (PBMC) datasets; bulk RNA sequencing data in FASTQ format of 15 Italian people with SALS (Zucca) (Zucca et al., 2019), and hg18-aligned log<sub>2</sub> transformed and quantile normalised microarray gene probe intensities of 397 Dutch people with ALS (van Rheenen) (van Rheenen et al., 2018). Accession numbers of these datasets are available in Chapter 3.5.1. To determine if the clusters could discriminate between ALS cases and controls, we also used RNA sequencing data in FASTQ format from 59 individuals from the KCL

BrainBank, and 34 samples from 19 individuals in TargetALS, as well as microarray data from 645 individuals from the van Rheenen study. We also obtained raw transcript counts for two additional TargetALS case datasets to determine if the expression signatures reflected a motor cortex-specific disease process, which included 45 samples from the occipital cortex, and 128 samples from 123 individuals from the cerebellum. The sequencing specific methods are described in more detail in Chapter 3.1.2.1. The basic demographics of each of the datasets used in this study are detailed in Table A29. We did not randomise the samples or conduct power analysis to estimate the appropriate sample size, as all available samples were used, nor were experimenters blinded to group assignment and outcome assessment.

#### **7.4.2 Bulk RNA Sequencing Data Processing**

The processing pipeline to convert paired FASTQ files from KCL BrainBank, TargetALS and Zucca datasets into raw transcript count matrices is described in Chapter 3.1.3. For the TargetALS occipital cortex and cerebellum datasets, transcripts were quantified with Salmon (Patro et al., 2017) before being converted into gene-specific expression counts with tximport (Soneson et al., 2015). For all datasets, raw counts were normalised using the *estimateSizeFactors* function of DESeq2, before lowly expressed genes and non-autosomal chromosomes were removed. Expression values were then standardized using the variance stabilising transformation (*vst*) function in DESeq2 (Love et al., 2014).

#### **7.4.3 Hierarchical Clustering of KCL BrainBank Samples**

Our hierarchical clustering was based on a protocol that was previously used to identify cortical molecular phenotypes of ALS (Tam et al., 2019). Briefly, the 5000 most variably expressed genes, selected based on the highest median absolute deviation values, were extracted from the KCL BrainBank gene expression matrix. Unsupervised hierarchical clustering was then performed with the non-smooth negative factorisation (nsNMF) algorithm, using helper functions outlined in the SAKE package (Ho et al., 2018). The optimal number of clusters was identified by running nsNMF with 100 runs and 1000 iterations for different values of k (two to ten). Cluster estimation results are available in Figure A12. We then ran the nsNMF algorithm with k = three, 100 runs and 1000 iterations, with the resulting consensus matrix showing a clear separation of samples (Figure A13). Informative gene and sample assignment for each of the three clusters was then extracted. The list of informative genes for each

cluster was then used to characterise their molecular phenotypes by performing gene enrichment analysis using the GProfiler2 R package (Kolberg et al., 2020). Genes from the whole KCL expression matrix were used as a custom gene background. The default g:SCS algorithm was used to assess significant enrichment for several process and pathway categories in the following databases: Gene Ontology (Biological Process (GO:BP), Molecular Function (GO:MF) and Cellular Component (GO:CC)), Kyoto Encyclopaedia of Genes and Genomes (KEGG), Reactome, CORUM, TRANSFAC, and miRTarBase. Additionally, MetaCore™ (available at <https://portal.genego.com>) was used to construct cluster-specific gene pathway networks using the 'analyze network' algorithm under default options, with the network that displayed the highest significance selected as the one that most defines the cluster.

#### 7.4.4 Validation of KCL BrainBank-derived clusters

To determine if the informative genes which defined each cluster could be used to successfully stratify samples in other ALS datasets, we applied linear discriminant analysis (LDA) models to the TargetALS, Zucca, and van Rheenen ALS datasets, using the MASS R package (Venables & Ripley, 2002). Each dataset-specific model was trained using the intersection of dataset-specific and informative cluster genes, which yielded 470, 381, and 535 genes for TargetALS, Zucca and van Rheenen, respectively. The linear discriminants were derived from the KCL BrainBank gene and sample cluster assignments. The same approach was carried out for KCL BrainBank (787 genes), TargetALS (787 genes) and van Rheenen (535 genes) controls, as well as the occipital cortex and cerebellum of people with ALS from TargetALS, with 651 and 622 genes shared between each respective dataset and KCL BrainBank cases. Classification probability was evaluated based on the average dataset-specific posterior probabilities of cluster assignment. Cluster stability was then assessed using bootstrapping, implemented in the resample function of the scikit-learn package (Pedregosa et al., 2011). Resampling with replacement was performed with 1000 iterations. For each iteration, the median and 95% confidence intervals for accuracy and silhouette of the cluster assignment was collected, before being averaged to form the final estimate.

As linear discriminant analysis is constrained to assign every sample to one class, we performed additional analyses to confirm that controls and post-mortem expression

data from different brain regions assigned to each molecular phenotype could be distinguished from cases. To determine the specificity of the cluster one signature for ALS in the KCL BrainBank dataset, we performed case-control differential expression analysis of the 131 genes which constituted its signature using DESeq2 (Love et al., 2014), applying the same standardisation and normalisation procedure that was used to pre-process the expression data for hierarchical clustering. Differentially expressed genes were identified via the independent hypothesis weighting multiple testing approach using Benjamini-Hochberg adjustment, with  $p$ -value  $< 0.050$  denoting significance. For the KCL BrainBank cluster 1 case-control dataset, the TargetALS and van Rheenen case-control datasets and TargetALS motor-occipital and motor-cerebellum case datasets for all clusters, we built logistic regression classifiers with ten-fold cross validation using the scikit-learn and imblearn Python libraries (Lemaître et al., 2017; Pedregosa et al., 2011), to ascertain the discriminative ability of each cluster-specific gene signature. Three scenarios were employed: 1) using all of the cluster-specific genes present in each dataset, 2) removing multicollinear features using the SelectNonCollinear function of the collinearity package with a correlation threshold of 0.4 and ANOVA F-value as the scoring parameter (Malato, n.d.), and 3) extracting the uncorrelated features present in all folds to subset the cluster-specific signatures before retraining the model. For all scenarios, the data was firstly normalised by removing the mean and scaling to unit variance using StandardScaler before oversampling was performed to address potential class imbalance using the synthetic-minority oversampling technique (SMOTE) function of *imblearn*. For each scenario, the best hyperparameters were selected using GridSearchCV with ROC\_AUC as the scoring parameter, before the model was evaluated using the average ROC\_AUC, precision, recall, and F1-score over all folds. Both hyperparameter tuning and cross-validation was performed using StratifiedKFold with ten splits and shuffling of the samples within each cluster.

We also performed two additional analyses to determine the robustness of our discovery and validation methods. The first analysis involved performing hierarchical clustering on the top 5000 variably expressed genes in TargetALS motor cortex samples to obtain informative-gene based cluster assignments in the same way as described for KCL BrainBank. By doing this, TargetALS was the discovery dataset, whilst KCL BrainBank served as the replication dataset. We then analysed the overlap

between the original assignments and new assignments to gather the natural grouping of samples. To support the discriminative performance of the KCL BrainBank classifier, we constructed ten additional logistic regression classifier models with 10-fold cross validation using the cases and controls assigned to cluster 1. Each classifier was supplied with 131 randomly sampled genes from the transformed expression matrix. The resulting performance metrics over all ten classifiers were averaged to form the final estimate before the performance was compared to the cluster 1 expression signature specific classifier.

#### **7.4.5 Interpretation of Predictor Genes**

The top predictors explained by each of the case-control classifier models for scenarios one and two in each cluster were obtained via calculation of SHapley Additive exPlanations (SHAP) values using the SHAP python package (v0.41.0; (Lundberg & Lee, 2017)), with the final values representing averaged SHAP values over all of the ten folds. These values were calculated using the model-agnostic permutation-based explainer approach.

To obtain the genes which favour assignment of cases into one cluster over the others, we performed dominance analysis using the dominance-analysis Python package (v1.1.9; (Luo & Azen, 2013)) for the KCL BrainBank, TargetALS and van Rheenen datasets. The expression data was normalised between 0 and 1 using the MinMaxScaler scikit-learn function before executing the analysis, where a one vs rest approach was adopted i.e., cluster one vs clusters two and three. The top 15 predictors were selected for each one vs rest scenario for each cluster. For the Zucca dataset, we chose to use permutation importance to obtain the top predictors as dominance analysis cannot be used if only one case is assigned to a cluster.

#### **7.4.6 Cell Type Deconvolution Analysis of Motor Cortex Case Datasets**

To assess whether the molecular phenotypes we identified in bulk RNAseq data could also be reflective of cell composition, we used the MuSiC R package (v1.0.0; (X. Wang et al., 2019)) to derive cell proportions in the KCL BrainBank and TargetALS case datasets for the following cell types: astrocytes, endothelial cells, microglia, neurons, and oligodendrocytes. We performed deconvolution with the raw RNAseq counts. The single-cell RNAseq reference dataset which was used to derive expression information for each cell type consisted of 8 adults and 4 embryonic samples (16-18 weeks

gestational age) from the temporal lobe (Darmanis et al., 2015), which was downloaded via the scRNAseq R package (v2.14.0; (Risso D, Cole M, 2023)). Differences in composition between clusters in each dataset were assessed using one-way ANCOVA corrected for sex assigned at birth and age of death, with post-hoc Tukey's test used to determine subcluster-specific trends. The normality of each variable for each dataset was assessed using the Shapiro-Wilk test, with any variables that were non-normally distributed (p-value < 0.050) being log-transformed before analysis.

#### 7.4.7 Subgroup Phenotype Analysis

To reveal and compare the phenotypic architecture of each cluster, we extracted several clinical and omics variables from each case-specific dataset. We performed the chi-square test of independence to assess if there were differences in the proportion of *C9orf72*-positive, limb-onset, bulbar-onset, and combined limb and bulbar onset cases between each of the clusters in the KCL BrainBank and TargetALS datasets, the limb:bulbar ratio in the van Rheenen datasets, and the male:female ratio in all four case-only datasets. A p-value < 0.05 denotes significance. Due to variations in the phenotypic information collected and accessibility of other omics data, we could not extract some phenotypic variables for all datasets. A breakdown of the collected phenotypic variables for each dataset is available in Table A30. Transcriptional age acceleration was calculated by using RNAAgeCalc to obtain tissue-specific transcriptional age estimates for each dataset (Ren & Kuan, 2020), before being subtracted from the chronological age (age at death for KCL BrainBank and TargetALS, age at last blood draw for Zucca and van Rheenen). Telomere length and mitochondrial DNA copy number were obtained by applying TelSeq v0.0.2 (Ding et al., 2014) and fastMitoCalc v1.2 (Qian et al., 2017) to the whole-genome sequencing BAM files, respectively. Biological age was estimated from the methylation beta-value matrix using CorticalClock (Shireby et al., 2020), before acceleration was calculated by subtracting each value from the age at death. Differences between clusters were assessed using one-way ANCOVA corrected for sex assigned at birth, with post-hoc Tukey's test used to determine subcluster-specific trends. The normality of each variable for each dataset was assessed using the Shapiro-Wilk test, with any variables that were non-normally distributed (p-value < 0.050) being log-transformed before analysis. Additionally, we applied a Cox proportional-hazards model to assess

differences in age of onset among clusters by combining samples from both KCL BrainBank and TargetALS datasets, with which  $p$ -value  $< 0.050$  denotes significance.

#### 7.4.8 Code Availability

The implementation of our class assignment model based on the KCL BrainBank data, can be used to assign class membership to new expression samples (both microarray and RNAseq) and is publicly available at <https://alsgeclustering.er.kcl.ac.uk>. The code for the analyses performed in this study is available at <https://github.com/KHP-Informatics/HierarchicalClusteringALS/>.

### 7.5 Results

The nsNMF algorithm identified 794 of the 5000 most variably expressed genes as being the most informative for defining the clusters. Each informative gene was uniquely assigned to one cluster, yielding three distinct clusters, each with a unique gene expression profile. There were 131, 291, and 372 genes which defined clusters one, two, and three, respectively (Figure 7-1A). The full list of genes which comprise each cluster are available in Table A31. The larger proportion of people with ALS (60; 53.6%) were assigned to cluster one, followed by cluster two (28; 25%) and cluster three (24; 21.4%), without substantial differences in male:female ratio in each cluster, based on sex assigned at birth (Figure 7-1B) or the proportion of males and females assigned to the clusters ( $X^2 = 0.43$ ,  $p$ -value = 0.81). Almost all *C9orf72* positive cases (7; 87.5%) were assigned to cluster one (Table 7-1), with no significant difference in the proportion of these cases between clusters ( $X^2 = 4.24$ ,  $p$ -value = 0.12).

Four known ALS-associated genes (*HSPB1*, *CAV1*, *CX3CR1*, *RNASE2*) were among the informative genes selected for the cluster signatures, with all four demonstrating significant differences in their average expression values between clusters when performing one-way ANCOVA corrected for sex assigned at birth, age at death and post-mortem delay (Figures A14A-D). When performing post-hoc analysis to assess which clusters show differential expression, only *CX3CR1*, which was assigned to cluster three, was significantly upregulated compared to cluster one (Tukey  $p$ -value =  $1.2E-05$ ) and cluster two (Tukey  $p$ -value =  $7.2E-05$ ) without difference in expression between clusters one and two (Figure A14C). The other gene's cluster assignments did not have a complete influence on their expression in cases assigned to the gene's

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cluster, although for the cluster three informative gene *RNASE2*, there was a trend for higher expression in cases assigned to that cluster compared to the others (Figure A14D). The full statistical results are available in Figure A14E.

### **7.5.1 Each cluster represents a molecularly distinct phenotype enriched for genes and pathways previously linked to ALS pathogenesis**

Characterising the molecular architectures of each cluster by using gene enrichment and gene network analyses, we found that each cluster represents a distinct molecular phenotype, with genes and pathways that have been previously linked to ALS pathogenesis. Cluster one was significantly enriched for various neuronal and synaptic signalling-related processes such as neuropeptide activity, cAMP signalling, and neuroactive ligand transcription, binding, and receptor interaction (Figure 7-2A, Table A32). Network analysis revealed that a mitochondria specific signalling network is also present (Figure 7-2B). Led by *NXPH2*, *ATP12A*, *PTPRV*, *SV2C* and *C18orf42*, this network is enriched for mitochondrial ATP synthesis coupled electron transport and the aerobic electron transport chain.



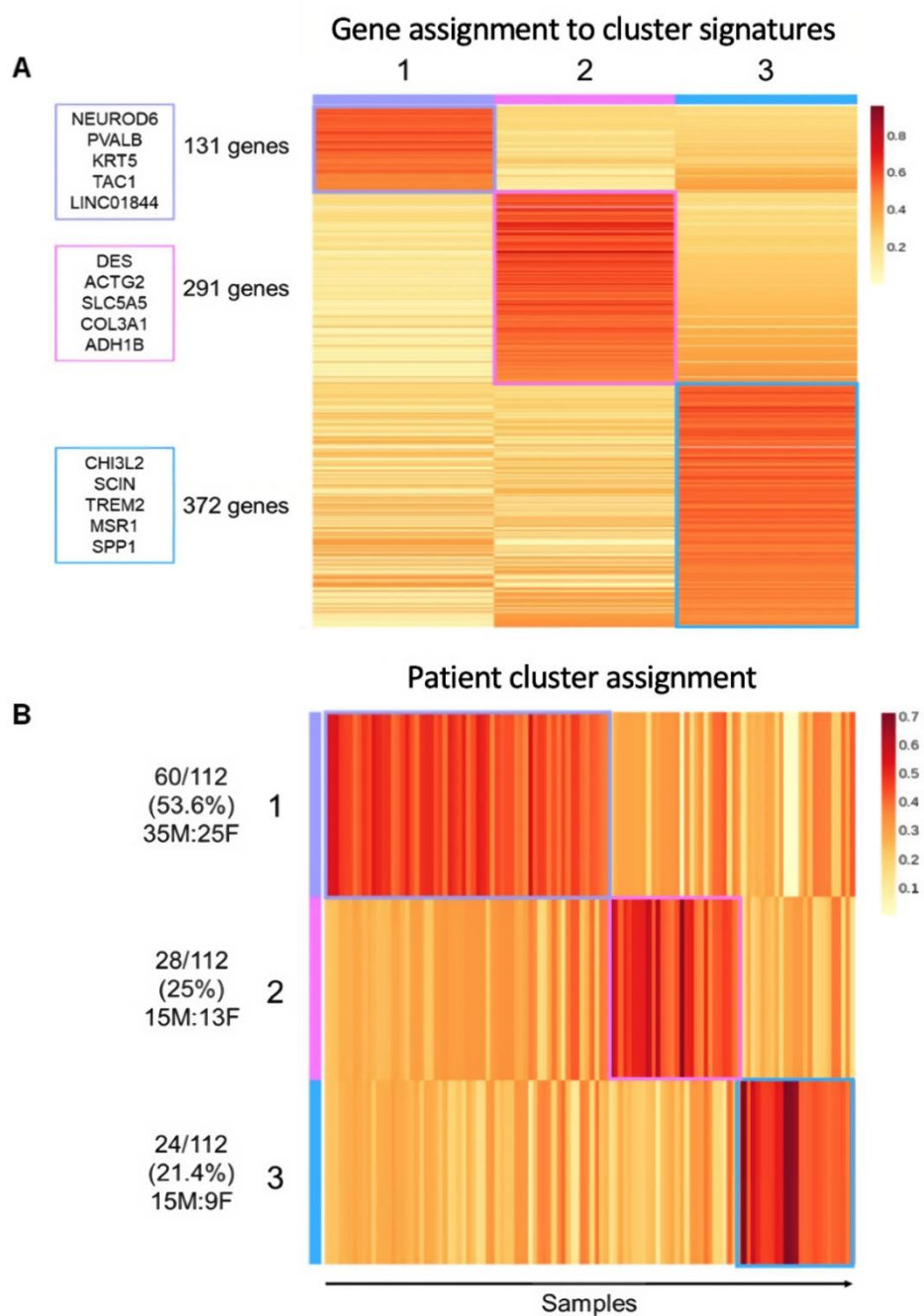


Figure 7-1. Informative gene and sample assignment for KCL BrainBank-generated clusters. A) Number of the 794 informative genes uniquely assigned to each cluster, with the top five contributing genes (defined by posterior probability) listed at the side. B) Distribution of cluster assignment of people with SALS alongside the male:female ratio, based on sex assigned at birth. The coloured scale refers to the posterior probability value.

|  | KCL BrainBank (motor cortex) |                             |                       | TargetALS (motor cortex) |                     |                    | Zucca (blood)     |                   |                   | van Rheenen (blood) |                    |                    |
|--|------------------------------|-----------------------------|-----------------------|--------------------------|---------------------|--------------------|-------------------|-------------------|-------------------|---------------------|--------------------|--------------------|
|  | 1                            | 2                           | 3                     | 1                        | 2                   | 3                  | 1                 | 2                 | 3                 | 1                   | 2                  | 3                  |
| Number of Samples (%)  | 60<br>(53.57)                | 28<br>(25.00)               | 24<br>(21.43)         | 97 (57.7)                | 28 (16.6)           | 43 (25.6)          | 13<br>(86.70)     | 1 (6.65)          | 1 (6.65)          | 335<br>(84.4)       | 33 (8.31)          | 29 (7.31)          |
| Number of Samples with a posterior probability $\geq 80\%$ (%) | NA                           | NA                          | NA                    | 88 (90.7)                | 22 (78.6)           | 31 (72.1)          | 9 (69.2)          | 1 (100)           | 0 (0)             | 275<br>(82.1)       | 31 (93.9)          | 11 (37.9)          |
| N Males: N Females (Ratio)                                     | 35:25<br>(1.4)               | 15:13<br>(1.15)             | 15:9<br>(1.67)        | 60:37<br>(1.62)          | 18:10<br>(1.80)     | 21:22<br>(0.95)    | 6:7 (0.86)        | 0:1 (0)           | 1:0 (0)           | 205:130<br>(1.58)   | 18:15<br>(1.20)    | 16:13<br>(1.23)    |
| C9 positive individuals (N)                                    | 7                            | 1                           | 0                     | 11                       | 0                   | 4                  | NA                | NA                | NA                | NA                  | NA                 | NA                 |
| Age at Symptom Onset in Years<br>(mean $\pm$ SD)               | 58.8 $\pm$<br>11.6           | 65.7 $\pm$<br>12.3          | 61.7 $\pm$<br>15.7    | 59.6 $\pm$<br>11.1       | 64.9 $\pm$<br>9.52  | 60.3 $\pm$<br>11.5 | 63.6 $\pm$<br>8.6 | 67.0 $\pm$<br>0.0 | 65.0 $\pm$<br>0.0 | 62.7 $\pm$<br>11.9  | 57.9 $\pm$<br>12.0 | 60.9 $\pm$<br>12.3 |
| Age at Blood Draw in Years (mean $\pm$ SD)                     | NA                           | NA                          | NA                    | NA                       | NA                  | NA                 | 66.1 $\pm$<br>9.8 | 69.0 $\pm$<br>0.0 | 68.0 $\pm$<br>0.0 | NA                  | NA                 | NA                 |
| Age At Death in Years<br>(mean $\pm$ SD)                       | 62.5 $\pm$<br>11.4           | 70.2 $\pm$<br>11.4          | 64.2 $\pm$<br>15.6    | 63.2 $\pm$<br>10.2       | 69.5 $\pm$<br>9.0   | 64.5 $\pm$<br>8.9  | NA                | NA                | NA                | NA                  | NA                 | NA                 |
| Limb Onset (N)   | 36                           | 10                          | 17                    | 65                       | 22                  | 17                 | NA                | NA                | NA                | 215                 | 21                 | 15                 |
| Bulbar Onset (N)   | 15                           | 7                           | 5                     | 14                       | 5                   | 21                 | NA                | NA                | NA                | 120                 | 12                 | 14                 |
| Limb + Bulbar Onset (N)  | 1                            | 1                           | 0                     | 7                        | 0                   | 1                  | NA                | NA                | NA                | NA                  | NA                 | NA                 |
| Diagnostic Delay in Years<br>(mean $\pm$ SD)                   | 0.0015 $\pm$<br>0.0013       | 0.00047<br>$\pm$<br>0.00085 | 0.001 $\pm$<br>0.0012 | 0.025 $\pm$<br>0.32      | 0.073 $\pm$<br>0.59 | 0.12 $\pm$<br>0.35 | NA                | NA                | NA                | NA                  | NA                 | NA                 |

|   |                     |                     |                     |                     |                    |                    |                      |                      |                      |                       |                       |                       |
|---|---------------------|---------------------|---------------------|---------------------|--------------------|--------------------|----------------------|----------------------|----------------------|-----------------------|-----------------------|-----------------------|
| Disease Duration in Years (median (IQR))                  | 3.16<br>(1.96)      | 2.30<br>(1.81)      | 2.38<br>(1.75)      | 3.00<br>(2.13)      | 4.00<br>(3.48)     | 2.00<br>(2.00)     | NA                   | NA                   | NA                   | 2.41<br>(2.02)        | 2.47<br>(1.14)        | 2.37<br>(1.53)        |
| Post-mortem Delay in Hours (mean $\pm$ SD)                | 26.1 $\pm$<br>12.10 | 26.0 $\pm$<br>10.70 | 25.9 $\pm$<br>13.90 | 9.9 $\pm$<br>6.10   | 10.0 $\pm$<br>7.45 | 12.0 $\pm$<br>8.26 | NA                   | NA                   | NA                   | NA                    | NA                    | NA                    |
| Mitochondrial DNA Copy Number (mean $\pm$ SD)             | 465 $\pm$<br>22.0   | 457 $\pm$<br>22.4   | 459 $\pm$<br>17.3   | NA                  | NA                 | NA                 | NA                   | NA                   | NA                   | NA                    | NA                    | NA                    |
| Telomere Length in Kilobytes (mean $\pm$ SD)              | 4.04 $\pm$<br>0.46  | 3.98 $\pm$<br>0.56  | 3.77 $\pm$<br>0.42  | NA                  | NA                 | NA                 | NA                   | NA                   | NA                   | NA                    | NA                    | NA                    |
| Transcriptional Age Acceleration in Years (mean $\pm$ SD) | 6.16 $\pm$<br>9.24  | 0.45 $\pm$<br>10.90 | 5.59 $\pm$<br>10.80 | 10.50 $\pm$<br>8.63 | 4.19 $\pm$<br>8.08 | 8.54 $\pm$<br>8.44 | -23.50 $\pm$<br>9.90 | -28.60 $\pm$<br>0.00 | -26.93 $\pm$<br>0.00 | -41.21 $\pm$<br>11.66 | -36.68 $\pm$<br>11.84 | -38.62 $\pm$<br>11.69 |
| Biological Age Acceleration in Years (mean $\pm$ SD)      | 5.99 $\pm$<br>2.92  | 4.06 $\pm$<br>4.65  | 7.93 $\pm$<br>4.67  | NA                  | NA                 | NA                 | NA                   | NA                   | NA                   | NA                    | NA                    | NA                    |

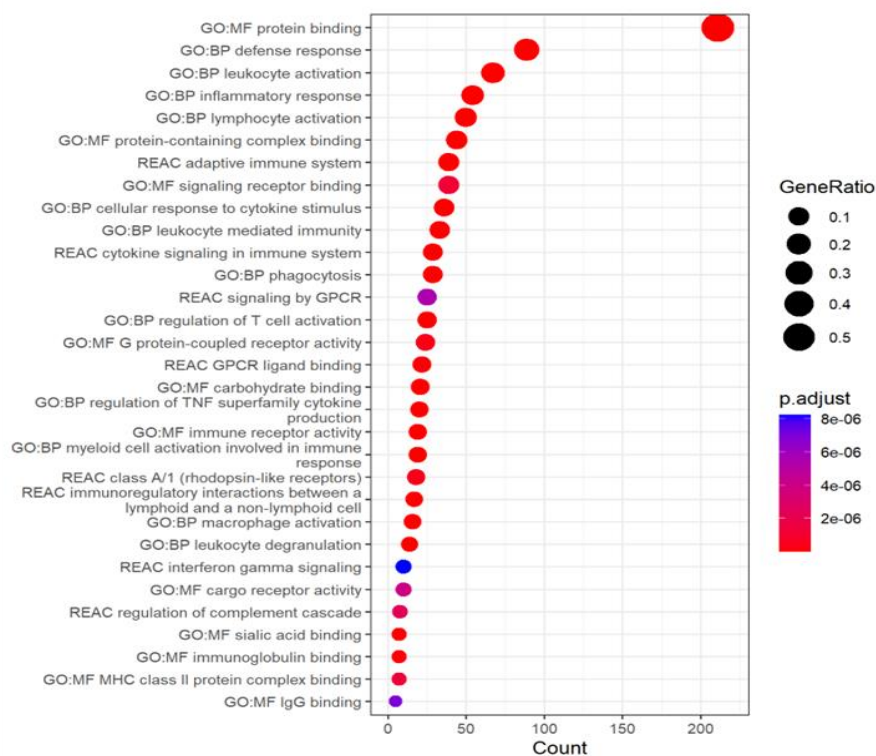
Table 7-1. Demographics and omics-based/clinical phenotypes for the samples assigned to each cluster, for each dataset. NA represents values that could not be collected due to omics and clinical data availability.

Cluster two was strongly linked with oxidative stress, apoptotic signalling, and vasculature related processes including angiogenesis, blood vessel development, epithelial cell differentiation and atherosclerosis (Figure 7-3A). Moreover, muscle-system and extracellular-matrix (ECM) specific enrichments (e.g., collagen synthesis and degradation, smooth muscle contraction, ECM proteoglycans and degradation), and anti-inflammatory pathways (interleukin-4 and interleukin-13 signalling, neutrophil degranulation) from Reactome were also associated with this cluster (Figure 7-3A). The muscle contraction theme was strengthened with GO:CC enrichments for banded collagen fibril, supramolecular fiber, myofibril, Z disc, I band, sarcomere, and the actin cytoskeleton (Table A33). Cluster two was also enriched for the ALS-gene related NOS3-CAV1 CORUM complex ( $p=0.018$ ). Furthermore, the cluster two network (Figure 7-4B), which was driven by *MFAP4*, *FPRL1*, *TUSC5*, *MRGPRF*, and *PLAUR*, was associated with muscle contraction and actin-myosin filament sliding as well as phospholipase C-activating G protein coupled signalling. Cluster three represents an inflammatory phenotype, with biological process enrichment strongly associated with immune response in GO:BP and KEGG (Table A34), as well as links with adaptive immunity, complement cascade, and interferon gamma signalling in Reactome and immunoglobulin activity and major histocompatibility complex (MHC) class II in GO:MF (Figure 7-4A). Furthermore, C1q and TLR1-TLR2 CORUM complexes and viral diseases present in KEGG, such as Epstein-Barr disease, herpes simplex virus 1, and influenza A were among the most significant enrichments. Nine microRNAs were also significantly enriched in cluster two (including hsa-miR-335-5p, hsa-miR-146a-5p, hsa-miR-124-3p, hsa-miR-29a-3p, and hsa-miR-204-5p), with hsa-miR-335-5p also being enriched in cluster three (Tables A33 and A34). The cluster three network (Figure 7-4B), defined by *GNLY*, *HSPA7*, *SLAMF8*, *CLEC17A*, and *Sgo1*, is MHC-class II specific and enriched for antigen processing, peptide antigen assembly, and presentation of peptides and polysaccharide antigens. Furthermore, the centre of the network, *GATA-2*, was the most significantly enriched TRANSFAC element in cluster three (*GATAD2A*,  $p=9.56E-17$ , Table A34).





A



B

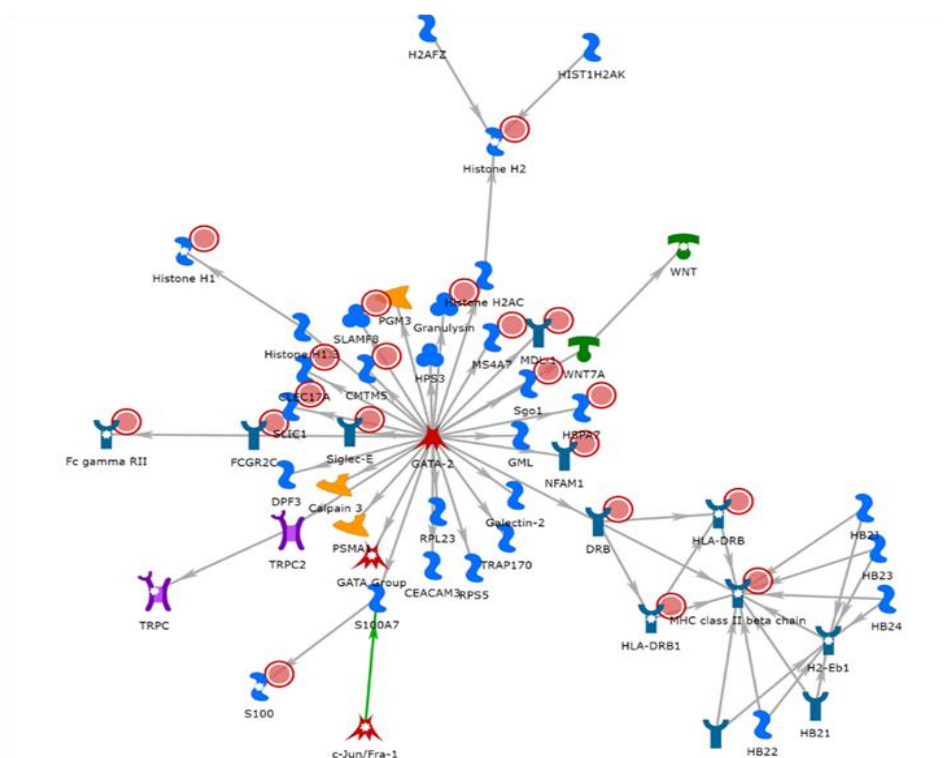


Figure 7-4. Results of gene enrichment and network analyses for Cluster 3. A) GProfiler2 reveals enrichment for pro-inflammatory processes. B) The most significant sub-cluster reinforces the link to inflammation with the identification of an MHC Class 2 specific network. Red circles present in each network represent informative genes identified in each cluster. The descriptions of what each symbol represents is available in Figure A11.

### **7.5.2 The molecular phenotypes are robust and validated in independent brain and blood datasets**

To validate the KCL BrainBank derived clusters, we performed linear discriminant-driven cluster assignments of the TargetALS, Zucca and van Rheenen samples, using the intersection between the genes expressed in each one of them and the 794 genes that were used to define the clusters in the KCL BrainBank. Samples from each dataset were assigned to one of the three clusters with high certainty (between 80-90%) based on average posterior probability (diagonal cells in Figures 7-5A, B and C). A breakdown of the sample to cluster composition for all case datasets is available in Table 7-1. For the Zucca dataset, the posterior probability of belonging to cluster three is marginally higher than cluster 2 as only one sample was assigned to it.

To determine whether the molecular phenotypes also withheld validity in control datasets, we applied the same approach to healthy controls from the KCL BrainBank, TargetALS and van Rheenen datasets as well as TargetALS case datasets of the occipital cortex and cerebellum (demographics available in Table A29). We found that all KCL BrainBank controls were assigned to cluster one (Figure 7-5D), whereas for the other control datasets and TargetALS datasets from different tissues, cluster accuracy was not degraded as there were similar average probability estimates for cluster assignment as in the motor cortex case datasets (diagonal cells in Figures 7-5E-H).

The intersection and union of the overall and cluster-specific genes for the case and control motor cortex and blood datasets are represented in Figures A15 (cases) and A16 (controls), with a visual inspection of the sample assignments based on the calculated linear discriminants in all datasets available in Figures A17 (cases) and A18 (controls). The posterior probability of assignment to each of the three clusters for each sample in the case datasets is available in Table A35. Bootstrapping to assess cluster assignment stability for each of the eight datasets revealed that all TargetALS datasets and the Zucca dataset had a 100% median assignment accuracy, with van Rheenen controls having an accuracy of 98.9% (Table 7-2), confirming that these cluster assignments are robust. In contrast, KCL BrainBank controls and van Rheenen cases had a poor-to-average assignment accuracy, therefore their cluster stability was deemed to be unstable.



We also performed a reverse validation of the TargetALS motor cortex case dataset by performing hierarchical clustering in the replication dataset (TargetALS) as initially performed on KCL BrainBank (the discovery dataset). The purpose of this was to assess whether unsupervised clustering in both datasets leads to similar clustering assignments. Three clusters were defined by a total of 238 informative genes, with 47, 42 and 79 samples assigned to three clusters when TargetALS was utilised for the hierarchical clustering. We found that high proportions of samples assigned to these clusters (81.4%, 67% and 71.4% respectively) were the same as when the UK BrainBank was utilised for clustering.

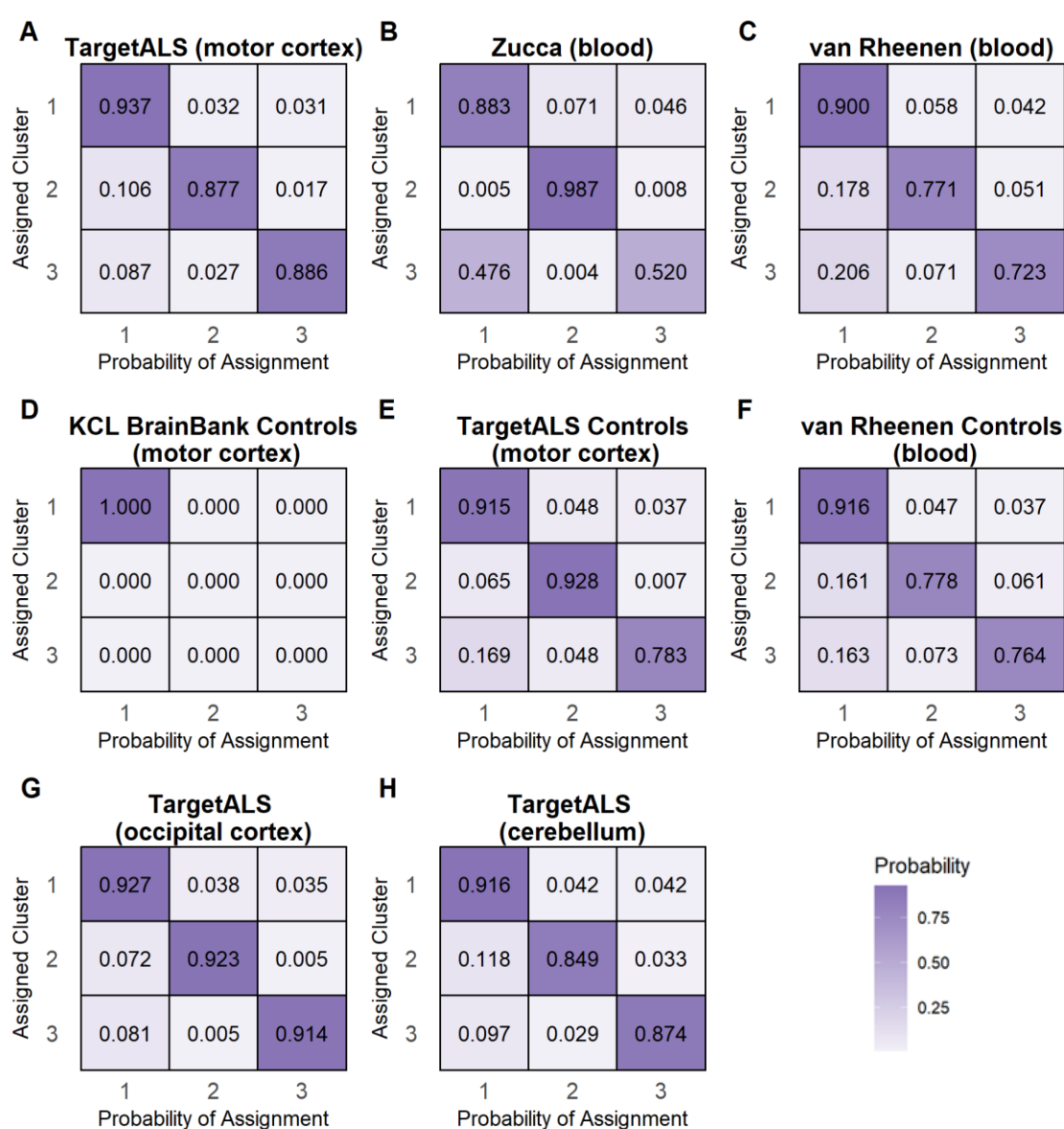


Figure 7-5. Posterior probabilities of cluster assignment for the eight independent expression datasets using linear discriminant analysis trained on the shared informative genes between each dataset and KCL BrainBank. The x-axis represents the average predicted posterior probability of being assigned to one of the three clusters, with the diagonals of the y-axis representing the average posterior probability of being assigned to the correct cluster.

| Dataset                      | Number of Genes | Accuracy                | Silhouette                  |
|------------------------------|-----------------|-------------------------|-----------------------------|
| TargetALS                    | 470             | 1.000<br>(1.000-1.000)  | 0.137<br>(0.109-0.168)      |
| Zucca                        | 381             | 1.000<br>(1.000-1.000)  | 0.127<br>(0.0560-0.234)     |
| Van Rheezen                  | 535             | 0.738<br>(0.693, 0.778) | 0.0185<br>(-0.0145, 0.0512) |
| BrainBank Controls           | 787             | 0.661<br>(0.543-0.780)  | 0.220<br>(0.167-0.281)      |
| TargetALS Controls           | 787             | 1.000<br>(1.000-1.000)  | 0.210<br>(0.131-0.305)      |
| Van Rheezen Controls         | 535             | 0.989<br>(0.981-0.997)  | 0.0782<br>(0.0539-0.103)    |
| TargetALS (occipital cortex) | 651             | 1.000<br>(1.000-1.000)  | 0.199<br>(0.132-0.283)      |
| TargetALS (cerebellum)       | 622             | 1.000<br>(1.000-1.000)  | 0.174<br>(0.139-0.217)      |

Table 7-2. Bootstrapping results for the linear discriminant analysis-derived sample assignments for the eight independent datasets. Bootstrapping was performed with 1000 iterations, with average accuracy of correct class assignment used as the evaluation metric. Average accuracy and silhouette values are reported as median and 95% confidence intervals.

### 7.5.3 The expression signatures of each molecular phenotype can discriminate between cases and controls and represent specific features of motor cortex gene expression

As all KCL BrainBank controls were assigned to cluster one, and the model is constrained to assign each sample to at least one class, we sought to see if there were differences in the expression of informative genes between cases and controls belonging to cluster one. We found that 87 genes (66.4%) were differentially expressed in cases (Figure A19, Table A36), which supports that this gene-specific expression profile is altered in ALS. We then constructed a logistic regression classification model with ten-fold cross-validation to determine if this expression profile is altered in such a way that it can accurately discriminate between ALS and control status (Figure 7-6A). We supplied the model with three different gene signature scenarios (one: all shared genes in the signature, two: removing multicollinear genes from each fold, three: genes common to all folds after removing multicollinearity). We found that training the models under scenarios one and two achieved excellent discriminative ability (one: ROC AUC  $0.88 \pm 0.10$ , two: ROC AUC  $0.82 \pm 0.11$ ). Notably,

scenario one also achieved the highest performance based on all metrics (precision =  $0.80 \pm 0.13$ , recall =  $0.82 \pm 0.19$ , and F1 =  $0.79 \pm 0.14$ ). Conversely, the discriminative power under scenario three was poor (ROC AUC  $0.61 \pm 0.14$ ). The specificity of the cluster one expression signature for ALS was further supported with the finding that the average performance over ten rounds of supplying the classifier with 131 randomly sampled genes for ROC AUC and the other metrics are in line with and below what would be expected by chance, regardless of scenario (Figure 7-6B).

We adopted the same approach with the TargetALS and van Rheenen case-control datasets, and found that regardless of dataset, training the models under scenarios one and two achieved excellent discriminative ability based on ROC AUC score, whereas the discriminative power under scenario three was highly variable (Figure 7-6). For all of the cluster-specific TargetALS models, the average ROC AUC score ranged between 0.93 and 1.00 (Figures 7-6C, D and E), which is the gold standard in research settings. However, in Cluster 3, after removing collinearity (scenario two), the recall and F1 score was relatively poor (recall =  $0.55 \pm 0.18$ , F1 =  $0.70 \pm 0.16$ ), despite the high ROC AUC ( $0.96 \pm 0.063$ ) and precision ( $1.00 \pm 0.00$ ) scores (Figure 7-6E). The performance of the van Rheenen cluster-specific classifiers was quite changeable, with the average ROC AUC score ranging from 0.69 to 1.00 (Figures 7-6F, G and H). For instance, the cluster one classifier (Figure 7-6F) could distinguish perfectly between cases and controls for scenarios one and two, according to ROC AUC score, but this dropped considerably in scenario three ( $0.69 \pm 0.056$ ). The discriminative power of cluster two under scenarios one and two (Figure 7-6G) was worse than cluster three (Figure 7-6H) based on all of the four performance metrics.

We then assessed whether these molecular phenotypes are truly representative of a motor-cortex based disease process by constructing motor cortex-occipital cortex and motor cortex-cerebellum logistic regression classifiers for each cluster and scenario. We found that each molecular phenotype did indeed reflect features of motor cortex gene expression as there was almost perfect discrimination between motor cortex and the other brain regions when supplying all of the cluster-specific informative genes to

the model. The full results, including the best hyperparameters and the number of genes supplied to each model, are available in Table A37.

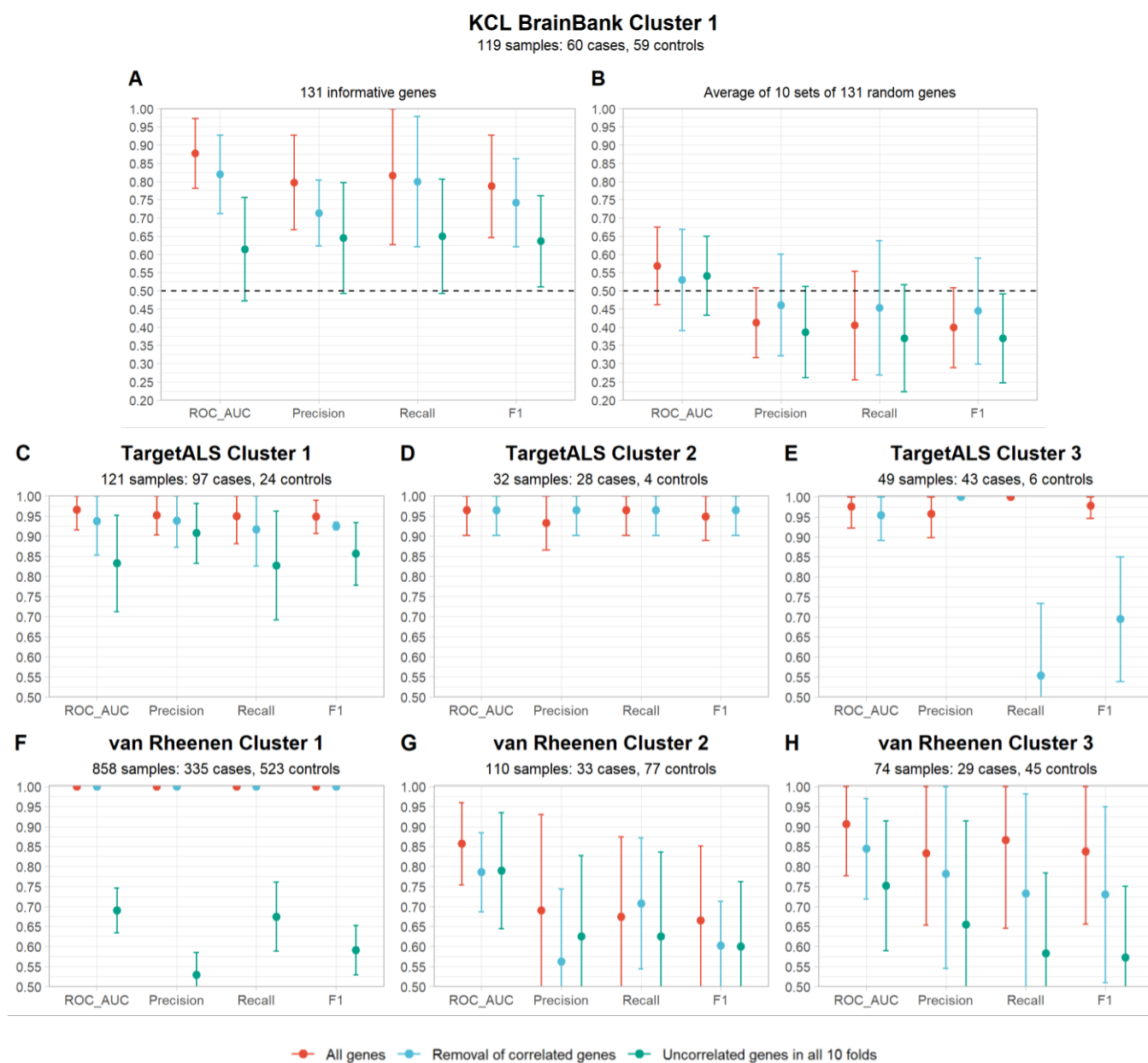


Figure 7-6. Averaged performance metrics over all ten cross-validation folds for each cluster under three scenarios in the three case-control datasets. KCL BrainBank: A) using all 131 informative gene of cluster one, B) random sets of 131 genes from the full expression matrix, TargetALS: Panels C-E, van Rheezen: Panels F-H. The x-axis represents each metric used to assess the discriminative performance of each model, with the average score of the metric represented on the y-axis. Each point represents the mean and the standard deviation. The y-axis starts from 0.5 in Panels C-H as this is the value that you would expect by chance, with the dotted line in Panels A and B representing this also.

### 7.5.4 There are common top predictor genes of case-control status and key driver genes of cluster assignment in case datasets

To gather the most important predictor genes in each model, SHAP importance analysis was performed, with the top 10 gene-based SHAP values being extracted for further examination and discussion (Table 7-3). The complete SHAP value results are available in Tables A38, A39 and A40 for the KCL BrainBank, TargetALS and van Rheenen datasets, respectively. As expected, when multicollinearity was removed, the relative SHAP importance values were higher as the influence of correlation with another predictor would have been removed, therefore making the importance estimate more accurate.

In the van Rheenen dataset, the 100% accuracy for scenarios 1 and 2 in cluster 1 (Figure 7-6F) is attributed to *NME1*, as its relative importance is 1462 and 1105 times larger than the next important predictor gene in scenarios 1 and 2, respectively, and when removing *NME1* from the scenario 1 model, the discriminative performance drops considerably (ROC AUC  $0.69 \pm 0.051$ ; Table A37). A similar but diluted effect was also observed for the Thioesterase gene for scenario 1 in cluster 3 with TargetALS (3.25x larger), *VIP* (3.07x larger) and *SLN* (2.61x larger) for scenario 2 in cluster 1 of KCL BrainBank and TargetALS, respectively, and for *ANGPTL4* (2.14x larger) for scenario 2 in cluster 2 of TargetALS (Table 7-3).

| Scenario         | Cluster | Gene Symbol (or Ensembl ID if no symbol is available) | SHAP Importance | Dataset       |
|------------------|---------|---|-----------------|---------------|
| 1<br>(All Genes) | 1       | <i>VIP</i>  | 0.0479          | KCL BrainBank |
|                  |         | <i>WIF1</i>   | 0.0391          | KCL BrainBank |
|                  |         | <i>SST</i>  | 0.0355          | KCL BrainBank |
|                  |         | <i>LINC01007</i>                                      | 0.0347          | KCL BrainBank |
|                  |         | <i>NPY2R</i>  | 0.0346          | KCL BrainBank |
|                  |         | <i>HSD11B1</i>  | 0.0342          | KCL BrainBank |
|                  |         | <i>LOC105374524</i>                                   | 0.0334          | KCL BrainBank |
|                  |         | <i>SV2C</i>   | 0.0326          | KCL BrainBank |
|                  |         | <i>Antisense to ADTRP</i>                             | 0.0324          | KCL BrainBank |
|                  |         | <i>LINC02055</i>                                      | 0.0323          | KCL BrainBank |
|                  |         | <i>SLN</i>  | 0.0600          | TargetALS     |
|                  |         | <i>LINC02192</i>                                      | 0.0336          | TargetALS     |
|                  |         | <i>miR-1255</i>                                       | 0.0321          | TargetALS     |
|                  |         | <i>LINC01107</i>                                      | 0.0311          | TargetALS     |
|                  |         | <i>HSD17B12</i><br><i>Pseudogene</i>                  | 0.0290          | TargetALS     |

|  |   |                     |            |             |
|--|---|---------------------|------------|-------------|
|  |   | <i>Lnc-DUSP22-2</i> | 0.0285     | TargetALS   |
|  |   | <i>SNORA74A</i>     | 0.0251     | TargetALS   |
|  |   | <i>KRT17P1</i>      | 0.0243     | TargetALS   |
|  |   | <i>GATD3</i>        | 0.0230     | TargetALS   |
|  |   | <i>FAM8A6P</i>      | 0.0224     | TargetALS   |
|  |   | <i>NME1</i>         | 0.484      | van Rheenen |
|  |   | <i>GPAT3</i>        | 0.000331   | van Rheenen |
|  |   | <i>LINC01844</i>    | 0.000112   | van Rheenen |
|  |   | <i>ADTRP</i>        | 0.0000820  | van Rheenen |
|  |   | <i>DNAJC22</i>      | 0.0000340  | van Rheenen |
|  |   | <i>CRH</i>          | 0.0000190  | van Rheenen |
|  |   | <i>DRD5</i>         | 0.0000120  | van Rheenen |
|  |   | <i>GATD3</i>        | 0.0000100  | van Rheenen |
|  |   | <i>CTXN3</i>        | 0.00000600 | van Rheenen |
|  |   | <i>OSTN</i>         | 0.00000400 | van Rheenen |
|  | 2 | <i>HILPDA</i>       | 0.0106     | TargetALS   |
|  |   | <i>STC1</i>         | 0.0104     | TargetALS   |
|  |   | <i>ANGPTL4</i>      | 0.00760    | TargetALS   |
|  |   | <i>SECTM1</i>       | 0.00730    | TargetALS   |
|  |   | <i>ADM</i>          | 0.00720    | TargetALS   |
|  |   | <i>RRAD</i>         | 0.00650    | TargetALS   |
|  |   | <i>ADAMTS9</i>      | 0.00630    | TargetALS   |
|  |   | <i>FCAR</i>         | 0.00540    | TargetALS   |
|  |   | <i>SAMD11</i>       | 0.00520    | TargetALS   |
|  |   | <i>IGFN1</i>        | 0.00440    | TargetALS   |
|  |   | <i>MIR3667HG</i>    | 0.0377     | van Rheenen |
|  |   | <i>HSPA1A</i>       | 0.0332     | van Rheenen |
|  |   | <i>CLEC4E</i>       | 0.0276     | van Rheenen |
|  |   | <i>ADGRG3</i>       | 0.0261     | van Rheenen |
|  |   | <i>HSPB7</i>        | 0.0246     | van Rheenen |
|  |   | <i>VNN2</i>         | 0.0238     | van Rheenen |
|  |   | <i>THBS1</i>        | 0.0237     | van Rheenen |
|  |   | <i>COL1A2</i>       | 0.0230     | van Rheenen |
|  |   | <i>VCAM1</i>        | 0.0220     | van Rheenen |
|  |   | <i>SOCS3</i>        | 0.0215     | van Rheenen |
|  | 3 | <i>Thioesterase</i> | 0.1406     | TargetALS   |
|  |   | <i>ITGAL</i>        | 0.0435     | TargetALS   |
|  |   | <i>NAPSB</i>        | 0.0312     | TargetALS   |
|  |   | <i>FCGR1CP</i>      | 0.0301     | TargetALS   |
|  |   | <i>C4A</i>          | 0.0285     | TargetALS   |
|  |   | <i>DHRS9</i>        | 0.0111     | TargetALS   |
|  |   | <i>CLEC7A</i>       | 0.0108     | TargetALS   |
|  |   | <i>POM121L9P</i>    | 0.00900    | TargetALS   |
|  |   | <i>LNCAROD</i>      | 0.00500    | TargetALS   |
|  |   | <i>LINC01299</i>    | 0.00370    | TargetALS   |
|  |   | <i>SLA</i>          | 0.0323     | van Rheenen |

|                                    |                    |                           |                |               |           |
|------------------------------------|--------------------|---------------------------|----------------|---------------|-----------|
|                                    |                    | <i>TMEM119</i>            | 0.0310         | van Rheenen   |           |
|                                    |                    | <i>FGD2</i>               | 0.0278         | van Rheenen   |           |
|                                    |                    | <i>MAG</i>                | 0.0266         | van Rheenen   |           |
|                                    |                    | <i>PKD1L2</i>             | 0.0226         | van Rheenen   |           |
|                                    |                    | <i>GPNMB</i>              | 0.0222         | van Rheenen   |           |
|                                    |                    | <i>FFAR1</i>              | 0.0216         | van Rheenen   |           |
|                                    |                    | <i>GPR62</i>              | 0.0215         | van Rheenen   |           |
|                                    |                    | <i>SLC31A2</i>            | 0.0200         | van Rheenen   |           |
|                                    |                    | <i>TAS2R39</i>            | 0.0176         | van Rheenen   |           |
| 2<br>(Removal of Correlated Genes) | 1                  | <i>VIP</i>                | 0.359          | KCL BrainBank |           |
|                                    |                    | <i>WIF1</i>               | 0.117          | KCL BrainBank |           |
|                                    |                    | <i>HSD11B1</i>            | 0.0436         | KCL BrainBank |           |
|                                    |                    | <i>ENSG00000254561</i>    | 0.0377         | KCL BrainBank |           |
|                                    |                    | <i>CR2</i>                | 0.0303         | KCL BrainBank |           |
|                                    |                    | <i>LINC00898</i>          | 0.0265         | KCL BrainBank |           |
|                                    |                    | <i>LINC01830</i>          | 0.0214         | KCL BrainBank |           |
|                                    |                    | <i>Antisense to ADTRP</i> | 0.0131         | KCL BrainBank |           |
|                                    |                    | <i>CSN1S1</i>             | 0.00670        | KCL BrainBank |           |
|                                    |                    | <i>ENSG00000286016</i>    | 0.00660        | KCL BrainBank |           |
|                                    |                    | <i>SLN</i>                | 0.129          | TargetALS     |           |
|                                    |                    | <i>LINC01107</i>          | 0.0494         | TargetALS     |           |
|                                    |                    | <i>KRT17P1</i>            | 0.0466         | TargetALS     |           |
|                                    |                    | <i>Lnc-MYB-5</i>          | 0.0449         | TargetALS     |           |
|                                    |                    | <i>miR-1255</i>           | 0.0445         | TargetALS     |           |
|                                    |                    | <i>LINC02192</i>          | 0.0424         | TargetALS     |           |
|                                    |                    | <i>GATD3</i>              | 0.0346         | TargetALS     |           |
|                                    |                    | <i>Lnc-DUSP22-2</i>       | 0.0304         | TargetALS     |           |
|                                    |                    | <i>VGF</i>                | 0.0293         | TargetALS     |           |
|                                    |                    | <i>ATP12A</i>             | 0.0289         | TargetALS     |           |
|                                    |                    | <i>NME1</i>               | 0.484          | van Rheenen   |           |
|                                    |                    | <i>GPAT3</i>              | 0.000488       | van Rheenen   |           |
|                                    |                    | <i>LINC01844</i>          | 0.0000820      | van Rheenen   |           |
|                                    |                    | <i>ADTRP</i>              | 0.0000440      | van Rheenen   |           |
|                                    |                    | <i>DNAJC22</i>            | 0.0000230      | van Rheenen   |           |
|                                    |                    | <i>GATD3</i>              | 0.0000160      | van Rheenen   |           |
|                                    |                    | <i>CRH</i>                | 0.0000150      | van Rheenen   |           |
|                                    | <i>CTXN3</i>       | 0.00000900                | van Rheenen    |               |           |
|                                    | <i>DRD5</i>        | 0.00000900                | van Rheenen    |               |           |
|                                    | <i>OSTN</i>        | 0.00000600                | van Rheenen    |               |           |
|                                    |                    | 2                         | <i>ANGPTL4</i> | 0.116         | TargetALS |
|                                    |                    |                           | <i>ADM</i>     | 0.0540        | TargetALS |
|                                    |                    |                           | <i>STC1</i>    | 0.0462        | TargetALS |
|                                    | <i>LINC02080</i>   |                           | 0.00930        | TargetALS     |           |
|                                    | <i>SNX31</i>       |                           | 0.00910        | TargetALS     |           |
|                                    | <i>Lnc-KCTD8-1</i> |                           | 0.00470        | TargetALS     |           |
|                                    | <i>HGFAC</i>       |                           | 0.00260        | TargetALS     |           |

|  |   |                     |          |             |
|--|---|---------------------|----------|-------------|
|  |   | <i>MUC19</i>        | 0.000700 | TargetALS   |
|  |   | <i>SLC22A8</i>      | 0.000700 | TargetALS   |
|  |   | <i>FOXD2</i>        | 0.000500 | TargetALS   |
|  |   | <i>MIR3667HG</i>    | 0.0433   | van Rheenen |
|  |   | <i>COL1A2</i>       | 0.0410   | van Rheenen |
|  |   | <i>SULT1B1</i>      | 0.0395   | van Rheenen |
|  |   | <i>CLEC4E</i>       | 0.0349   | van Rheenen |
|  |   | <i>HSPB7</i>        | 0.0345   | van Rheenen |
|  |   | <i>TENT5C</i>       | 0.0344   | van Rheenen |
|  |   | <i>HSPA1A</i>       | 0.0325   | van Rheenen |
|  |   | <i>VCAM1</i>        | 0.0304   | van Rheenen |
|  |   | <i>ADH1B</i>        | 0.0287   | van Rheenen |
|  |   | <i>VNN2</i>         | 0.0281   | van Rheenen |
|  | 3 | <i>C4A</i>          | 0.321    | TargetALS   |
|  |   | <i>Thioesterase</i> | 0.171    | TargetALS   |
|  |   | <i>RASSF9</i>       | 0.00180  | TargetALS   |
|  |   | <i>FGD2</i>         | 0.0493   | van Rheenen |
|  |   | <i>SLA</i>          | 0.0472   | van Rheenen |
|  |   | <i>TMEM119</i>      | 0.0401   | van Rheenen |
|  |   | <i>PKD1L2</i>       | 0.0325   | van Rheenen |
|  |   | <i>TLR2</i>         | 0.0311   | van Rheenen |
|  |   | <i>GPR62</i>        | 0.0285   | van Rheenen |
|  |   | <i>SERPINA5</i>     | 0.0279   | van Rheenen |
|  |   | <i>RASSF9</i>       | 0.0277   | van Rheenen |
|  |   | <i>AQP1</i>         | 0.0272   | van Rheenen |
|  |   | <i>MYO1G</i>        | 0.0255   | van Rheenen |

Table 7-3. The top 10 most important predictors for each case-control dataset obtained via calculation of SHAP values, for each cluster-based model under scenarios one and two.

Examination of the top 30 most important predictors of each of the cluster-specific models for each scenario in each dataset revealed 19 genes which were shared in at least 2 of the case-control datasets (Table 7-4). Only one gene which resided in cluster one, *CTXN3*, was important in all three case-control datasets when considering all genes in the signature. Regardless of scenario, a total of 8 genes were shared between KCL BrainBank and TargetALS datasets, with 1 present in KCL BrainBank and van Rheenen and 9 in both TargetALS and van Rheenen.

We then performed dominance analysis for the KCL BrainBank, TargetALS and van Rheenen case datasets, to determine key genes which drove assignment into one particular cluster in a one vs rest strategy. For the three strategies, the top 15 predictors (or fewer if 15 predictors were not available) were extracted from each dataset. For the Zucca dataset, permutation importance was performed (as only one



sample was present in clusters two and three), with the top 45 predictors extracted and combined with the results from the dominance analysis before identifying the shared genes. There were a total of 15 genes which were shared key drivers of cluster assignment in at least two datasets (Table 7-5). Interestingly, the drivers of assignment in the cluster two vs others and cluster three vs others strategies are assigned to those clusters, but for cluster one vs others, the driver genes are from clusters two and three. This trend continues when looking at the full dominance analysis results for each dataset, available in Tables A41 (cluster one vs others), A42 (cluster two vs others) and A43 (cluster 3 vs others). This suggests that the cluster one gene signature is not distinct enough in individuals assigned to this cluster: instead, perhaps the divergence in the gene expression profiles of the other clusters is driving their assignment. This is feasible, especially given that the linear discriminant analysis model is constrained to assign samples to one of the three clusters. Regardless, the McFadden's pseudo R-squared of each dataset under each scenario (Tables A41, A42 and A43) ranged from 0.34 to 0.89, which indicates that the top predictors contribute to a good to excellent model fit. The full permutation importance results for the Zucca dataset is available in Table A44.

| Scenario                           | Cluster | Gene Symbol                   | Datasets                              |                        |
|------------------------------------|---------|-------------------------------|---------------------------------------|------------------------|
| 1<br>(All Genes)                   | 1       | <i>CTXN3</i>                  | KCL BrainBank, TargetALS, van Rheenen |                        |
|                                    |         | <i>NPY2R</i>                  | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>AKAIN1</i>                 | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>CR2</i>                    | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>DUSP4</i>                  | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>LINC02427</i>              | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>HSD11B1</i>                | KCL BrainBank, van Rheenen            |                        |
|                                    |         | <i>OSTN</i>                   | TargetALS, van Rheenen                |                        |
|                                    |         | <i>CRH</i>                    | TargetALS, van Rheenen                |                        |
|                                    |         | <i>GATD3</i>                  | TargetALS, van Rheenen                |                        |
|                                    | 2       | 2                             | <i>IGFN1</i>                          | TargetALS, van Rheenen |
|                                    |         |                               | <i>HILPDA/C7orf68</i>                 | TargetALS, van Rheenen |
|                                    |         |                               | <i>PLA1A</i>                          | TargetALS, van Rheenen |
| <i>VNN1</i>                        |         |                               | TargetALS, van Rheenen                |                        |
| 3                                  | 3       | <i>TNFSF14</i>                | TargetALS, van Rheenen                |                        |
| 2<br>(Removal of Correlated Genes) | 1       | <i>LERFS</i>                  | KCL BrainBank, TargetALS              |                        |
|                                    |         | Antisense to <i>ADTRP</i>     | KCL BrainBank, TargetALS              |                        |
|                                    |         | <i>LOC124908056/LINC01830</i> | KCL BrainBank, TargetALS              |                        |

|  |   |                |                            |
|--|---|----------------|----------------------------|
|  |   | <i>DUSP4</i>   | KCL BrainBank, TargetALS   |
|  |   | <i>HSD11B1</i> | KCL BrainBank, van Rheenen |
|  |   | <i>GATD3</i>   | TargetALS, van Rheenen     |
|  | 3 | <i>RASSF9</i>  | TargetALS, van Rheenen     |

Table 7-4. Shared predictors for each case-control dataset obtained via calculation of SHAP values, for each cluster-based model under scenarios one and two. These were determined based on the top 30 predictors for each dataset.

| Scenario (one vs (rest))               | Gene Symbol      | Cluster | Datasets                   |
|--|------------------|---------|----------------------------|
| Cluster 1 vs (Cluster 2 and Cluster 3) | <i>CD44</i>      | 3       | TargetALS, KCL BrainBank   |
|  | <i>CP</i>        | 2       | TargetALS, KCL BrainBank   |
|  | <i>COL14A1</i>   | 2       | KCL BrainBank, van Rheenen |
|  | <i>LINC01088</i> | 2       | TargetALS, Zucca           |
|  | <i>CPAMD8</i>    | 2       | TargetALS, Zucca           |
|  | <i>TNFSF14</i>   | 3       | TargetALS, Zucca           |
|  | <i>ADGRE1</i>    | 3       | KCL BrainBank, Zucca       |
|  | <i>PDLIM1</i>    | 2       | van Rheenen, Zucca         |
| Cluster 2 vs (Cluster 1 and Cluster 3) | <i>SLC22A2</i>   | 2       | TargetALS, KCL BrainBank   |
|  | <i>ACTG2</i>     | 2       | TargetALS, KCL BrainBank   |
|  | <i>ITGA5</i>     | 2       | KCL BrainBank, van Rheenen |
|  | <i>MYL9</i>      | 2       | KCL BrainBank, van Rheenen |
|  | <i>COL14A1</i>   | 2       | KCL BrainBank, van Rheenen |
|  | <i>IHO1</i>      | 2       | TargetALS, Zucca           |
| Cluster 3 vs (Cluster 1 and Cluster 2) | <i>HOXD3</i>     | 3       | KCL BrainBank, van Rheenen |
|  | <i>LRRRC63</i>   | 3       | TargetALS, KCL BrainBank   |
|  | <i>ADGRE1</i>    | 3       | KCL BrainBank, Zucca       |
|  | <i>TNFSF14</i>   | 3       | KCL BrainBank, Zucca       |
|  | <i>PDLIM1</i>    | 2       | KCL BrainBank, Zucca       |

Table 7-5. Shared top predictors of the case datasets with dominance analysis (KCL BrainBank, TargetALS, van Rheenen) and permutation importance (Zucca). For each one vs rest scenario, the gene and original cluster assignment is shown, along with the datasets the respective genes are found to be highly predictive in. For the Zucca dataset, dominance analysis could not be performed as there was perfect convergence between class assignment, given only one sample resided in clusters two and three, therefore, the shared predictor genes for this dataset were taken from the top 45 genes identified with permutation importance, which was ran with 50 iterations.

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### **7.5.5 Cell composition analysis of the ALS motor cortex reinforces the biological interpretation of each molecular subtype**

When performing cell deconvolution analysis for the KCL BrainBank and TargetALS case datasets, we found that the samples that were assigned to each cluster had distinctive cell-type profiles, which were reflective of the predominant biological processes of each molecular phenotype. These profiles were almost identical in both datasets (Figure 7-7), with significant overall differences in the proportion of all five cell types. Samples residing in cluster one had a significantly higher proportion of neurons compared to clusters two and three. A higher proportion of astrocytes and endothelial cells were present in samples assigned to cluster two than in cluster one, whilst samples residing in cluster three displayed higher proportions of microglia than cluster one, and oligodendrocytes than clusters one and two. The full results are available in Tables A45 (KCL BrainBank) and A46 (TargetALS).

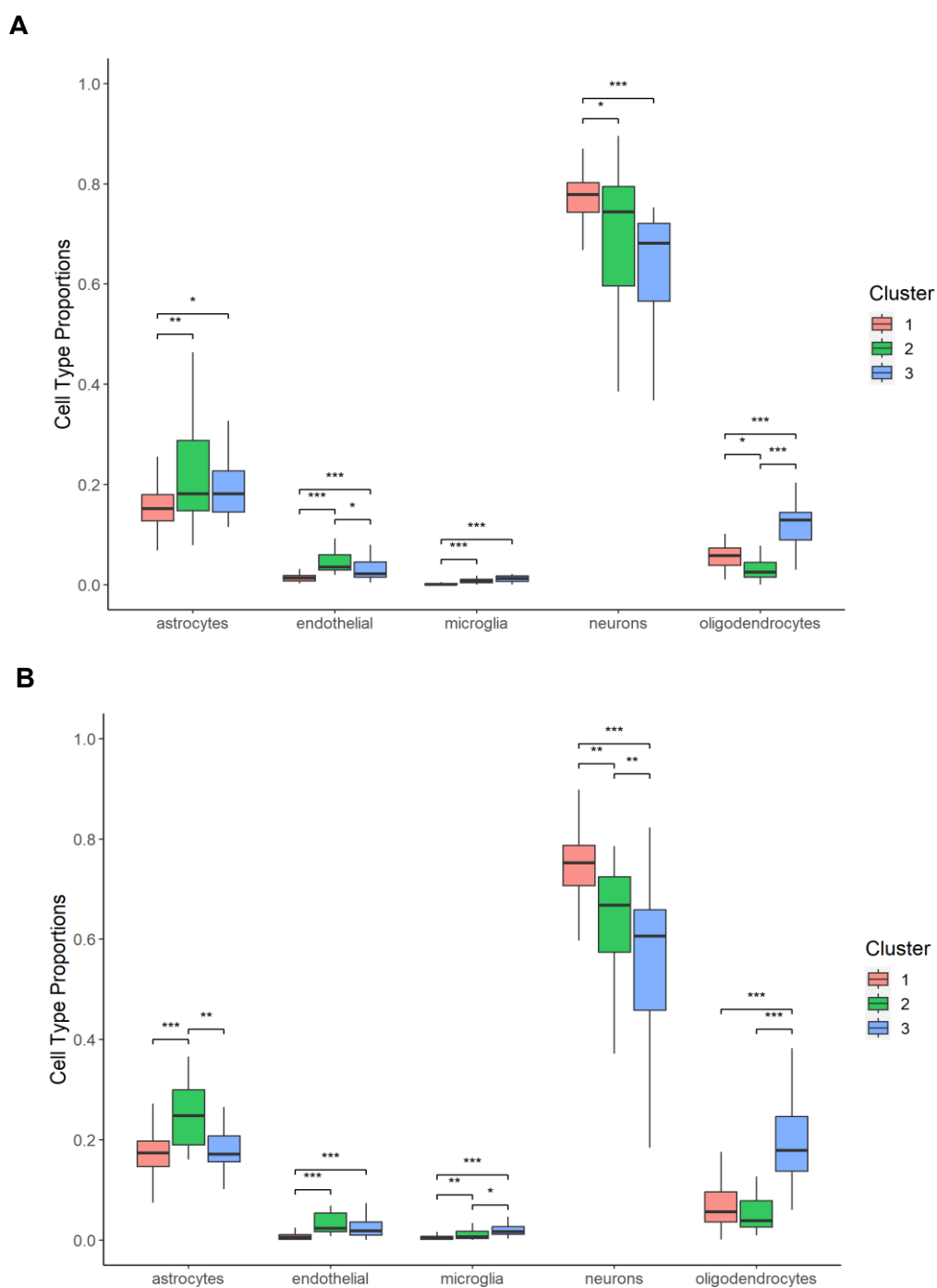


Figure 7-7. Results of the cell type deconvolution analysis for A) KCL BrainBank cases and B) TargetALS cases. Results were corrected for age of death and sex assigned at birth. Asterisks refer to one-way ANCOVA post-hoc Tukey p-values: \* < 0.05, \*\* < 0.01, \*\*\* < 0.001.

### 7.5.6 Cluster assignment is correlated with different clinical outcomes and omics measures

In both KCL BrainBank and TargetALS, we observed that cluster two demonstrated differences in several phenotypic and omics measures (full results available in Table 7-6). For instance, cluster two compared to cluster one had a higher age of death (Figures 7-8A and 7-8B) and smaller transcriptional age acceleration (Figures 7-8C and 7-8D). This trend continues when looking at variables present in one of the two datasets, with a 3.87 year slower biological age acceleration being observed in cluster two compared to cluster three in KCL BrainBank ( $p=0.020$ ), and a longer but albeit non-significant increase in disease duration in TargetALS samples assigned to cluster two. We also found trends for higher mitochondrial DNA copy number in cluster one, and shorter telomere length in cluster 3 in KCL BrainBank samples (Table 7-2). When assessing differences in age of onset based on samples combined from KCL BrainBank and TargetALS, we found that samples residing in cluster one had a lower age of onset compared to clusters two and three (Figure 7-8E;  $p=0.013$ ). For the Zucca and van Rheenen datasets, there was no significant alteration in age of onset and transcriptional age acceleration between clusters, although samples assigned to the van Rheenen dataset displayed a borderline significant increase in transcriptional age acceleration and also reduced disease duration, which contradicts what was found in the motor cortex datasets.

When assessing potential differences in the site of onset between clusters, we found that in KCL BrainBank, there was a borderline significant difference in the proportion of people with limb-onset SALS assigned to the clusters ( $X^2 = 6.05$ ,  $p\text{-value} = 0.05$ ). Bulbar-onset and combined limb and bulbar onset SALS were not overrepresented in any of the clusters (bulbar:  $X^2 = 0.18$ ,  $p\text{-value} = 0.91$ ; limb and bulbar:  $X^2 = 0.95$ ,  $p\text{-value} = 0.62$ ). As found with the KCL BrainBank dataset, the proportion of limb-onset TargetALS cases differed significantly between clusters ( $X^2 = 13.49$ ,  $p\text{-value} = 1.2E-03$ ). The distribution of bulbar-onset cases also varied significantly ( $X^2 = 20.10$ ,  $p\text{-value} = 4.3E-05$ ). There was no difference in the proportion of *C9orf72*-positive ( $X^2 = 3.45$ ,  $p\text{-value} = 0.18$ ) or combined limb and bulbar onset cases ( $X^2 = 3.25$ ,  $p\text{-value} = 0.20$ ). In the van Rheenen dataset, there was no association between limb: bulbar ratio and cluster assignment ( $X^2 = 1.78$ ,  $p\text{-value} = 0.41$ ). Across the three case-only datasets,

there was no difference in the male:female ratio (TargetALS:  $X^2 = 2.48$ , p-value = 0.29; Zucca:  $X^2 = 2.02$ , p-value = 0.36; van Rheenen:  $X^2 = 0.88$ , p-value = 0.64).

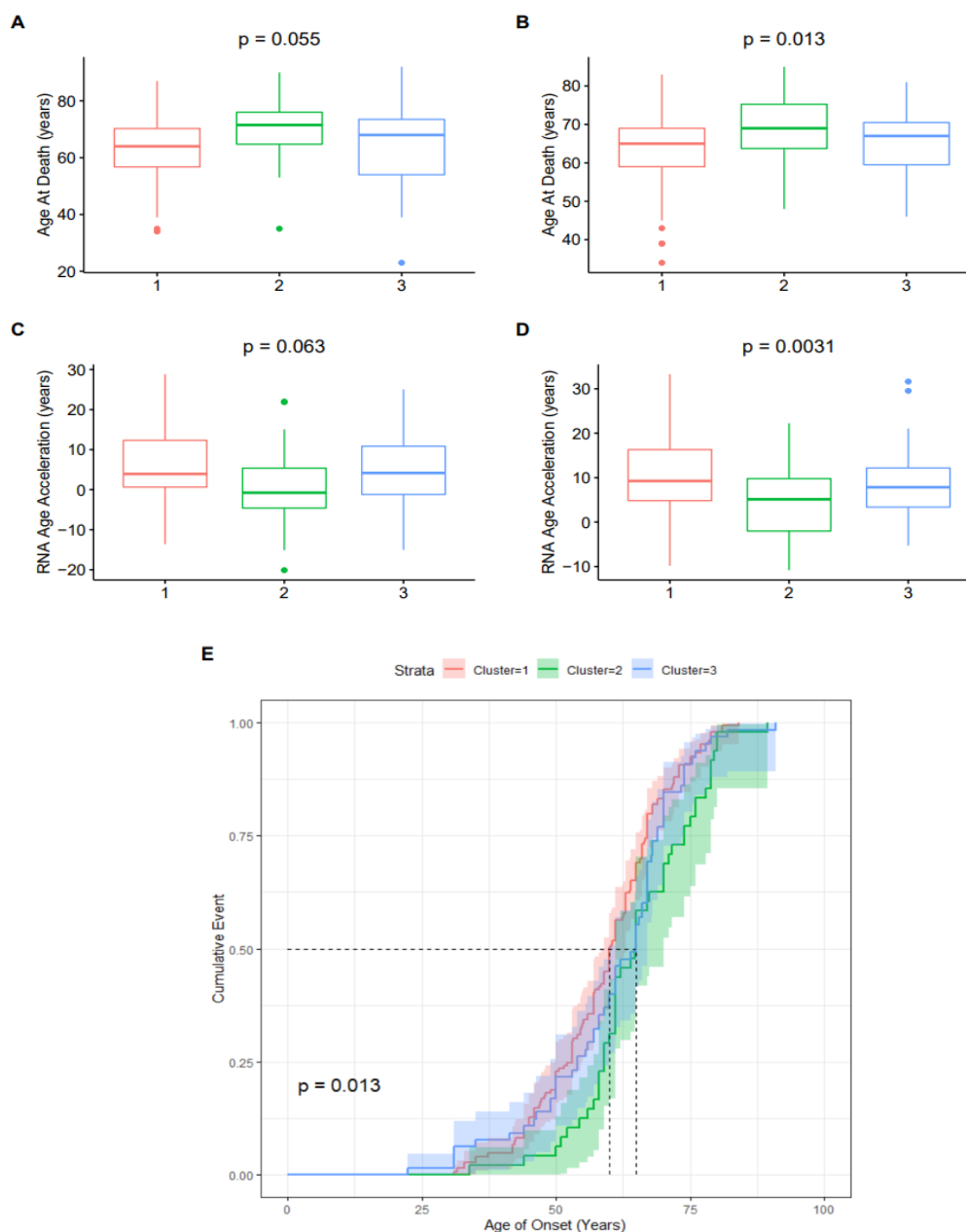


Figure 7-8. Subgroup phenotype analysis between samples residing in each cluster for KCL BrainBank and TargetALS. Variables visualised here includes the age of death for A) KCL BrainBank and B) TargetALS, and transcriptional age acceleration for C) KCL BrainBank and D) TargetALS. P-values are from performing one-way ANCOVA, corrected for sex. E) Cox proportional hazards model for the age of onset of samples from both BrainBank and TargetALS datasets, showing that samples from Cluster 1 have a significantly lower age of onset than Clusters 2 and 3.

| <b>KCL BrainBank (motor cortex)</b> |  |   |   |
|-------------------------------------|--|---|---|
| <b>Phenotype</b>                    | <b>Normality (Shapiro-Wilk <i>W</i>, <i>p</i>-value)</b> | <b>One-Way ANCOVA (F-statistic, <i>p</i>-value)</b> | <b>Post-Hoc Analysis (Tukey <i>p</i>-value)</b>     |
| Age at Onset                        | 0.983, 0.22  | 2.160, 0.121  | 1 vs 2; 0.107, 1 vs 3; 0.622, 2 vs 3; 0.569         |
| Age at Death                        | 0.976, <b>0.042</b>                                      | 2.979, 0.055  | 1 vs 2; 0.051, 1 vs 3; 0.988, 2 vs 3; 0.168         |
| Disease Duration (years)            | 0.943; <b>3.5E-04</b>                                    | 4.211; <b>0.018</b>                                 | 1 vs 2; <b>0.036</b> , 1 vs 3; 0.092, 2 vs 3; 0.890 |
| Post-mortem Delay                   | 0.951, <b>4.4E-04</b>                                    | 0.178, 0.837  | 1 vs 2; 0.997, 1 vs 3; 0.851, 2 vs 3; 0.855         |
| mtDNA Coverage                      | 0.944, <b>3.2E-04</b>                                    | 1.886, 0.157  | 1 vs 2; 0.988, 1 vs 3; 0.145, 2 vs 3; 0.294         |
| mtDNA Copy Number                   | 0.966; <b>9.9E-03</b>                                    | 1.643, 0.199  | 1 vs 2; 0.231, 1 vs 3; 0.458, 2 vs 3; 0.945         |
| Telomere Length                     | 0.972, <b>0.028</b>                                      | 2.451, 0.092  | 1 vs 2; 0.810, 1 vs 3; 0.074, 2 vs 3; 0.350         |
| Biological Age Acceleration         | 0.971, <b>0.025</b>                                      | 3.858, <b>0.025</b>                                 | 1 vs 2; 0.110, 1 vs 3; 0.414, 2 vs 3; <b>0.020</b>  |
| RNA Age Acceleration                | 0.981, 0.142   | 2.847, 0.063  | 1 vs 2; 0.055, 1 vs 3; 0.973, 2 vs 3; 0.203         |
| <b>TargetALS (motor cortex)</b>     |  |   |   |
| <b>Phenotype</b>                    | <b>Normality (Shapiro-Wilk <i>W</i>, <i>p</i>-value)</b> | <b>One-Way ANCOVA (F-statistic, <i>p</i>-value)</b> | <b>Post-Hoc Analysis (Tukey <i>p</i>-value)</b>     |
| Age at Onset                        | 0.977, <b>7.1E-03</b>                                    | 2.463, 0.088  | 1 vs 2; 0.075, 1 vs 3; 0.968, 2 vs 3; 0.194         |
| Age at Death                        | 0.984, 0.053   | 4.456, <b>0.013</b>                                 | 1 vs 2; <b>0.009</b> , 1 vs 3; 0.765, 2 vs 3; 0.089 |
| Diagnostic Delay                    | 0.776, <b>2.9E-14</b>                                    | 0.926, 0.398  | 1 vs 2; 0.840, 1 vs 3; 0.373, 2 vs 3; 0.867         |
| Disease Duration (years)            | 0.705, <b>2.2E-16</b>                                    | 2.403, 0.094  | 1 vs 2; 0.114, 1 vs 3; 0.944, 2 vs 3; 0.110         |
| Post-mortem Delay                   | 0.883, <b>6.8E-10</b>                                    | 1.176, 0.311  | 1 vs 2; 0.892, 1 vs 3; 0.405, 2 vs 3; 0.349         |
| RNA Age Acceleration                | 0.989, 0.292   | 6.004, <b>3.1E-03</b>                               | 1 vs 2; <b>0.002</b> , 1 vs 3; 0.420, 2 vs 3; 0.092 |
| <b>Zucca (blood)</b>                |  |   |   |
| <b>Phenotype</b>                    | <b>Normality (Shapiro-Wilk <i>W</i>, <i>p</i>-value)</b> | <b>One-Way ANCOVA (F-statistic, <i>p</i>-value)</b> | <b>Post-Hoc Analysis (Tukey <i>p</i>-value)</b>     |
| Age at Onset                        | 0.926, 0.242   | 0.078, 0.926  | 1 vs 2; 0.926, 1 vs 3; 0.987, 2 vs 3; 0.986         |
| RNA Age Acceleration                | 0.990, 0.999   | 0.178, 0.839  | 1 vs 2; 0.868, 1 vs 3; 0.936, 2 vs 3; 0.992         |
| <b>van Rheenen (blood)</b>          |  |   |   |
| <b>Phenotype</b>                    | <b>Normality (Shapiro-Wilk <i>W</i>, <i>p</i>-value)</b> | <b>One-Way ANCOVA (F-statistic, <i>p</i>-value)</b> | <b>Post-Hoc Analysis (Tukey <i>p</i>-value)</b>     |
| Age at Onset                        | 0.975, <b>2.0E-06</b>                                    | 2.282, 0.103  | 1 vs 2; 0.100, 1 vs 3; 0.738, 2 vs 3; 0.634         |
| Disease Duration (years)*           | 0.815; <b>&lt; 2.2E-16</b>                               | 0.00950, 0.991                                      | 1 vs 2; 0.990, 1 vs 3; 1.000, 2 vs 3; 0.992         |
| RNA Age Acceleration                | 0.973, <b>9.1E-07</b>                                    | 2.788, 0.063  | 1 vs 2; 0.082, 1 vs 3; 0.479, 2 vs 3; 0.787         |

Table 7-6. Statistical results of clinical and omics-based phenotype analysis. Variables that demonstrated non-normality via Shapiro Wilk were log transformed before running one-way ANCOVA (corrected for sex) and post-hoc Tukey's to assess cluster-specific trends. \* Disease duration was calculated using all of the data, regardless of censoring status.

## 7.6 Discussion

In this study, we used KCL BrainBank motor cortex gene expression data and machine learning to identify expression signatures which constitute three biologically homogeneous subgroups of SALS: synaptic and neuropeptide signalling (cluster one), oxidative stress and apoptosis (cluster two), and neuroinflammation (cluster three). These molecular phenotypes reflect three previously hypothesised key mechanisms of ALS pathogenesis, which have recently been identified using a deep learning-based approach, albeit using expression data from human iPSC-derived *C9orf72*, *TARDBP*, *SOD1* and *FUS* mutant motor neurons (Catanese et al., 2023). The biological interpretation of each cluster is further reinforced by the fact that in KCL BrainBank and TargetALS case datasets, there are significantly higher proportions of neurons, endothelial cells, and microglia in clusters one, two and three, respectively.

Genes which constitute the three main subgroups of cortical inhibitory GABAergic interneurons (*PVALB*, *SST*, *VIP*) were identified in cluster one (Tremblay et al., 2016), which is interesting given alterations in their excitability patterns cause global hyperexcitability of corticospinal neurons (Brunet et al., 2020), of which has long been hypothesised as a trigger for the spread of ALS pathology (Eisen et al., 2017; Scekcic-Zahirovic et al., 2021). There were also several informative genes related to body mass index, metabolism, and energy homeostasis (*LINC01844*, *ADCYAP1*, *CRH*, *CRHBP*, *CARTPT*, *VGF*). These processes are linked with worse survival and progression outcomes in ALS (Dardiotis et al., 2018; He et al., 2022; Jésus et al., 2018; Steyn et al., 2018).

Several oxidative stress, apoptosis and muscle system related enrichments defined cluster two, as well as anti-inflammatory signalling processes. In fact, this cluster contained several neuroprotective microglial secretory markers (*IL4R*, *TGFB111*, *TGFBI*, *CD163*) (Jurga et al., 2020), as well as the *MMP9* metalloproteinase gene, whose knockdown slows disease progression in ALS mutant models (Kaplan et al., 2014; Kiaei et al., 2007; Spiller et al., 2016). With microglia contributing minimally to this cluster, based on cell deconvolution analysis of KCL BrainBank cases, and better clinical and omics-based age outcomes defining the clusters phenotypic profile in this dataset, we can postulate that a reversal of pro-inflammatory processes may be occurring in this SALS subpopulation. This is further supported by evidence that knockout of the ALS risk gene *CAV1* (Cooper-Knock et al., 2021) in endothelial cells,



whose proportion in samples assigned to this cluster was significantly higher, can reduce innate immune system signalling via activation of endothelial nitric oxide synthase (*NOS3*) (Mirza et al., 2010); a complex of which was observed in our enrichment analysis. Moreover, this cluster was enriched for several potential microRNA biomarkers. The most encouraging in terms of its impact on the molecular phenotype are miR-335-5p and miR-29b-3, as they are downregulated in ALS patients (Banack et al., 2022). Additionally, their downregulation in model systems induces reactive oxygen species-mediated excitotoxicity (De Luna et al., 2020), and intrinsic apoptosis mediated motor neuron loss (Klatt et al., 2019); key processes which defined this cluster.

In cluster three, there was clear involvement of the major histocompatibility complex class II and the HLA complex (*HLA-DRA*, *HLA-DMB*, *HLA-DOA*, *HLA-DPA1*, *HLA-DRB1*, *HLA-DRB5*, *HLA-DRB6*), M1 or activated microglia (*CD14*, *CD86*, *TREM2*, *TYROBP*, *TMEM119*, *TMEM125*) (Jurga et al., 2020), and pro-inflammatory metalloproteinases (*MMP14*), as well as many immune related genes which were identified in other motor cortex and spinal cord SALS expression studies (Aronica et al., 2015; Dols-Icardo et al., 2020; Humphrey et al., 2023). The tentative ALS-related modifier gene *CX3CR1* (Lopez-Lopez et al., 2014)), which is thought to protect against proinflammatory processes and microglial-induced neuronal cell loss (C. Liu et al., 2019), was also present in this cluster. Several well studied serum and CSF biomarkers of ALS progression were also present, such as *SPP1* (de Luna et al., 2022), the human chitinases *CHI3L1* and *CHI3L2* (Thompson et al., 2019; Vu et al., 2020), and complement C3 (Thompson et al., 2022), in addition to prognostic and predictive CSF biomarkers such as *TREM2*, *LILRA2* and *ITGB2* (Cooper-Knock et al., 2017).

We also demonstrated that these molecular phenotypes can also define distinct subgroups of people with SALS across independent motor cortex (TargetALS) and blood (Zucca et al.; van Rheenen et al.,) datasets of European ancestry, by applying separate linear discriminant models trained on the KCL BrainBank case-derived sample assignments and gene intersections. The average probability of being assigned to the cluster that the samples from each dataset were allocated to was very high (between 0.8-0.9). Because this model is constrained to assign samples to one class, the same approach was carried out in three additional control datasets (KCL

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BrainBank, TargetALS, van Rheenen et al.), and the occipital cortex and cerebellum of TargetALS, which yielded varying results. All KCL BrainBank controls were assigned to cluster one, whereas for the TargetALS and van Rheenen control datasets, the probability estimates for cluster assignment were similar to cases, with similar average probability estimates found for the TargetALS datasets from other regions compared to the motor cortex. With the exception of KCL BrainBank controls, the cluster stability estimates were robust for the motor cortex and other region control dataset, which demonstrates that the cluster assignments are valid. When also performing reverse validation by applying hierarchical clustering to the TargetALS motor cortex dataset and comparing the grouping of samples to the linear discriminant analysis derived assignments with KCL BrainBank-derived clusters and genes, we found a 67-81% overlap in sample assignment which demonstrates that the cluster assignments, regardless of gene composition, is adequate.

Because the probability estimates for cluster assignments were comparable in cases and controls, we cannot confidently state that the entirety of the informative genes within each molecular phenotype are ALS-specific, but we can identify differential drivers of assignment within and across clusters by comparing cases and controls that fall into each. To determine if the expression signature of cluster one could distinguish between cases and controls in KCL BrainBank, we constructed a logistic regression classifier and found that the signature had excellent discriminative power, which indicates that expression of certain genes in this molecular phenotype are differentially regulated in ALS. This was also aided by the fact that when supplying the classifier with sets of random genes, the performance is the same as what would be expected by chance. Case-control logistic regression classifiers were also constructed for each cluster with TargetALS and van Rheenen motor cortex datasets. We discovered that regardless of dataset, the gene signature of each molecular phenotype had excellent power in discriminating cases from controls, indicating again that expression of certain genes in this molecular phenotype are differentially regulated in ALS. Furthermore, key driver analysis of the case-only datasets revealed that there was considerable overlap in genes which determine a sample assignment to one cluster over another, which reinforces the robustness of cluster assignments across datasets.

Analysis of the 30 most important predictors for each model revealed a total of 19 genes (13 in cluster one, 4 in cluster two, and 2 in cluster three) which were shared in

at least two case-control datasets. Only one gene, *CTXN3*, which is part of cluster one, was present in all three datasets when all genes in the molecular phenotype were used to construct the model. *CTXN3*, which encodes for the highly conserved integral membrane protein cortexin 3, resides in the genomic region which has been associated with schizophrenia (5q23.2-q34) in individuals of European ancestry (Lewis et al., 2003), with the AG genotype of the rs6595788 polymorphism conferring a 1.5 fold increase in schizophrenia risk in males (Šerý et al., 2015). This is an interesting result as ALS and schizophrenia overlap in terms of their genetic correlations, heritability and polygenic risk scores (McLaughlin et al., 2017; Spargo et al., 2023). Other notable genes which were shared predictors in both motor cortex and blood tissues and therefore show potential for further investigation as potential patient stratification biomarkers includes the cluster one genes *CRH*, *HSD11B1*, and *LERFS*, and the cluster two genes *PLA1A* and *VNN1*. Both *CRH*, which encodes for corticotrophin releasing hormone, and *HSD11B1*, which encodes for the 11-beta hydroxysteroid dehydrogenase type 1 enzyme, modulate the hypothalamic-pituitary-adrenal (HPA) axis, which is primarily responsible for regulating the stress response. Dysregulation of the HPA axis can induce alterations in autonomic nervous system responses, which has been consistently reported as a main non-motor symptom in ALS (Papadopoulou et al., 2022; Pimentel et al., 2019; Shojaie et al., 2023). HPA axis dysregulation is also linked to cortical hyperexcitability and changes in metabolism, which as previously mentioned, is a predominant molecular process which defines cluster one and is linked to differential outcomes in ALS. Release of CRH has also been associated with a reduction in mitochondrial activity and accompanying modification of neuronal activity in hippocampal neurons (Battaglia et al., 2020); two other processes which define the cluster one phenotype. Furthermore, *LERFS*, a non-coding RNA gene, interacts with heterogeneous nuclear ribonucleoprotein Q, which is present in cytoplasmic and internuclear inclusions of people with FTLD-FUS (Gittings et al., 2019). With regard to cross-tissue predictors of cluster two, *VNN1* (vanin 1) plays a role in regulating the glutathione-dependent oxidative stress response (Berruyer et al., 2004). Dysregulation of glutathione metabolism is thought to be one harbinger of reactive oxygen species-mediated toxicity contributing to ALS pathogenesis (K. Kim, 2021), with reduced levels of glutathione reported in the CSF of people with ALS (Tohgi et al., 1999). Finally, *PLA1A* (phospholipase A1 member A)

is responsible for regulating the phosphorylation and kinase activity of *TBK1* (X. Gao et al., 2018), which is a causative ALS gene (Cirulli et al., 2015; Freischmidt et al., 2015) whose missense mutations contribute to protein aggregation via defects in autophagy and mitophagy (Gerbino et al., 2020; Harding et al., 2021); another key element of the molecular phenotype of this cluster. We noticed that for the van Rheenen dataset, the predictor that was driving the perfect discrimination in cluster one was *NME1* (nucleoside diphosphate kinase A), as removing this from the model led to a 35% decrease in discriminative power. Not much is known about *NME1* in relation to ALS, although a recent study revealed that its overexpression can stimulate neurite outgrowth and increase mitochondrial function in cell models of Parkinson's disease (Anantha et al., 2022).

In regard to the sample assignment to different clusters, specifically cluster one, the proportion of samples varied based on tissue type (approximately 60% for the motor cortex versus 85% for the blood datasets). A potential explanation for this is that as the motor cortex represents the end stage of disease, perhaps other biological processes explained by the remaining molecular phenotypes more strongly influence the progression of disease in samples assigned to those clusters. This may not be as apparent in the blood datasets given that the samples were collected at different stages of the disease.

We also discovered that there were distinct clinical and omics-related outcomes that correlated with cluster assignment in both motor cortex case datasets. Cluster two was associated with a higher age of death and longer disease duration, accompanied by a decrease in transcriptional age acceleration. There are several plausible explanations as to why this trend was observed; the first is that more people assigned to this cluster may have had a history of Riluzole usage than other clusters, as it modulates apoptosis, autophagy and other excitotoxicity-related processes which are prevalent biological processes in this cluster (Koh et al., 1999; Storch et al., 2000). Another possibility is that genomic variants present in inflammatory genes assigned to this cluster may diminish their effects. This theory is supported by the example of *IL18RAP*, which is an M1 secretory marker present in this cluster (Jurga et al., 2020), of whom 3'UTR variants were recently found to protect against ALS, by impeding microglial-dependent motor neuron degeneration (Eitan et al., 2022). However, this must be interpreted with caution as information on Riluzole usage was not available, and

genetic data was not used in this study. In KCL BrainBank cases assigned to cluster two, there was also a significant decrease in biological age acceleration. Whether this phenomena is also apparent in TargetALS, and the blood datasets could not be analysed because biological age acceleration could only be measured in KCL BrainBank as there was matching epigenetic information available. However, this warrants further investigation in additional datasets as evidence links increased serum levels of the chronic inflammation marker suPAR, encoded by the cluster two gene *PLAUR*, with higher biological age acceleration in the normal population (Rasmussen et al., 2021). Telomere length was shorter in cluster three in KCL BrainBank, which despite being non-significant, is also an important trend to investigate as although mounting evidence supports the association between longer telomere length and worsened severity of ALS (Al Khleifat et al., 2019; Al Khleifat, Iacoangeli, Jones, et al., 2022), there is also an established link between chronic inflammatory states and telomere shortening in aging and disease (Jurk et al., 2014; Lex et al., 2020; Niveta et al., 2022). Finally, we found that samples in cluster one had a lower age of onset in a combined analysis of KCL BrainBank and TargetALS, which makes sense given that this cluster is linked to neuronal dysfunction and therefore motor neuron degeneration. The proportion of people with limb-onset ALS assigned to the clusters also differed significantly in both motor cortex datasets. Despite the association between distinct age of onset with each cluster in the motor cortex datasets, this was not replicated in the blood datasets, therefore further examination is needed to establish if clear phenotype differences exist across clusters.

There are several limitations of this study which will require further investigation in the context of our findings. First, only samples belonging to the KCL BrainBank dataset had matching multi-omics data, which meant that cluster-specific effects on omics variables could not be assessed in the other datasets. Likewise, both blood datasets had limited clinical information, which did not allow us to validate all possible clinical phenotype associations. Furthermore, the van Rheenen blood dataset did not replicate the association between disease duration and age at onset with class membership, with the opposite trends occurring for disease duration and transcriptional age with cluster two, and age of onset with cluster one. Some potential explanations are that microarray technology was used to obtain the transcriptomic profiles in this dataset, translating in a lower number of genes available that were part of the subtype

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signatures and lower class assignment accuracy. Indeed, clusters two and three represented approximately 25% of ALS patients each in the brain datasets, while only ~8% each in the van Rheenen blood dataset. Moreover, the Dutch population might present a more distinct structure compared to other European countries (Byrne et al., 2020). Also, as this dataset has nearly twice the number of controls than cases, the effects of the predictor genes, specifically *NME1* in cluster one, for discriminating cases and controls needs to be evaluated, despite our analysis oversampling for the minority class to address class imbalance before supplying to the classifier models. Finally, we did not integrate genomic variants into our analysis to further enhance our molecular classification, like recent studies that built upon their previous clustering analyses (La Cognata et al., 2020; Morello et al., 2019), as this would have resulted in underpowered analyses given our sample sizes, or correlated our clustering findings with neuropathological findings and co-existing pathologies in the motor cortex datasets, as this data was not available to us when the study took place. As we did not perform a comparative analysis of the cluster assignment of people with familial ALS or other neurodegenerative diseases i.e., FTD, Parkinson's disease, we cannot be absolutely sure that the molecular phenotypes identified in this study are truly ALS-specific. Although, we can discern that the expression of genes in these phenotypes that distinguish cases from controls represent sporadic ALS subtypes as the clusters were validated in three independent ALS datasets which did not contain samples from those with familial ALS. They also represent motor-cortex specific aspects of the disease process as the expression signatures of each molecular phenotype can distinguish samples from the motor cortex from other brain regions for TargetALS cases.

In conclusion, we have demonstrated that people with ALS can be successfully stratified into molecularly distinct subgroups using gene expression data. Our results support the hypothesis that different subgroups could underly previously investigated forms of ALS pathogenesis and can be identified in patients via specific expression signatures. These molecular phenotypes discovered in a UK cohort, were validated in independent motor cortex and blood datasets and could be used to distinguish patients from controls, showing potential to be used for clinical trial stratification and the development of biomarkers for personalised treatments and diagnostics. Our analysis also revealed several known candidate gene biomarkers which could be exploited in

future stratification studies to verify our findings. We have developed a publicly available web app (<https://alsgeclustering.er.kcl.ac.uk>) to allow the broader scientific and clinical community to use our model for the stratification of pre- and post-mortem samples in their studies.

## **Chapter 8. Summary of Findings and Future Directions**

### **8.1 Chapter 4: Development of a next-generation sequencing bioinformatics analysis pipeline**

The development of DNAscan2 expands the potential target audience to include both bioinformaticians and researchers in basic and translational scientific fields with limited access to computational resources and experience in NGS analysis. This application allows for the straightforward and efficient identification and characterisation of several types of genetic variation, which is particularly useful in the big-data era as the popularity of NGS exceeds that of traditional approaches.

Future revisions of the pipeline should focus on incorporating tools which can identify other types of genomic variation which can modulate disease risk and progression, particularly in relation to ALS. These include non-canonical structural variation, such as telomere length and mitochondrial DNA copy number. Telomeres are highly conserved TTAGGG hexameric non-coding DNA repeats responsible for maintaining chromosomal stability and integrity during cellular replication (Shammas, 2011), whilst mitochondrial copy number acts as a proxy for mitochondrial function (O'Hara et al., 2019), which is dysregulated in ALS due to mutations in several ALS-linked genes responsible for regulating varying mitochondrial processes (e.g. *FUS*, *TARDBP*, *SOD1*, *C9orf72*, *CHCHD10*, *TBK1*, *KIF5A*, *VCP*, *VAPB*, *SIGMAR1*, *OPTN*, *SQSTM1*, *ALS2*; (Jankovic et al., 2021)). Decreased telomere length and mitochondrial DNA (mtDNA) copy number have consistently been linked to aging and mortality in both neurologically normal people (Ghimire et al., 2019; Praveen et al., 2020; R. Zhang et al., 2017) and people with Alzheimer's disease (Forero et al., 2016; Guo & Yu, 2019; Wei et al., 2017), however, an opposite trend is noted in ALS, through the adoption of bioinformatics tools. The quantification of telomere length from WGS using the TelSeq tool (Ding et al., 2014) in over 6,500 people with ALS and controls from Project MinE found people with ALS harboured telomere lengths which were 20% longer than

controls, with shorter telomere lengths in people with ALS conferring a 10% increase in survival (Al Khleifat, Iacoangeli, Jones, et al., 2022), in accordance with a previous pilot study in the British cohort of Project MinE (Al Khleifat et al., 2019). Thus, telomere length could be incorporated as a prognostic biomarker. Why telomere lengths seem to be larger in ALS than other neurodegenerative diseases remains unclear, although a Mendelian randomisation study found that in European populations, the changes in telomere length may be driven by low density lipoprotein and overall cholesterol levels (Y. Gao et al., 2020). Likewise, a bioinformatics analysis quantifying leukocyte mtDNA copy number in the Project MinE cohort confirmed that this is increased in ALS after adjusting for mitochondrial haplotype and correlates with worse survival outcomes, albeit with small effect sizes (Harvey et al., 2022). This had previously been found in smaller SALS and FALS cohorts using qualitative PCR (Stocco et al., 2018, 2020). This phenomenon is likely to be representative of a compensatory mechanism against TDP-43 mislocalisation or reduction in mitochondrial energy metabolism function, as demethylation of the regulatory D-loop and mitochondrial haplotype are associated with mtDNA copy number and reduced survival (Harvey et al., 2022; Stocco et al., 2020).

The need for incorporating long-read WGS technology processing and analysis into this pipeline for the identification of other types of structural variation not characterisable with short-read NGS, such as variable number tandem repeats (VNTRs), is also warranted. Despite short-read WGS prevailing in genetic diagnostics and counselling practices, and the population-wide characterisation of genomic variation, complex chromosomal rearrangements, segmental duplications, VNTRs which are longer than the 150-bp read length and repeat expansions with high GC content are notoriously problematic to capture, as coverage, depth and mapping biases incurred by paired-end WGS can make approximately 480kb of protein coding exons (Barbitoff et al., 2020) and nearly 38,000 majority intronic and non-coding RNA regions (Ebbert et al., 2019) inaccessible to conventional alignment tools. Furthermore, most protein coding gene regions are also camouflaged i.e., had low mapping quality due to the presence of segmental duplications and tandem repeats creating multi-mapping reads (Ebbert et al., 2019). Furthermore, as VNTRs are longer than 20 base-pairs in length, this far exceeds the capabilities of current tools employed in this pipeline, such as ExpansionHunter and ExpansionHunterDenovo, which



currently deal with tandem repeats up to 6 base-pairs in length. VNTR profiling in ALS using long-read sequencing is highly relevant as the identification and characterisation of the first SALS-linked 69 base-pair VNTR in the last intron of the vacuolar-ATPase gene *WDR7* was discovered using this technology (Course et al., 2020). As it resides within the ALS3 locus, which has yet to have a causal gene formally linked with it, *WDR7* may be involved in ALS3 pathogenesis. Despite having a similar repeat unit distribution as Parkinson's disease genomes, people with SALS carry higher copy numbers of this VNTR (Course et al., 2020). Furthermore, like TDP-43 and FUS (Lim et al., 2016; Loughlin et al., 2019), this VNTR can also self-interact and form aggregable RNA stem-loop structures, increasing the prospect of its involvement in abnormal DNA repair, transcription and splicing processes.

Besides the addition of tools capable of identifying more complex variation, it is important that the current and future developments to DNAscan2 should incorporate strategies to ensure that the tool reaches the correct target user group. The two key strategies that should be adopted concern wider dissemination of the tool beyond publication (which applies to both current and future versions), and also providing the opportunity for target users to be involved with the implementation of new features. Dissemination of the tool would most likely be achieved via social media platforms such as X/Twitter and LinkedIn, in combination with the departmental and school specific media offices to ensure the tool reaches institutional and scientific audiences as well as the wider bioinformatics community. Up-to-date video walkthrough tutorials for different use cases could also be considered in order to better highlight what the tool delivers. Concerning the implementation of new features in future versions, it would be pertinent to create shareable online surveys (e.g. SurveyMonkey, Google Forms) to allow potential target users to give their opinions and suggestions on what they would like to be added to the tool to enhance their research. This could be followed by further email communication and a user meeting to keep them informed about what suggestions we will be taking forward.

## **8.2 Chapter 5: Investigating the role of *NEFH* as an ALS risk gene**

This study illuminates how performing meta-analyses of the literature and leveraging large-scale WGS data in combination with screening and a variant effect and frequency stratified burden analysis can assist in confirming or discovering variant associations in the *NEFH* gene with ALS susceptibility. We confirmed the association

of rare variants (MAF <1%) in the *NEFH* gene with ALS risk by performing meta-analysis and rare variant burden analysis of a combined cohort of 18,500 people with ALS and controls across previous reports from the literature and Project MinE. Both of these analyses were significant when taking multiple testing into account, highlighting that this result is highly reconcilable. We also revealed that missense tail domain variants likely drove this association, as our variant-based rare meta-analysis of 1164 people with ALS and 2177 controls, for which the majority of variants were pathogenic, and ultra-rare (MAF < 0.1%) burden analysis of pathogenic variants in Project MinE found these to be significantly associated with ALS. Despite the lower OR and nominal association with burden analysis, the direction and size of the effect was similar, which argues for a consistent effect of missense tail variants with ALS susceptibility.

Furthermore, we also found that rare in-frame deletions in the KSP segment of the tail domain nominally confer susceptibility to ALS in Project MinE, which agrees with previous reports using smaller sample sizes and traditional sequencing-based approaches, and that ultra-rare intronic variants in the rod domain were also nominally dominant factors of association with ALS risk in the Project MinE cohort, albeit nominal. Although our SV analysis in Project MinE identified a 113bp deletion in the KEP segment that seems to have a protective effect against ALS, and there is a report of a protective intronic rod domain repeat polymorphism that could be protective also, both of these mutations are common, which indicates that subdomain-specific effects for different classes of variants at different MAF cut-offs may play different roles for ALS susceptibility. This may also be a phenomenon occurring for other causal, modifier or predicted ALS genes, which could not have been investigated using whole exome sequencing and conventional burden analysis, as it usually considers the whole gene, or exons within a gene as the functional unit studied and would therefore dilute any region-specific effects which could span multiple exons. In light of this, I am now currently adopting a large-scale unbiased and systematic genome-wide approach using the burden test framework in the Project MinE cohort to see if mutations of different frequencies and classes that cluster in single annotated protein domains are indeed responsible for driving genetic associations with ALS risk. This is highly relevant given that for example in known ALS genes such as *FUS* and *TARDBP*, the

majority of identified pathogenic missense mutations reside within the nuclear localisation signal domain (Boer et al., 2021; Shang & Huang, 2016).

As the effect of missense *NEFH* variants and the protective 113bp deletion on ALS susceptibility has not been established previously, this finding also opens new avenues for future work in our team to explore if the rare missense variants identified computationally here are not false positives, with qPCR validation. Functional characterisation of selected missense variants could also be carried out to determine their impact on phosphorylation with techniques such as Western blot or ELISA. As for the deletion mutation, it would be better suited to perform in-silico computational dynamics simulations to determine how it could alter the phosphorylation and aggregation propensity of the NF-H protein as it would be quite difficult to introduce such a mutation into a model system.

Despite these findings, the effect sizes of the associations even in this large cohort are fairly small and have nominal significance, which argues against the presence of *NEFH* in genetic screening panels and suggests that perhaps *NEFH* should either remain an amber classification in the NHS screening panel or be classified as red. Of course, further screening and in-silico / model system characterisation needs to be performed to solidify this interpretation.

### **8.3 Chapter 6: Differential gene expression analysis of two large ALS sequencing consortia**

By performing independent differential gene expression in KCL BrainBank and TargetALS bulk RNAseq datasets, we identified ALS gene expression profiles that explicate various biological processes and modulatory themes as harbingers of ALS pathogenesis. There was strong evidence to suggest that alterations in the neuropeptide signalling pathway may be a key feature of the ALS phenotype, as in both cohorts we observed that this pathway was enriched amongst their differentially expressed genes, the melanocortin receptor 4 gene (*MC4R*) was significantly upregulated, and higher expression levels of two neuropeptide-related genes, *TACR1* and *NPBWR1*, correlated with longer disease duration and lower age of onset, respectively. There were also links between many of the 45 common differentially expressed genes with other previously studied themes of ALS pathogenesis, such as lipid metabolism and mitochondrial energy homeostasis.

Despite these findings, there was considerable divergence in the number of differentially expressed genes as well as the overall biological enrichments in the two datasets, which we attributed to the inevitability of differences in RNA collection and storage methods, sample demographics (especially the influence of a significantly older control group in the KCL BrainBank cohort, the gender effect which existed in the TargetALS cohort, and lower RIN numbers and a higher post-mortem delay in controls in both datasets), and populational variability in gene expression.

It is promising that even though these cohorts are inherently different, we managed to find an association with neuropeptide signalling at several levels, although further investigation is warranted to assess the potentiality of neuropeptide-coding genes and regulators of neuropeptide signalling as potential prognostic biomarkers as our results are only suggestive of a potential link between expression levels and modulation of phenotype. Future work therefore will exploit pre-mortem transcript expression of PBMCs and iPSC-derived motor neurons, and serum or CSF-based protein expression in publicly available datasets such as GEO and AnswerALS to confirm if the correlations between *TACR1* and *NPBWR1* remain. If these associations can be replicated, we could generate iPSCs or other cell lines or mice models with overexpression and knockdown of *TACR1* and *NPBWR1*, respectively, to determine if they can improve functional outcomes and alter the efficiency of neuropeptide signalling.

Likewise, because we only performed differential expression analysis for this study, it would be beneficial to implement other expression-based designs, like differential transcript usage and isoform expression analysis and the integration and analysis of alternative splicing variation such as intron retention, and the presence of cryptic exons to quantify splicing alterations at both a global level and for specific enrichments and shared differentially expressed genes observed in our analysis.

#### **8.4 Chapter 7: Utilising hierarchical clustering to identify molecular subtypes of ALS**

We demonstrated that the application of unsupervised machine learning to bulk motor RNAseq expression data of KCL BrainBank can identify three distinct expression signatures which constitute biologically homogeneous subgroups of SALS and contain several known candidate gene biomarkers which could be exploited for further

investigation of SALS heterogeneity. When combined with supervised machine learning trained on KCL BrainBank gene and sample assignments, these molecular phenotypes (synaptic and neuropeptide signalling, oxidative stress and apoptosis, and inflammation) can be used to successfully stratify people with ALS across three independent motor cortex and blood datasets (TargetALS, Zucca, van Rheenen), can distinguish between people with ALS and controls assigned to the same subgroup with high discriminative power and reflect motor-cortex disease relevant signatures as there was near perfect discrimination between motor cortex and other brain regions from TargetALS; the occipital cortex and cerebellum. Although, one limitation of the classification of the molecular subtype expression signatures between the motor cortex and other brain regions is that despite being processed in the same manner as the motor cortex and blood datasets, a different aligner was used to gather raw gene counts for the other regions in TargetALS.

To ensure that each molecular phenotype was robust and valid across datasets, we performed several sanity checks. Firstly, higher proportions of cell types predominantly involved in the biological processes of each molecular phenotype were found in people with ALS from the KCL BrainBank and TargetALS motor cortex datasets, which reinforces their biological interpretation. Moreover, cluster stability estimates were robust for all datasets except KCL BrainBank controls, as they were all assigned to cluster one. Reverse validation by applying unsupervised machine learning to TargetALS motor cortex revealed a 67-81% overlap in sample assignment with grouping using KCL BrainBank-derived clusters, with the performance of the cluster one case-control KCL BrainBank classifier being the same as expected by chance when supplying with 10 sets of random genes instead of the 131-gene signature of the molecular phenotype. Finally, there was a high overlap in the driver genes of sample assignment in the case-only datasets.

Our analysis of the predictors of case-control status in KCL BrainBank, TargetALS and van Rheenen datasets revealed that the schizophrenia-linked gene *CTXN3* was a shared top predictor of cluster one, which offers fresh insights into the well-established similarities in genomic architecture between ALS and schizophrenia. There were also shared predictors in at least two of these datasets; the most remarkable being *CRH*, *HSD11B1* and *LERFS* for cluster one, and *PLA1A* and *VNN1* in cluster two. A logical next step in determining if these are a true predictor of molecular phenotype

assignment is to perform feature ablation studies i.e. remove each gene and then see how the predictor values (feature driver proportion) and posterior probability assignment of molecular phenotype assignment changes.

Assignment to molecular phenotypes were also correlated with differential clinical and omics-based outcomes in the motor-cortex case datasets; individuals assigned to cluster two exhibited with significantly higher age of death, longer disease duration and decrease in transcriptional age acceleration. Therefore, the expression signature of cluster two needs to be investigated in more depth to identify isolated genomic biomarkers of onset and progression.

These molecular phenotypes show great potential to be used in clinical trial settings to prevent enrolment of potential non-responders or stratify people with ALS into appropriate treatment arms. Currently, the individuals' genomic response to a therapeutic being tested in clinical trial is only carried out after the trial has ended, as the primary outcome for the effectiveness of a candidate drug in ALS is a slowing of clinically observable functional decline as assessed with progression severity scales like ALSFRS-R (Cedarbaum et al., 1999). These post-hoc analyses have uncovered important interactions between therapeutics and genetic variation, such as carriers of the C/C genotype and C allele of the *UNC13A* survival modifier-linked SNP (rs12608932). Individuals carrying the C/C genotype had a 30% increase in the probability of survival when treated with lithium carbonate (van Eijk et al., 2017), with the presence of at least one C allele conferring the opposite effect with valproic acid treatment (van Eijk et al., 2020). This result has now led to the creation of a new clinical trial of lithium carbonate specifically for people with ALS that are homozygous for the C allele (Willemse et al., 2022). Despite this, there are a paucity of clinical trial inclusion criteria frameworks or prognostic prediction models of survival and functional decline (Elamin et al., 2015; Kjældgaard et al., 2021; Xu et al., 2021; Westeneng et al., 2018) that incorporate schemes to account for molecular heterogeneity of ALS at the level of recruitment or primary outcome assessment.

We do acknowledge, like in Chapter 6, that there are several factors such as the use of post-mortem tissue, differential RNA expression protocol, and demographic and population-based variability, that could influence the likelihood of belonging to a certain molecular phenotype. Furthermore, we did not supplement this analysis with enough

multi-omics data i.e methylation and genomic variants of informative genes or include data from people with known ALS mutations or other related neurodegenerative diseases, which means that we cannot definitively say that these molecular subtypes are ALS-specific or pinpoint the molecular subtypes to even further defined mechanisms of pathogenesis. This, coupled with the fact that our method did pick up several informative genes for each cluster that have already been recognised as potential candidate biomarkers for ALS stratification, means that I am currently embarking on a larger scale multi-omics stratification study as part of my post-doctoral training to verify our findings.

There are a few avenues which I am going to pursue to improve this method and then hopefully develop a more robust ALS subtype detection tool. For one, I am going to use the method here (LDA projections of molecular subtypes trained on KCL BrainBank gene and sample assignments) with additional pre-mortem datasets from the MNDA collection (static measurements) and AnswerALS (longitudinal) to ascertain if the posterior probabilities of assignment are similar as the other pre-mortem datasets used in Chapter 7. I will then use several different preprocessing, gene/marker selection and machine learning approaches for multi-omics stratification of MNDA and AnswerALS datasets. For feature selection, I will 1) use an unbiased approach like used in Chapter 7 to select the genes with the highest variability, 2) knowledge graph-based methods to refine the gene list to those predicted to be causal for ALS, and 3) use the informative genes identified as those defining the clusters from the hierarchical clustering analysis in Chapter 7. Different machine learning approaches employed depends on the nature of the temporal measurements in the datasets, but for the longitudinal datasets, I would like to use an approach like hidden Markov models, generative adversarial networks or Gaussian processes to determine if cluster assignment remains stable over the time course. For the static datasets, I hope to use latent factor and multi-set correlation based analysis in addition to hierarchical clustering to compare their performance in identification of both expression- and multi-omics-based subtype identification. Throughout this process, I will keep mindful of the limitations that we faced in Chapter 7 regarding how to handle data from different tissues and disease stages, and any possible batch and site effects that arise from utilising several cohorts which may pose issues in training and testing of the models.

## Appendix I. Figures

## Chapter 4

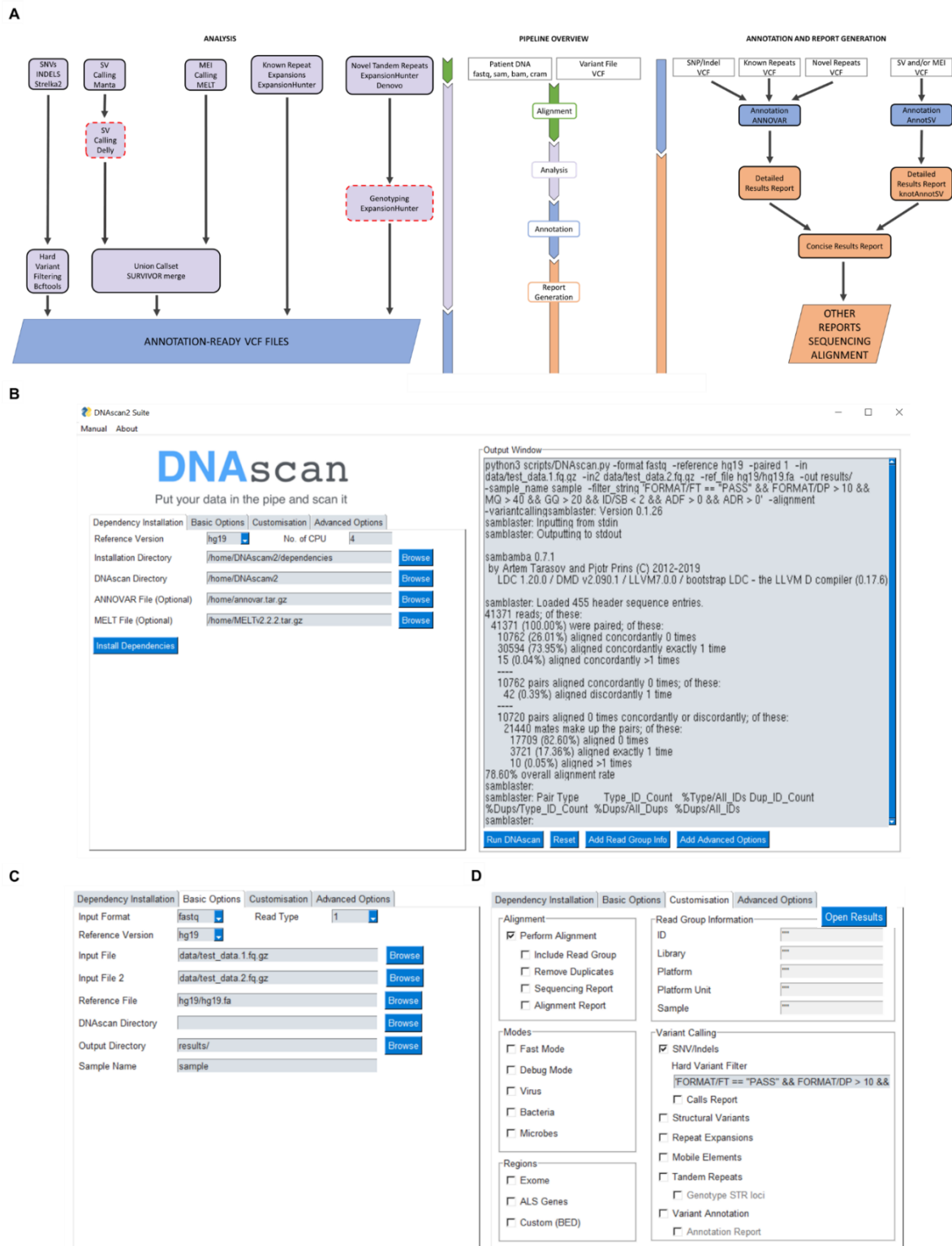


Figure A1. Panel A: Overview of the DNAscan2 pipeline, which consists of four main stages: Alignment, Analysis, Annotation and Report Generation, following input of patient DNA in several different formats. Steps in red dotted lines are removed if the '-fast\_mode' flag is set, which massively increases computational efficiency for those with limited computing resources. Panel B: Screenshot of the main DNAscan2 GUI window with an example alignment and variant calling output. Panel C: 'Basic Options' tab displaying the default settings. Panel D: 'Customisation' tab.



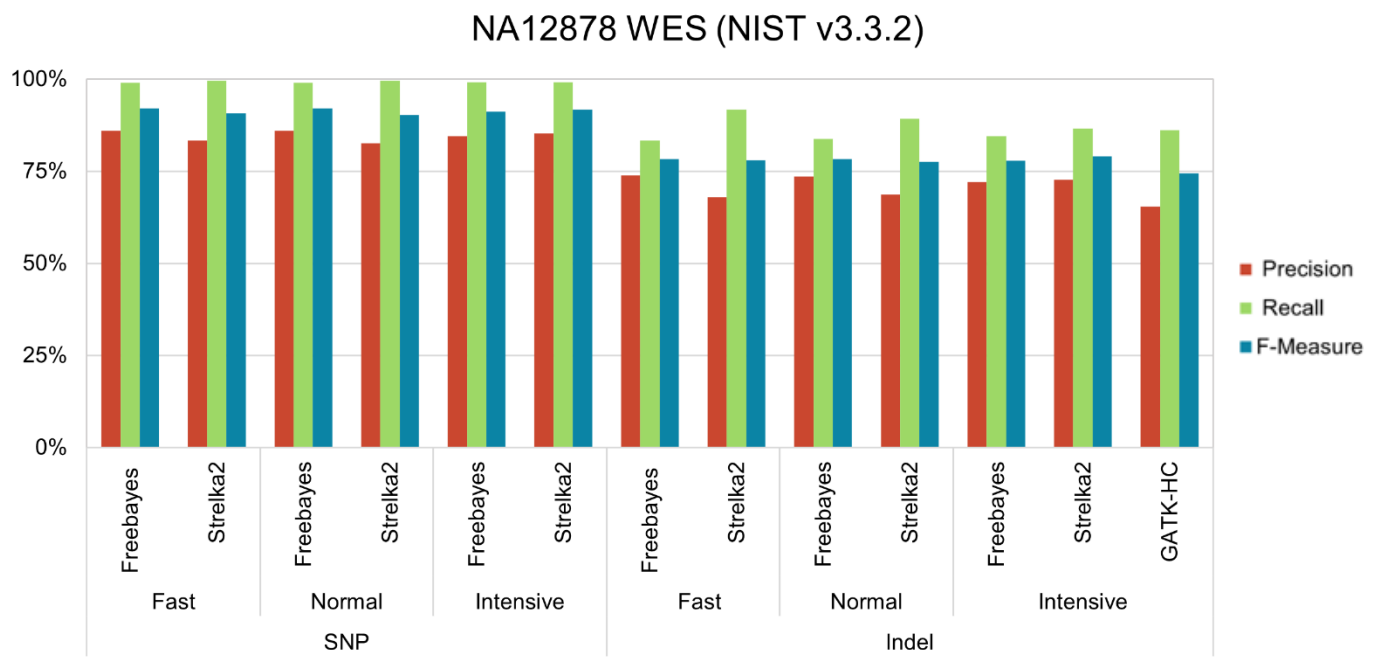


Figure A2. SNV and indel calling performance of Freebayes, Strelka2 and GATK HaplotypeCaller on the whole exome sequencing of NA12878, against the NIST small variant benchmarking callset (v3.3.2). DNAscan was run in fast, normal and intensive mode.

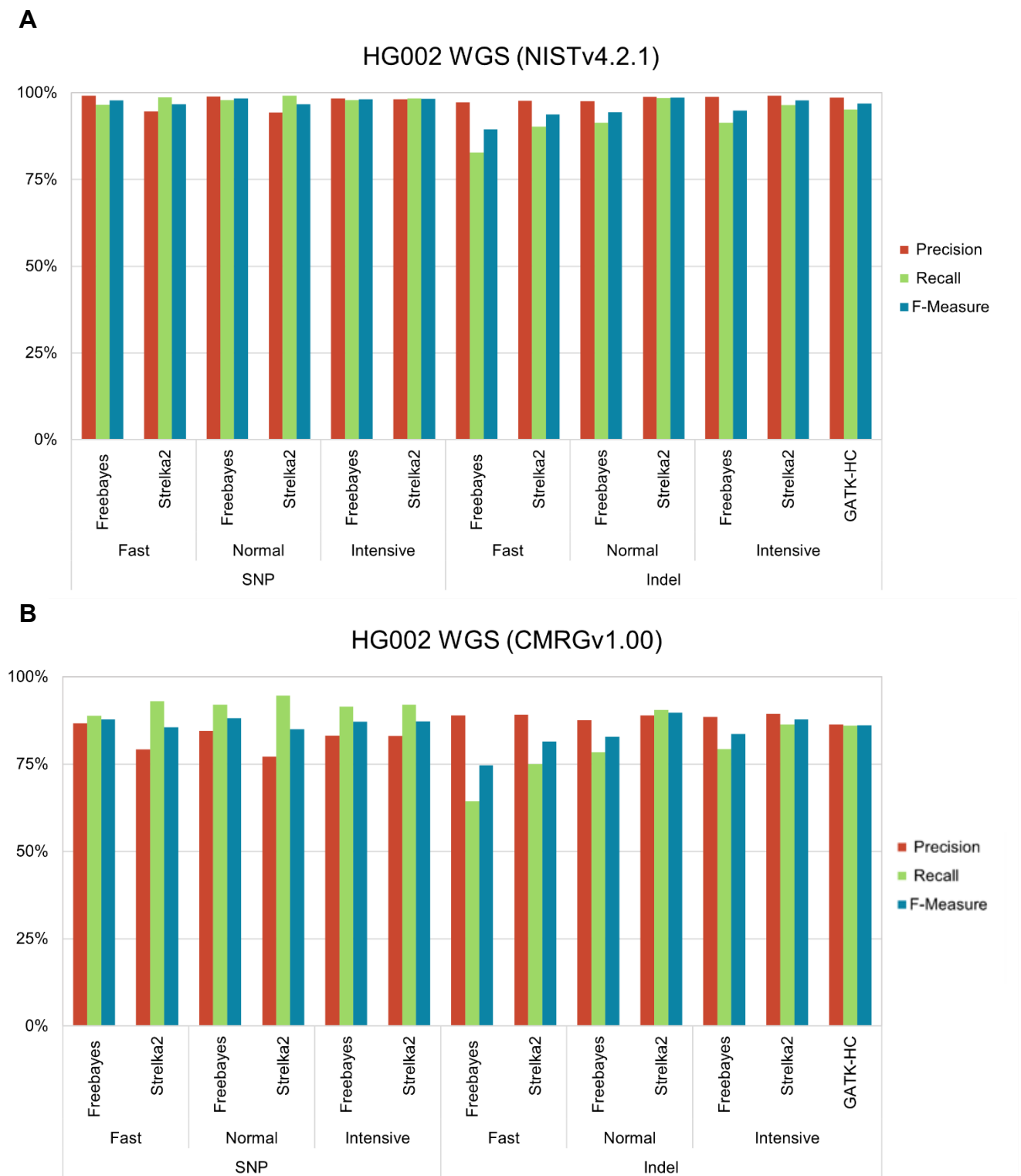
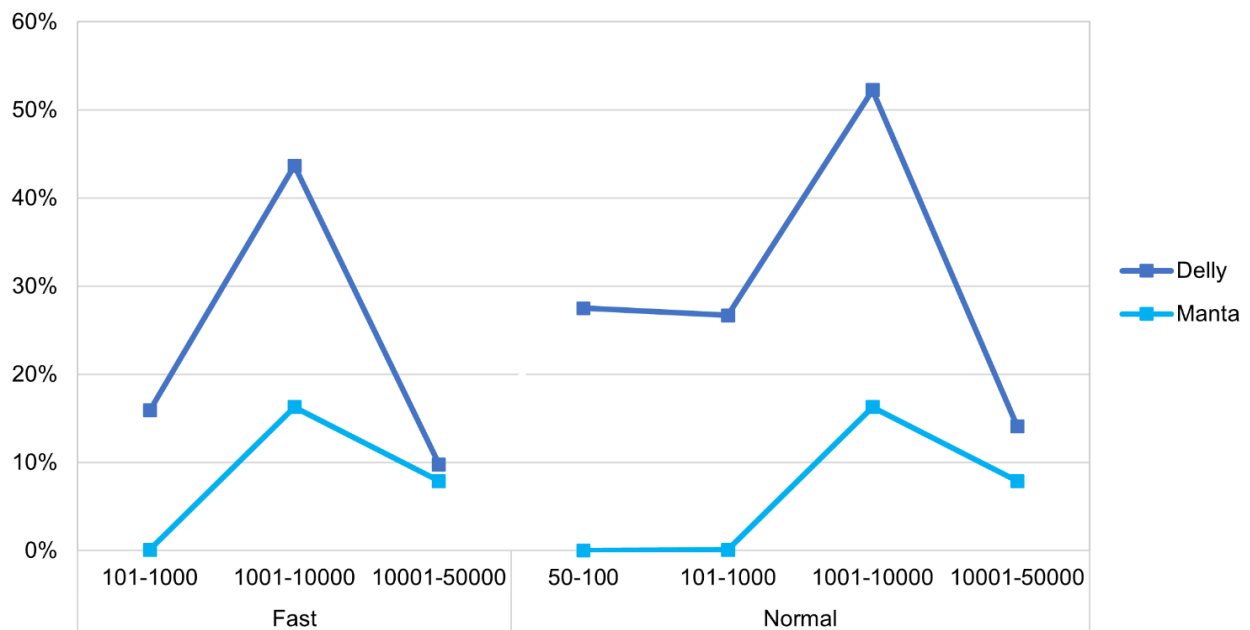


Figure A3. SNP and indel calling performance of Freebayes, Strelka2 and GATK HaplotypeCaller on the whole genome sequencing of HG002, against the A) NIST small variant benchmarking callset (v4.2.1), and the B) GIAB CMRG structural variant callset (v1.00). DNAscan was run in fast, normal and intensive mode.

**A**

## F-Measure of Deletion Calls - HG002 NIST v0.6

**B**

## Percentage of True Positive Deletion Calls - HG002 NIST v0.6

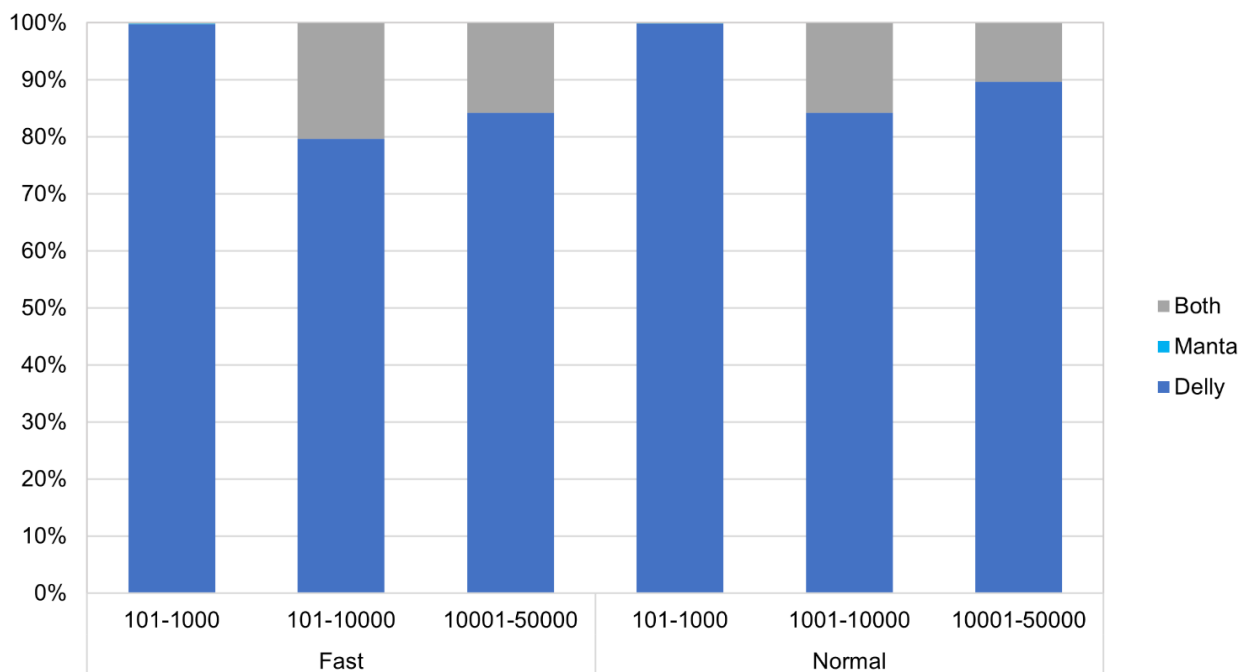
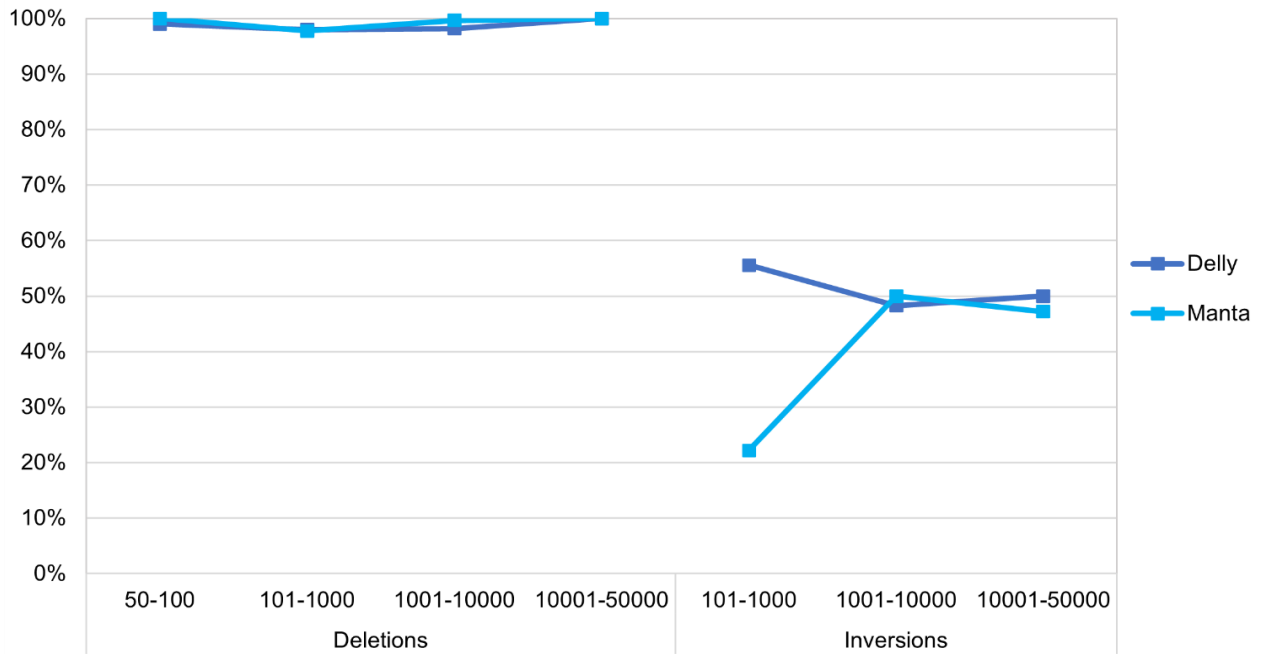


Figure A4. Deletion SV calling performance of Manta and Delly on the whole genome sequencing of HG002 against the NIST SV benchmarking callset (v0.6). Fast and normal modes refer to the alignment specifics as defined by DNAscan. Fast: HISAT2 alignment. Normal: HISAT2 alignment and BWA-mem realignment of soft-clipped and/or unaligned reads. A) F-Measure of calls, and B) Percentage of true positive calls shared by or exclusive to Manta and Delly, in fast and normal mode for multiple deletion variant sizes.

**A**

Precision of Deletion and Inversion Calls - NA12878



**B**

Percentage of True Positive Deletion and Inversion Calls - NA12878

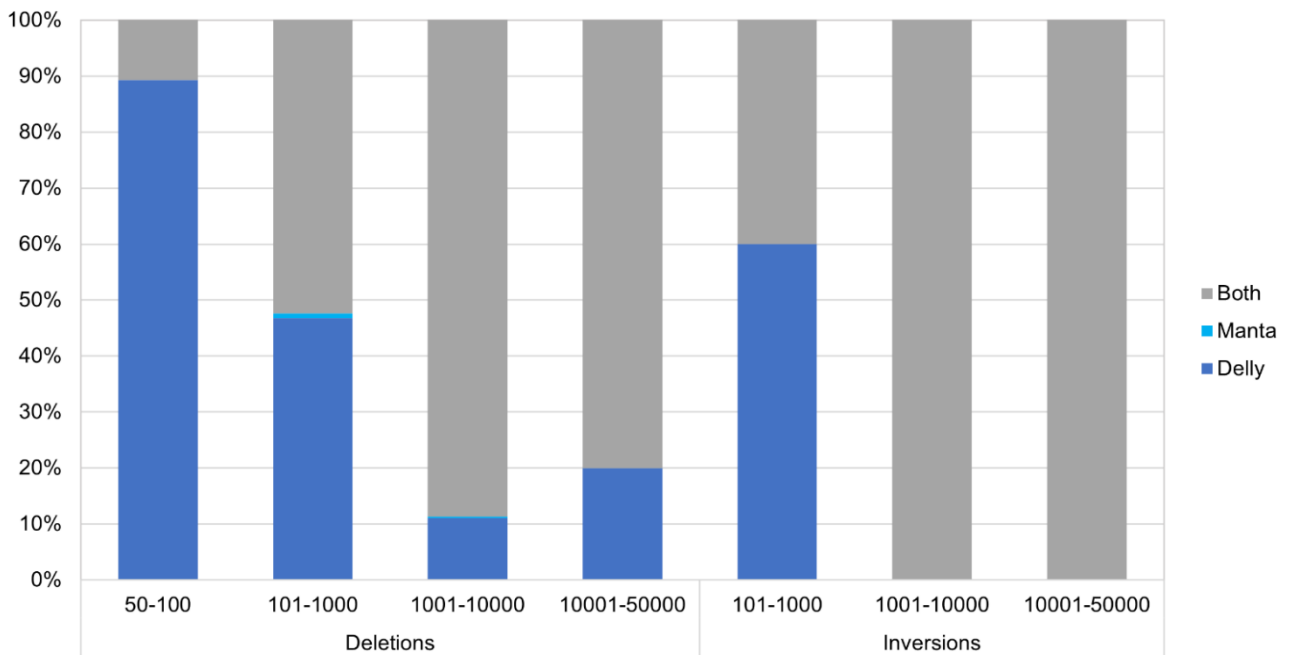


Figure A5. Deletion and inversion SV calling performance of Manta and Delly on simulated whole genome sequencing reads of NA12878 generated with VISOR. A) Precision of calls, and B) Percentage of true positive calls shared by or exclusive to Manta and Delly, for multiple deletion and inversion variant sizes.

| AnnotSV ID                   | ACMG class | SV type | Annotation mode | Gene name   | Location          | OMIM ID   | Exomiser score         | Overlapped regulatory elements | Pathogenic SV | Number of pathogenic SNV/indel overlapped | Benign SV   | Left breakpoint annotations | Right breakpoint annotations |
|------------------------------|------------|---------|-----------------|---|-------------------|---|------------------------|--------------------------------|---------------|---|---|-----------------------------|------------------------------|
| 21 10441055 10441056 ALU 1   | NA         | ALU     | full            | <a href="#">BAGE1</a> , <a href="#">BAGE2</a> , <a href="#">BAGE3</a> , <a href="#">BAGE4</a> [...4genes] | -                 | -   | NA                     | TPTE, BAGE2,                   | -             | -   | DDD:55340   | High Signal Region          | High Signal Region           |
| 21 10441055 10441056 ALU 1   | full=NA    | ALU     | split           | <a href="#">BAGE4</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | DDD:55340   | -                           | -                            |
| 21 10441055 10441056 ALU 1   | full=NA    | ALU     | split           | <a href="#">BAGE</a>  | intron3-intron3   | -   | NA                     | -                              | -             | -   | DDD:55340   | -                           | -                            |
| 21 10441055 10441056 ALU 1   | full=NA    | ALU     | split           | <a href="#">BAGE3</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | DDD:55340   | -                           | -                            |
| 21 10441055 10441056 ALU 1   | full=NA    | ALU     | split           | <a href="#">BAGE2</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | DDD:55340   | -                           | -                            |
| 13 21320641 21320642 ALU 1   | NA         | ALU     | full            | <a href="#">GRK6P1</a> , <a href="#">LINC00539</a> , <a href="#">MIFEPF3</a> [...3genes]                  | -                 | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 13 21320641 21320642 ALU 1   | full=NA    | ALU     | split           | <a href="#">GRK6P1</a>  | exon1-exon1       | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 13 21320641 21320642 ALU 1   | full=NA    | ALU     | split           | <a href="#">MIFEPF3</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 13 21320641 21320642 ALU 1   | full=NA    | ALU     | split           | <a href="#">LINC00539</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 12 11125814 11125815 ALU 1   | NA         | ALU     | full            | <a href="#">PRH1</a> , <a href="#">PRH1-PRR4</a> , <a href="#">PRH1-TAS2R14</a> [...3genes]               | -                 | -   | NA                     | -                              | -             | -   | DDD:37842   | -                           | -                            |
| 12 11125814 11125815 ALU 1   | full=NA    | ALU     | split           | <a href="#">PRH1</a>  | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842   | -                           | -                            |
| 12 11125814 11125815 ALU 1   | full=NA    | ALU     | split           | <a href="#">PRH1-TAS2R14</a>  | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842   | -                           | -                            |
| 12 11125814 11125815 ALU 1   | full=NA    | ALU     | split           | <a href="#">PRH1-PRR4</a>   | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842   | -                           | -                            |
| 12 11066593 11066594 LINE1 1 | NA         | LINE1   | full            | <a href="#">PRH1</a> , <a href="#">PRH1-PRR4</a> , <a href="#">PRH1-TAS2R14</a> [...3genes]               | -                 | -   | NA                     | -                              | -             | -   | DDD:37842; IMH; dpr454e212; gnomAD-SV_v2.1_DUI... | -                           | -                            |
| 12 11066593 11066594 LINE1 1 | full=NA    | LINE1   | split           | <a href="#">PRH1</a>  | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842; IMH; dpr454e212; gnomAD-SV_v2.1_DUI... | -                           | -                            |
| 12 11066593 11066594 LINE1 1 | full=NA    | LINE1   | split           | <a href="#">PRH1-TAS2R14</a>  | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842; IMH; dpr454e212; gnomAD-SV_v2.1_DUI... | -                           | -                            |
| 12 11066593 11066594 LINE1 1 | full=NA    | LINE1   | split           | <a href="#">PRH1-PRR4</a>   | intron1-intron1   | -   | NA                     | -                              | -             | -   | DDD:37842; IMH; dpr454e212; gnomAD-SV_v2.1_DUI... | -                           | -                            |
| 18 55478844 55478845 ALU 1   | NA         | ALU     | full            | <a href="#">TCF4</a> , <a href="#">TCF4-AS1</a> [...2genes]   | -                 | <a href="#">602228</a> , <a href="#">602272</a> | NA                     | MIR4529;                       | -             | -   | 1000g   | -                           | -                            |
| 18 55478844 55478845 ALU 1   | full=NA    | ALU     | split           | <a href="#">TCF4</a>  | intron1-intron1   | <a href="#">602228</a> , <a href="#">602272</a> | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 18 55478844 55478845 ALU 1   | full=NA    | ALU     | split           | <a href="#">TCF4-AS1</a>  | intron1-intron1   | <a href="#">602228</a> , <a href="#">602272</a> | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 12 106497183 106497184 ALU 1 | NA         | ALU     | full            | <a href="#">LOC100287944</a> , <a href="#">POLR3B</a> [...2genes]   | -                 | -   | <a href="#">614366</a> | -                              | -             | -   | 1000g   | -                           | -                            |
| 12 106497183 106497184 ALU 1 | full=NA    | ALU     | split           | <a href="#">POLR3B</a>  | intron25-intron25 | -   | <a href="#">614366</a> | -                              | -             | -   | 1000g   | -                           | -                            |
| 12 106497183 106497184 ALU 1 | full=NA    | ALU     | split           | <a href="#">LOC100287944</a>  | intron3-intron3   | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |
| 3 45501170 45501171 ALU 1    | NA         | ALU     | full            | <a href="#">LARS2</a> , <a href="#">LARS2-AS1</a> [...2genes]   | -                 | -   | <a href="#">604544</a> | -                              | -             | -   | 1000g   | -                           | -                            |
| 3 45501170 45501171 ALU 1    | full=NA    | ALU     | split           | <a href="#">LARS2</a>   | intron14-intron14 | -   | <a href="#">604544</a> | -                              | -             | -   | 1000g   | -                           | -                            |
| 3 45501170 45501171 ALU 1    | full=NA    | ALU     | split           | <a href="#">LARS2-AS1</a>   | intron2-intron2   | -   | NA                     | -                              | -             | -   | 1000g   | -                           | -                            |

Figure A6. Screenshot of the transposable element report generated by DNAscan2 using knotAnnotSV for 1 Project MinE control sample.

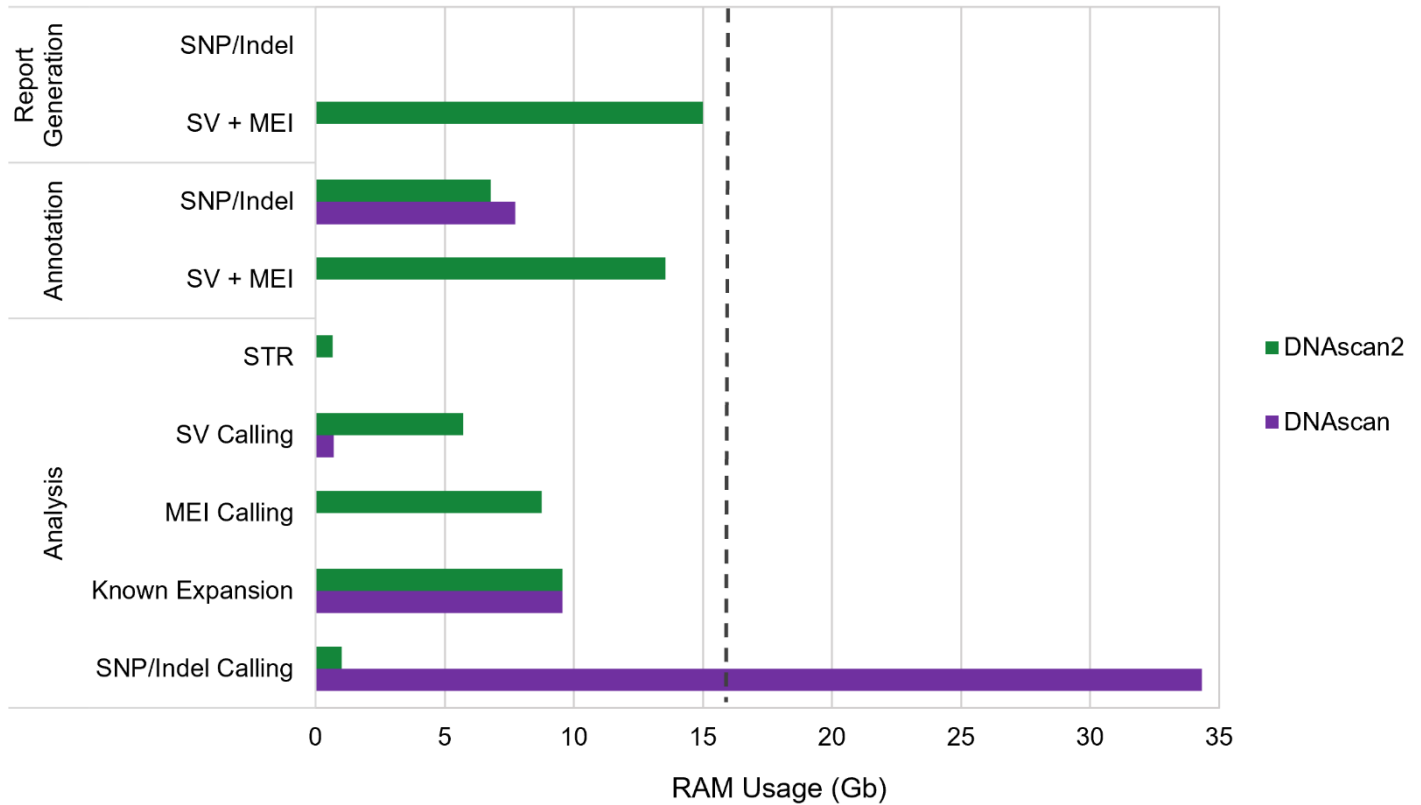


Figure A7. Comparison of average memory usage (in gigabytes) between DNAscan and DNAscan2 for each step following alignment, using whole genomes of 10 Project MinE control samples. The steps were categorised by the main stage of the workflow (Analysis, Annotation, Report Generation). The dotted line represents the average RAM of a standard midrange personal computer.

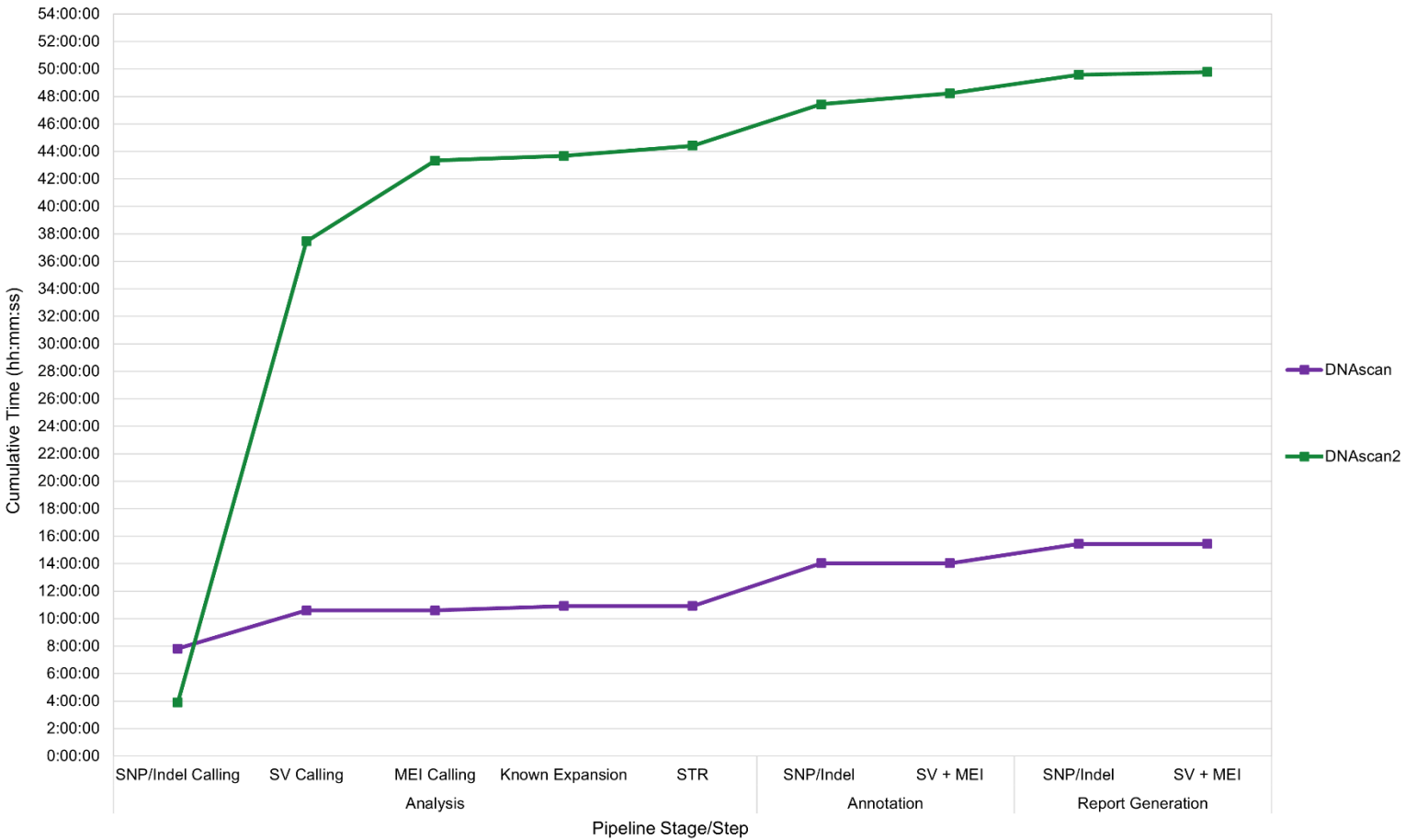


Figure A8. Average cumulative elapsed time (in hours:minutes:seconds format) between DNAscan and DNAscan2 for each step following alignment, using whole genomes of 10 Project MinE control samples. The steps were categorised by the main stage of the workflow (Analysis, Annotation, Report Generation).

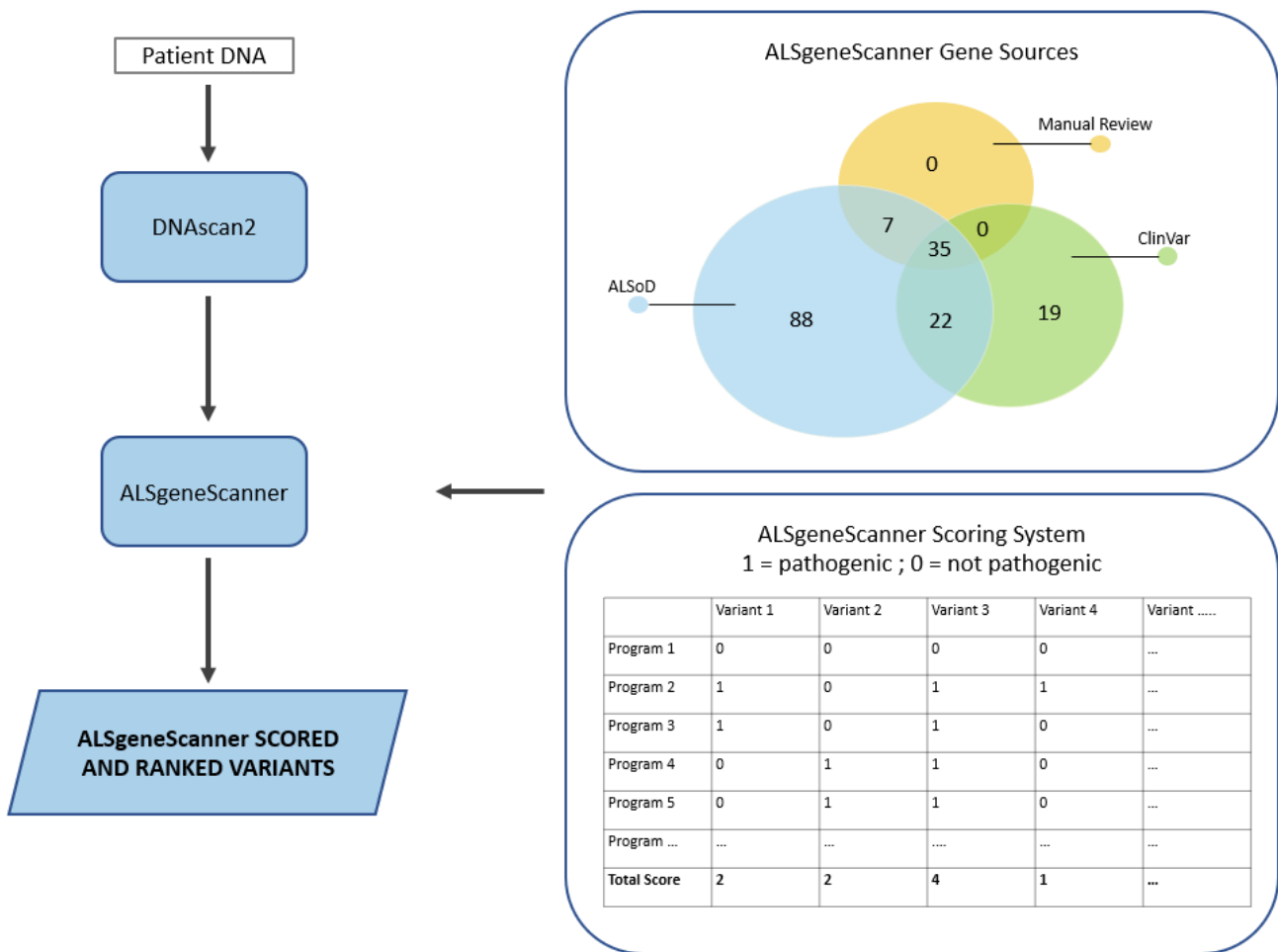


Figure A9. The ALSgeneScanner scoring module of DNAscan2. After the main DNAscan pipeline has completed, ALSgeneScanner takes SNV and indel annotation files as input and keeps only the variants whose genes are identified to be associated with ALS (171 in total, from three different sources). Afterwards, each of these filtered variants are scored based on the pathogenicity prediction assigned by each of the 13 prediction databases (SIFT, Polyphen-2 HDIV, PolyPhen-2 HVAR, LRT, MutationTaster, MutationAssessor, FATHMM, PROVEAN, FATHMM-mkl coding, MetaSVM, CADD and Intervar) and then ranked based on the total cumulative score from all programs.



## Chapter 6

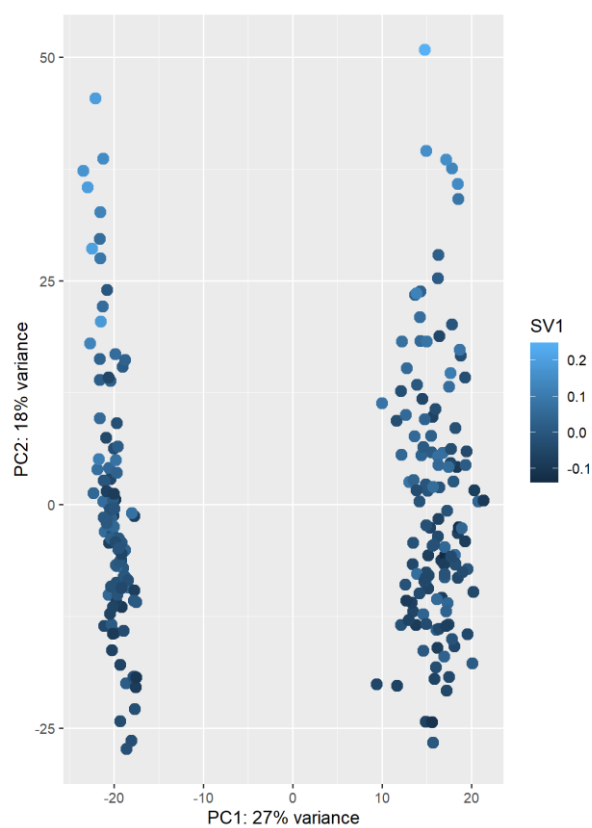


Figure A10. Principal component analysis of 234 samples from a total of 132 individuals in the TargetALS dataset (112 ALS cases and 20 controls) for the surrogate variable derived with SVA analysis. The inclusion of the surrogate variable accounted for the natural grouping of the TargetALS dataset.

## Chapters 6 and 7

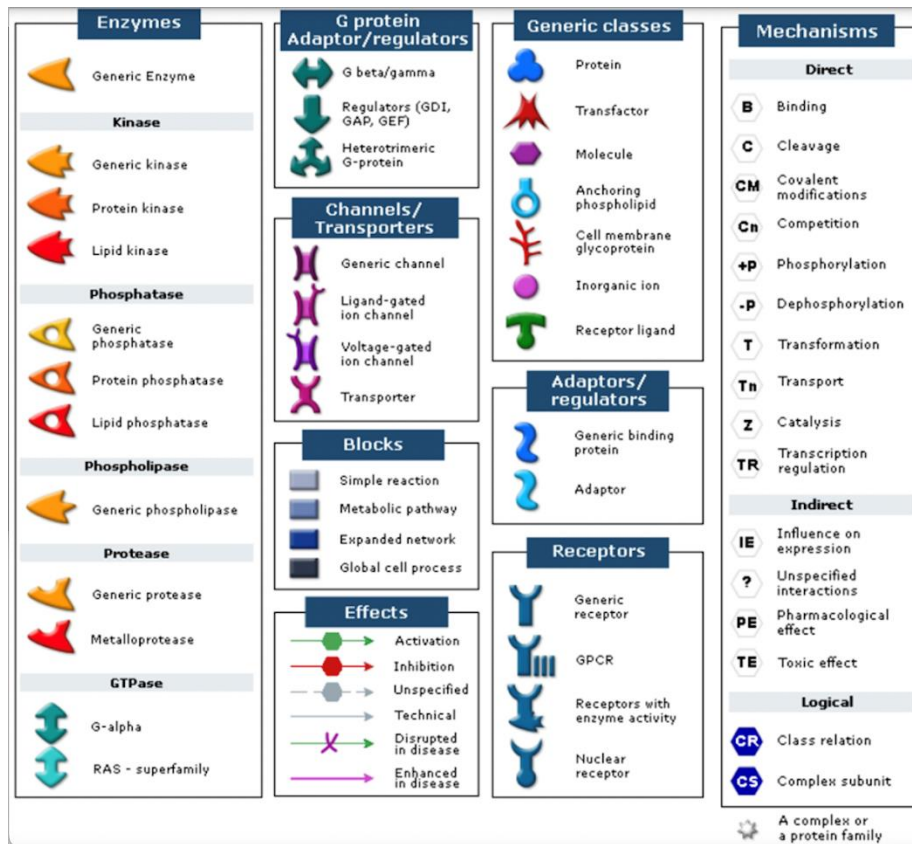


Figure A11. Key of the MetaCore pathway network symbols.

## Chapter 7

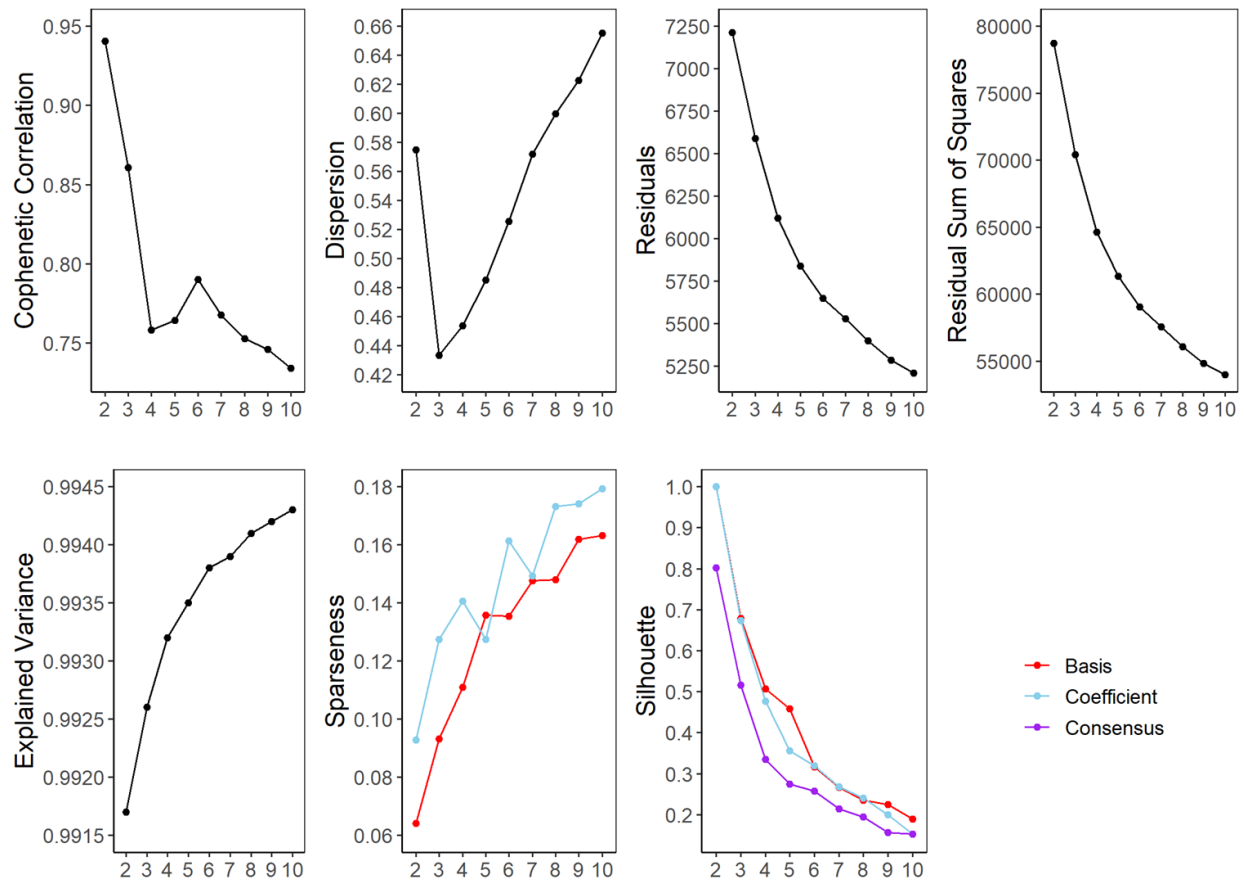


Figure A12. Cluster estimation metrics produced when running nsNMF with  $k = 2-10$ , 100 runs and 1000 iterations.

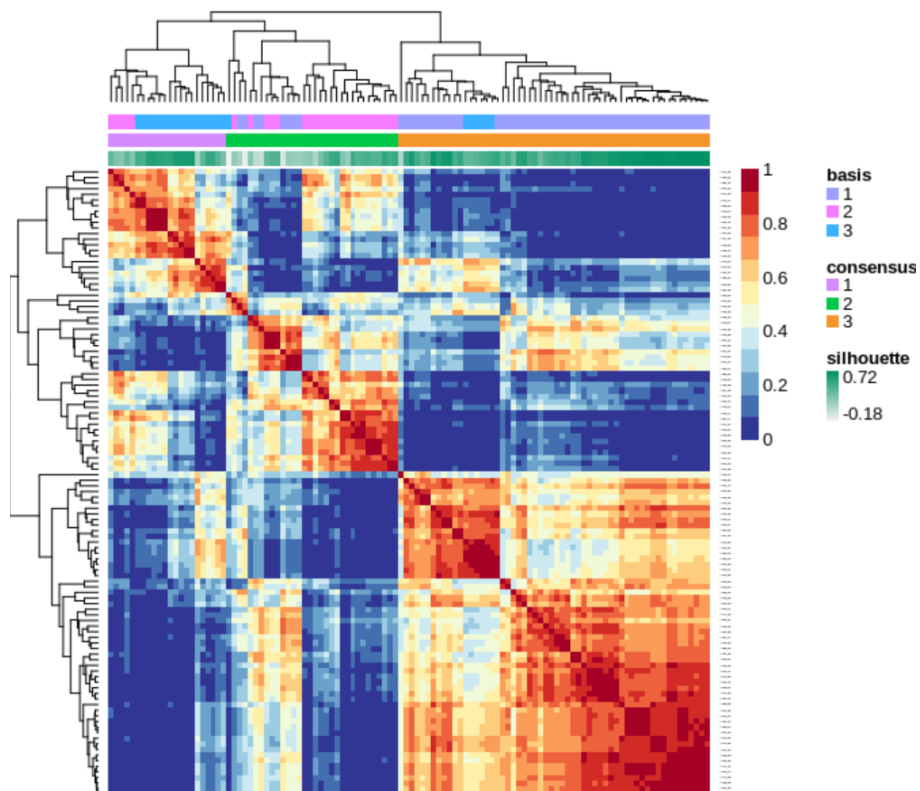
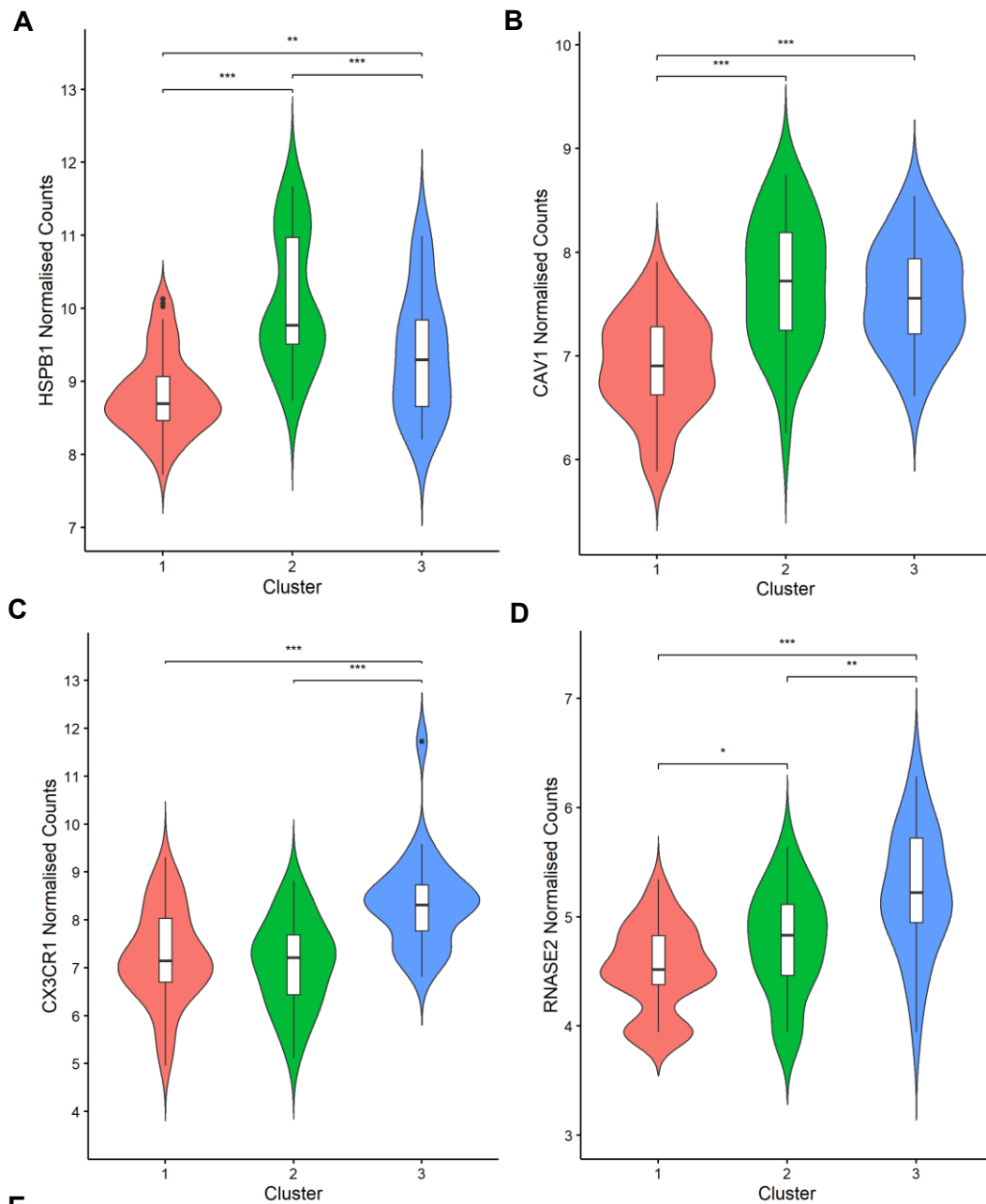


Figure A13. Cluster construction with the KCL BrainBank sample matrix, sorted by consensus, for the KCL BrainBank dataset. The nsNMF clustering algorithm was run with  $k = 3$ , 100 runs and 1000 iterations.



**E**

| <b>Informative ALS-linked Gene</b> | <b>Cluster</b> | <b>One-Way ANOVA (F-statistic, p-value)</b> | <b>Post-Hoc Analysis (Tukey p-value)</b>                                     |
|------------------------------------|----------------|---|--|
| HSPB1                              | 1              | 31.45, <b>1.9E-11</b>                       | 1 vs 2; <b>&lt;0.001</b> , 1 vs 3; <b>4.9E-03</b> , 2 vs 3; <b>&lt;0.001</b> |
| CAV1                               | 2              | 28.12, <b>1.6E-10</b>                       | 1 vs 2; <b>&lt;0.001</b> , 1 vs 3; <b>&lt;0.001</b> , 2 vs 3; 0.58           |
| CX3CR1                             | 3              | 14.72; <b>2.3E-06</b>                       | 1 vs 2; 0.94, 1 vs 3; <b>1.2E-05</b> , 2 vs 3; <b>7.2E-05</b>                |
| RNASE2                             | 3              | 19.65, <b>5.5E-08</b>                       | 1 vs 2; <b>0.036</b> , 1 vs 3; <b>&lt; 0.001</b> , 2 vs 3; <b>4.5E-03</b>    |

Figure A14. Comparison of the expression of the four identified ALS-related genes. Genes are as follows: A) HSPB1, B) CAV1, C) CX3CR1, and D) RNASE2, in each cluster. Asterisks represent significance levels of \* < 0.05, \*\* < 0.01, \*\*\* < 0.0001 with post-hoc Tukey's test after running one-way ANCOVA corrected for sex, age at death and post-mortem delay. E) Summary of the ANCOVA results assessing the differences in gene expression levels in ALS-linked genes between clusters. Bold p-values denote significance (< 0.05).

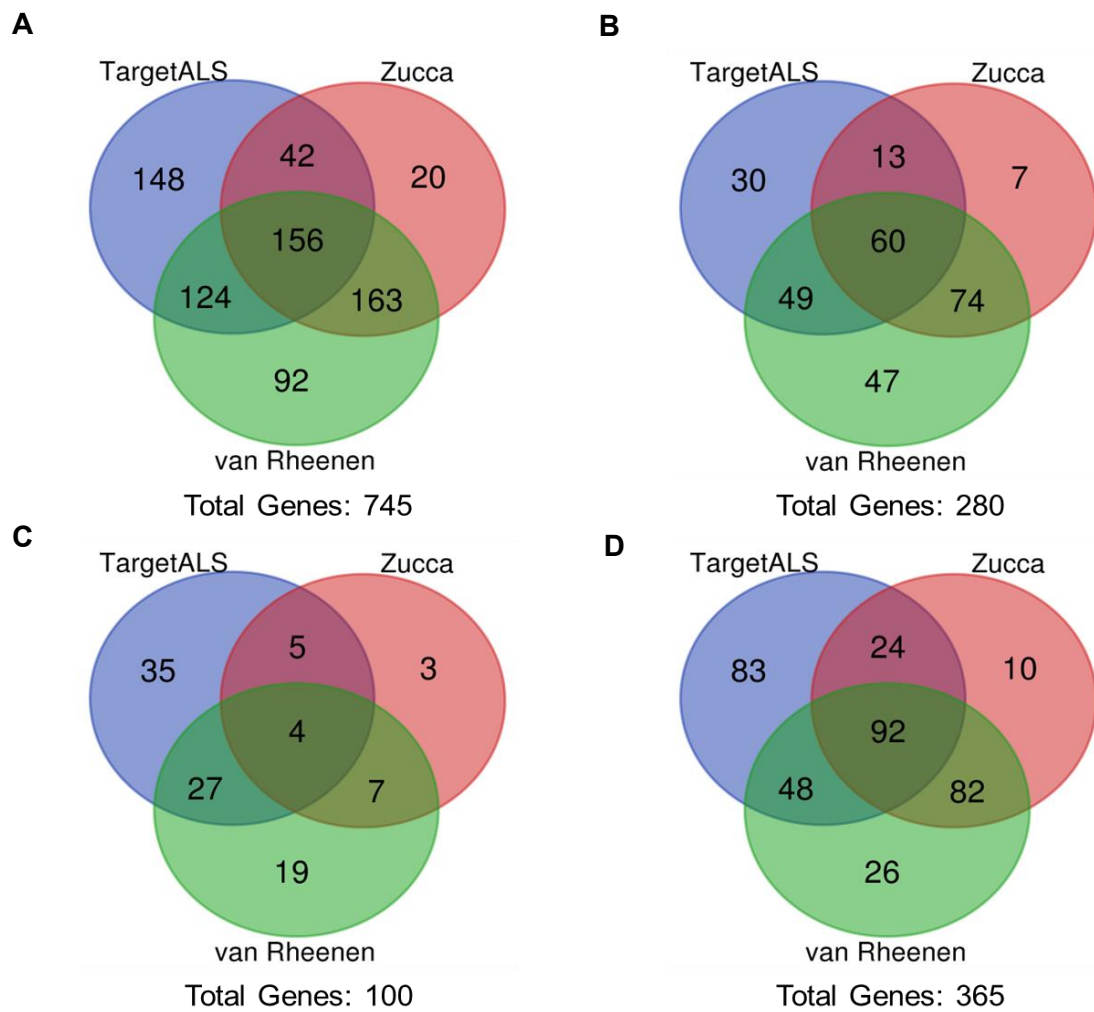


Figure A15. Union and intersection of genes for the three case datasets. A) All genes (TargetALS: 470, Zucca: 381, van Rheenen: 535), B) Cluster one genes, C) Cluster two genes and D) Cluster three genes. The 'total genes' at the bottom of each panel represents the sum of all genes in each Venn diagram.

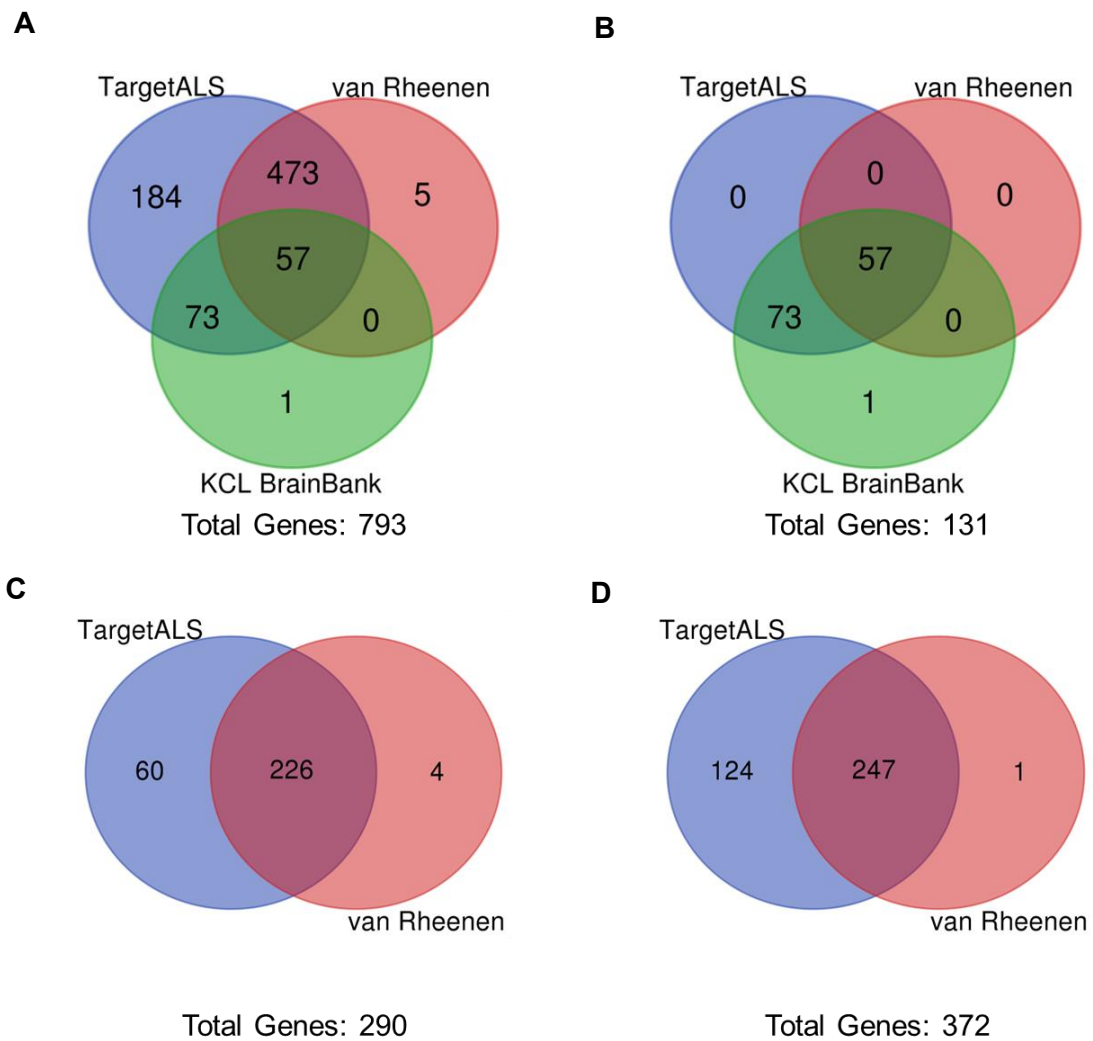


Figure A16. Union and intersection of genes for the three control datasets. A) All genes (KCL BrainBank: 787, TargetALS: 787, van Rheezen: 535), B) Cluster one genes, C) Cluster two genes and D) Cluster three genes. The 'total genes' at the bottom of each panel represents the sum of all genes in each Venn diagram.

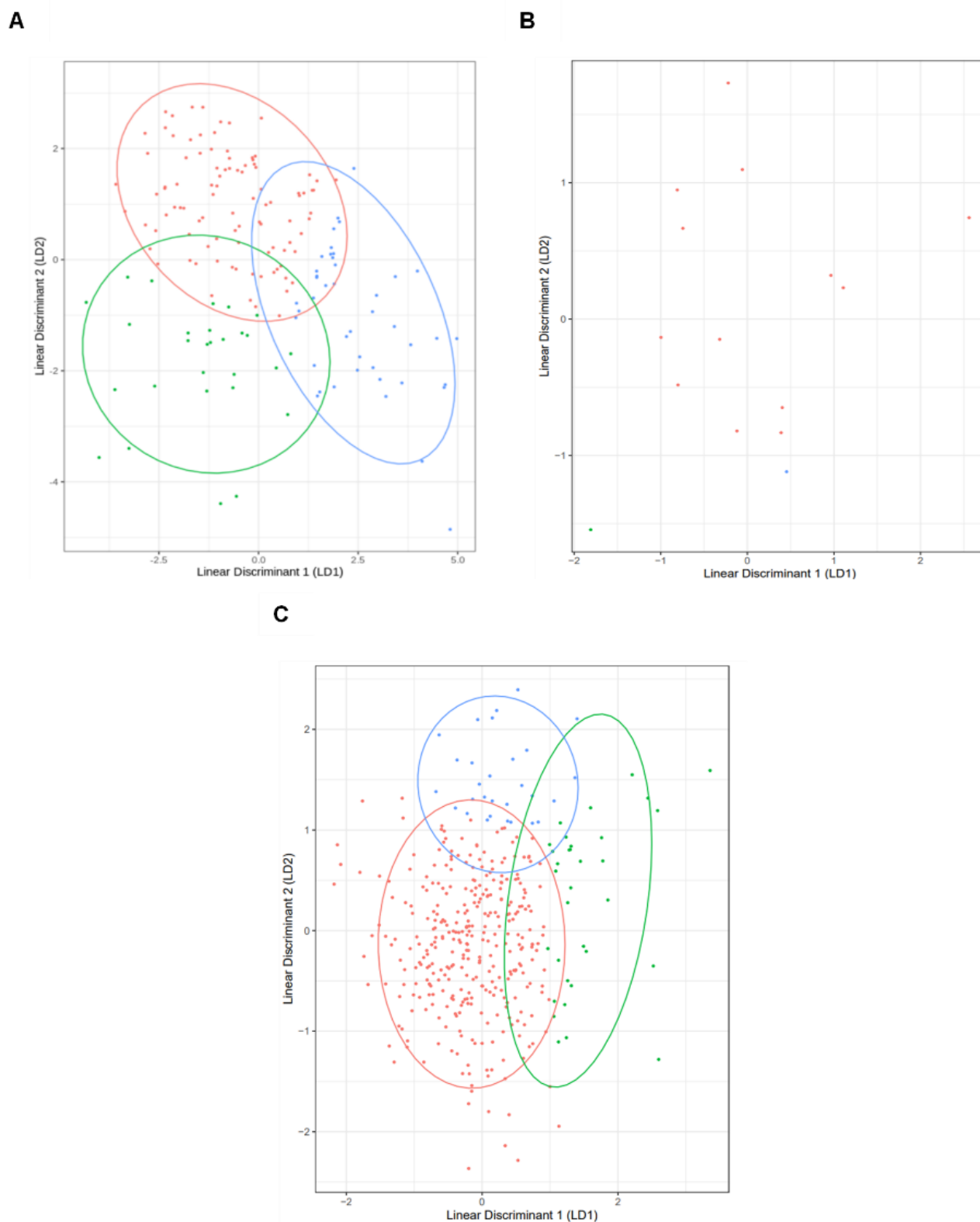
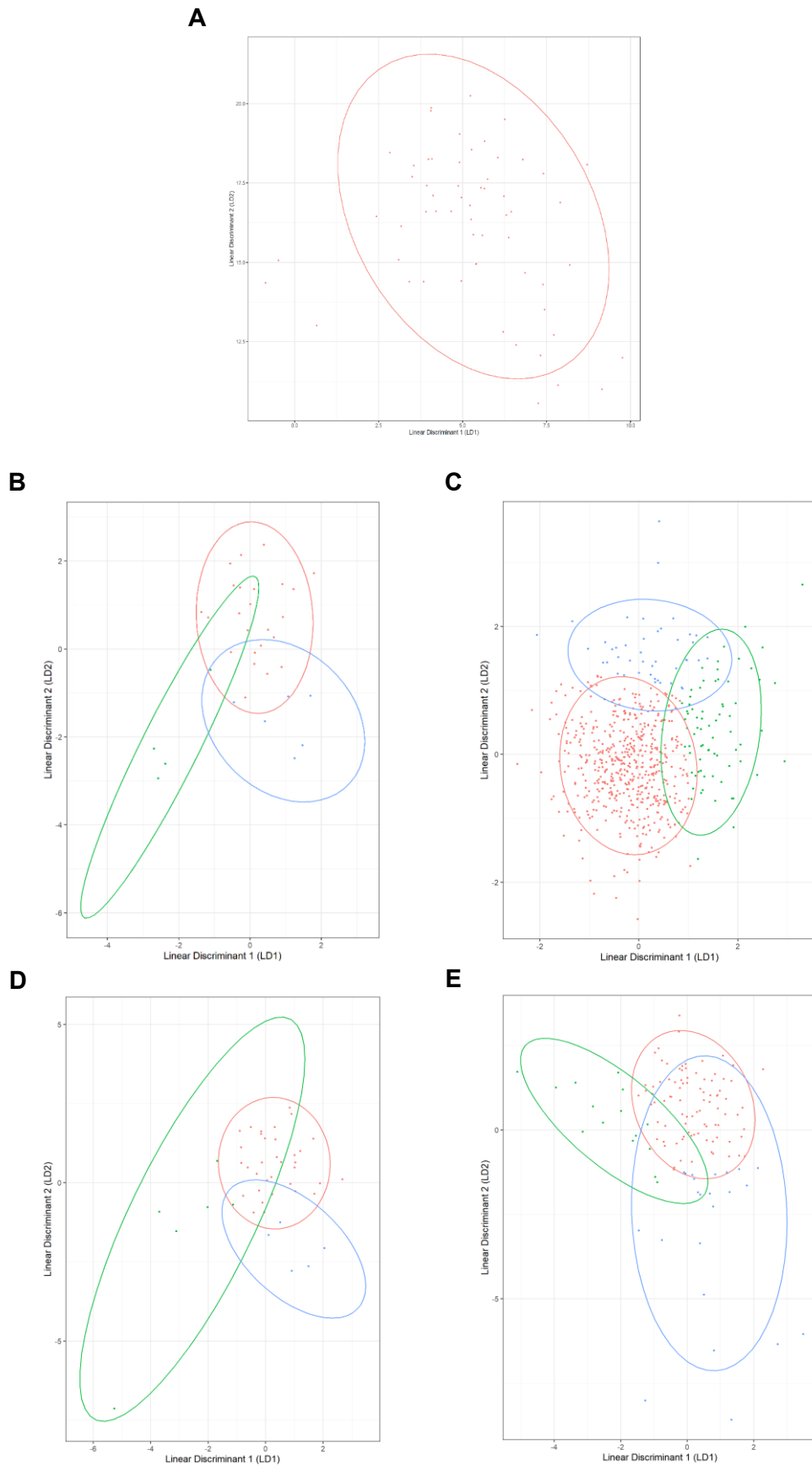


Figure A17. Sample assignment of A) TargetALS, B) Zucca, and C) van Rheezen case datasets to the KCL BrainBank case-defined clusters. Linear discriminant analysis models were trained on the KCL sample assignments and informative genes shared with each dataset. The number of genes for each dataset are as follows: A) 470, B) 381 and C) 535. Red: Cluster 1; Green: Cluster 2, Blue: Cluster 3.





**Figure A18.** Sample assignment of A) KCL BrainBank controls, B) TargetALS controls, C) van Rheenen controls, D) TargetALS occipital cortex and E) TargetALS cerebellum control datasets to the KCL BrainBank case-defined clusters. Linear discriminant analysis models were trained on the KCL sample assignments and informative genes shared with each dataset. Red: Cluster 1; Green: Cluster 2, Blue: Cluster 3.

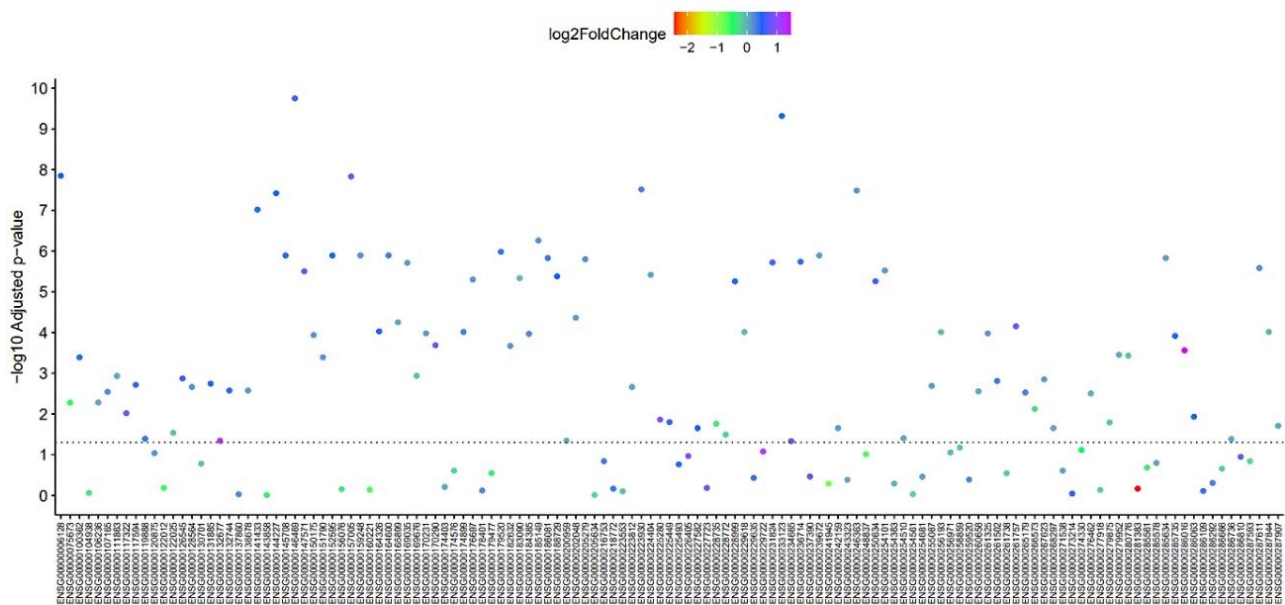


Figure A19. Dot chart demonstrating significant differences in expression of 87 of the 131 cluster one genes between KCL BrainBank cases and controls, coloured by log2 fold change. An increase in log2 fold change means the gene is upregulated in cases, and vice versa. The dotted line represents the  $-\log_{10}$  adjusted p-value that corresponds to a Benjamini-Hochberg p-value of 0.05.

## Appendix II. Tables

### Chapter 4

| Dependency Category      | Dependency Details                | Required Storage (Gb) |               |
|--------------------------|-----------------------------------|-----------------------|---------------|
|                          |                                   | hg19                  | hg38          |
| References               | Reference Genome and Index        | 3.16                  | 3.27          |
|                          | BWA-mem Index                     | 5.42                  | 5.62          |
|                          | HISAT2 Index                      | 4.37                  | 4.66          |
| Databases and Catalogues | ExpansionHunter Variant Catalogue | < 0.01                | < 0.01        |
|                          | ANNOVAR Databases*                | 91.34                 | 91.67         |
|                          | AnnotSV Databases**               | 3.31                  | 3.31          |
| Tools                    | Conda Installation                | 0.10                  | 0.10          |
|                          | Conda-Installed Tools             | 1.50                  | 1.50          |
|                          | Manually Installed Tools          | 12.01                 | 12.01         |
| Miscellaneous            | Additional Disk Space***          | 20.00                 | 20.00         |
| Total free space needed: |                                   | <b>141.21</b>         | <b>142.14</b> |

*Table A1. Storage requirements of all dependencies necessary to run DNAscan2, divided by reference version. \*Default DNAscan2 ANNOVAR databases (refGene, dbnsfp33a, clinvar\_20210501, intervar\_20180118, avsnp147, exac03, 1000g2015aug, gnomad211\_genome) were used. \*\*AnnotSV was only run using databases that do not require a commercial licence to download. \*\*\*This refers to the additional overhead storage space that MELT requires to temporarily hold intermediate files.*

| Pipeline Stage    | Tool                   | Tool Version | Installation Method              | Reference                                |
|-------------------|------------------------|--------------|----------------------------------|--|
| Alignment         | BWA-mem                | 0.7.17       | Conda                            | (H. Li, 2013)                            |
|                   | HISAT2                 | 2.2.1        | Conda                            | (Kim et al., 2019)                       |
|                   | Sambalster             | 0.1.26       | Conda                            | (Faust & Hall, 2014)                     |
|                   | Sambamba               | 0.7.1        | Conda                            | (Tarasov et al., 2015)                   |
| Analysis          | Strelka2               | 2.9.10       | Manual Download                  | (Kim et al., 2018)                       |
|                   | Manta                  | 1.6.0        | Manual Download                  | (X. Chen et al., 2016b)                  |
|                   | Delly                  | 0.8.3        | Conda                            | (Rausch et al., 2012)                    |
|                   | MELT                   | 2.2.2        | Manual Registration and Download | (Gardner et al., 2017)                   |
|                   | ExpansionHunter        | 3.2.2        | Conda                            | (Dolzhenko et al., 2019)                 |
|                   | ExpansionHunter Denovo | 0.9.0        | Manual Download                  | (Dolzhenko et al., 2020)                 |
|                   | SURVIVOR               | 1.0.7        | Manual Download                  | (Jeffares et al., 2017)                  |
| Annotation        | ANNOVAR                | 08/06/2019   | Manual Registration and Download | (K. Wang et al., 2010)                   |
|                   | AnnotSV                | 3.0.9        | Manual Download                  | (Geoffroy et al., 2018)                  |
| Report Generation | FastQC                 | 0.11.9       | Conda                            | (FastQC, no date)                        |
|                   | MultiQC                | 1.10.1       | Conda                            | (Ewels et al., 2016)                     |
|                   | knotAnnotSV            | 1.0.0        | Manual Download                  | (Geoffroy et al., 2021)                  |
| General           | Miniconda              | 4.10.3       | Manual Download                  | (Anaconda Software Distribution. (2022)) |
|                   | Perl                   | 5.26.2       | Conda                            |  |
|                   | Python                 | 3.8          | Conda                            |  |
|                   | Biopython              | 1.78         | Conda                            | (Cock et al., 2009)                      |
|                   | Pysam                  | 0.16.0.1     | Conda                            | (Pysam, 2014/2021)                       |
|                   | SAMtools               | 1.9          | Conda                            | (H. Li et al., 2009)                     |
|                   | BEDTools               | 2.25.0       | Conda                            | (Quinlan & Hall, 2010)                   |
|                   | BCFtools               | 1.9          | Conda                            | (H. Li, 2011)                            |
|                   | VCFtools               | 0.1.16       | Conda                            | (Danecek et al., 2011)                   |
|                   | PySimpleGUI*           | 4.40.0       | Conda                            | (PySimpleGUI, n.d.)                      |
|                   | Snakemake**            | ≥ 5.32.1     | Conda                            | (Mölder et al., 2021)                    |

Table A2. List of tools and corresponding versions that DNAscan2 requires for each pipeline stage. 'General' refers to tools which are necessary for the basic execution of DNAscan2. The 'Installation Method' column lists the easiest way to obtain the software to avoid software version clashes. \*This is only required if you want to run DNAscan2 as a standalone application and not as a command-line tool. \*\*This is only required if you want to deploy DNAscan2 on a high performance computing facility or execute the workflow in a multi-sample parallel fashion.

| <b>Variant Calling Metrics per Variant Type</b> | <b>DNAscan</b> | <b>DNAscan2</b> |
|---|----------------|-----------------|
| <b>SNV/Indel Calling</b>                        |                |                 |
| - Total called variants                         | 29192123       | 30000110        |
| - Total called and filtered variants            | 4285989        | 4611498         |
| - Number of filtered non-synonymous variants    | 10165 (0.237%) | 10727 (0.250%)  |
| - Number of filtered synonymous variants        | 21304 (0.497%) | 22285 (0.483%)  |
| <b>Structural Variant Calling</b>               |                |                 |
| - Total called variants                         | 28831          | 56970           |
| • Deletions                                     | 8478           | 16069           |
| • Insertions                                    | 6455           | 6189            |
| • Inversions                                    | 3410           | 7280            |
| • Duplications                                  | 4031           | 9285            |
| • Translocations                                | 6457           | 18147           |
| <b>MEI Calling</b>                              |                |                 |
| - Total called variants                         | N/A            | 1694            |
| • ALU   | N/A            | 1287            |
| • SVA   | N/A            | 148             |
| • LINE1   | N/A            | 259             |
| <b>Expansion/Repeat Scanning</b>                |                |                 |
| - Total called and genotyped expansions         | 37             | 37              |
| - Total Identified STR loci                     | N/A            | 3043            |

*Table A3. Comparison of the variant calling power of DNAscan and DNAscan2 for several variant classes. 'N/A' represents tasks that could not be performed in DNAscan due to lack of available software. Synonymous and non-synonymous SNV and indel variants were obtained from the corresponding refGene annotation classification. Values here denote the average number of variant types identified using whole genomes of 10 Project MinE control samples.*

|                   | Pipeline Stage    | Pipeline Step   | Elapsed Time (hh:mm:ss) | CPU Time (hh:mm:ss) | RAM Usage (Gb) | MaxDiskRead | MaxDiskWrite |
|-------------------|-------------------|-----------------|-------------------------|---------------------|----------------|-------------|--------------|
| <b>DNAscan</b>    | Analysis          | SNV/Indel       | 07:48:52                | 32:10:31            | 34.34          | 144046      | 71073        |
|                   |                   | SV              | 02:46:41                | 11:06:44            | 0.69           | 827571      | 338          |
|                   |                   | MEI             | N/A                     | N/A                 | N/A            | N/A         | N/A          |
|                   |                   | Known Expansion | 00:19:48                | 01:19:10            | 9.55           | 23669       | 1            |
|                   |                   | STR             | N/A                     | N/A                 | N/A            | N/A         | N/A          |
|                   | Annotation        | SNV/Indel       | 03:06:26                | 12:25:44            | 7.74           | 402697      | 71254        |
|                   |                   | SV + MEI        | N/A                     | N/A                 | N/A            | N/A         | N/A          |
|                   | Report Generation | SNV/Indel       | 01:24:58                | 05:39:51            | 0.02           | 1953279     | 8            |
|                   |                   | SV + MEI        | N/A                     | N/A                 | N/A            | N/A         | N/A          |
|                   | <b>DNAscan2</b>   | Analysis        | SNV/Indel               | 03:54:10            | 15:36:41       | 1.00        | 81794        |
| SV                |                   |                 | 33:32:53                | 133:53:30           | 5.70           | 1222044     | 55738        |
| MEI               |                   |                 | 05:53:05                | 23:32:20            | 8.75           | 2710405     | 38612        |
| Known Expansion   |                   |                 | 00:19:48                | 01:19:10            | 9.55           | 23669       | 1            |
| STR               |                   |                 | 00:44:51                | 02:59:24            | 0.66           | 28505       | 30           |
| Annotation        |                   | SNV/Indel       | 03:00:48                | 12:03:12            | 6.78           | 353781      | 35076        |
|                   |                   | SV + MEI        | 00:47:15                | 03:08:58            | 13.54          | 8653        | 8386         |
| Report Generation |                   | SNV/Indel       | 01:22:17                | 05:29:06            | 0.02           | 1840523     | 10           |
|                   |                   | SV + MEI        | 00:11:52                | 00:47:27            | 15.00          | 980         | 2331         |

*Table A4. Comparison of the average elapsed time of DNAscan and DNAscan2 for each step following alignment, using whole genomes of 10 Project MinE control samples. The steps were categorised by the main stage of the workflow (Analysis, Annotation, Report Generation). 'N/A' represents tasks that could not be performed in DNAscan due to lack of available software.*

| Gene Name      | Chromosome | Sources of Identification |       |         | Reference                           |
|----------------|------------|---------------------------|-------|---------|-------------------------------------|
|                |            | Manual Review             | ALSoD | ClinVar |                                     |
| <i>DNAJC7</i>  | 17q21.2    | ✓                         |       |         | (Farhan et al., 2019)               |
| <i>ERBB4</i>   | 2q34       | ✓                         |       |         | (Takahashi et al., 2013)            |
| <i>ANXA11</i>  | 10q22.3    |                           | ✓     |         | (Smith et al., 2017)                |
| <i>ARPP21</i>  | 3p22.3     |                           | ✓     |         | (Cooper-Knock et al., 2019)         |
| <i>ATXN1</i>   | 6p22.3     |                           | ✓     |         | (Tazelaar et al., 2020)             |
| <i>C21orf2</i> | 21q22.3    |                           | ✓     | ✓       | (van Rheenen et al., 2016b)         |
| <i>CAV1</i>    | 7q31.2     |                           | ✓     |         | (Cooper-Knock et al., 2021)         |
| <i>CAV2</i>    | 7q31.2     |                           | ✓     |         | (Cooper-Knock et al., 2021)         |
| <i>CCNF</i>    | 16p13.3    |                           | ✓     | ✓       | (Williams et al., 2016)             |
| <i>DNMT3A</i>  | 2p23.3     |                           | ✓     |         | (Chestnut et al., 2011)             |
| <i>DNMT3B</i>  | 20q11.21   |                           | ✓     |         | (Chestnut et al., 2011)             |
| <i>ENAH</i>    | 1q42.12    |                           | ✓     |         | (Cirulli et al., 2015)              |
| <i>EPHA3</i>   | 3p11.1     |                           | ✓     |         | (Uyan et al., 2013)                 |
| <i>ERLIN1</i>  | 10q24.31   |                           | ✓     | ✓       | (Tunca et al., 2018)                |
| <i>GLT8D1</i>  | 3p21.1     |                           | ✓     |         | (Cooper-Knock et al., 2019)         |
| <i>GPX3</i>    | 5q33.1     |                           | ✓     |         | (Benyamin et al., 2017)             |
| <i>KIF5A</i>   | 12q13.3    |                           | ✓     |         | (Nicolas et al., 2018)              |
| <i>MOBP</i>    | 3p22.1     |                           | ✓     | ✓       | (van Rheenen et al., 2016b)         |
| <i>NEFL</i>    | 8p21.2     |                           | ✓     | ✓       | (Benatar et al., 2018)              |
| <i>NEK1</i>    | 4q33       |                           | ✓     |         | (Kenna et al., 2016)                |
| <i>PGRN</i>    | 17q21.31   |                           | ✓     |         | (Philips et al., 2010)              |
| <i>PNPLA6</i>  | 19p13.2    |                           | ✓     | ✓       | (Pensato et al., 2020)              |
| <i>RFTN1</i>   | 3p24.3     |                           | ✓     |         | (Zhai et al., 2009)                 |
| <i>SCFD1</i>   | 14q12      |                           | ✓     | ✓       | (van Rheenen et al., 2016b)         |
| <i>TIA1</i>    | 2p13.3     |                           | ✓     | ✓       | (Mackenzie et al., 2017)            |
| <i>UBQLN1</i>  | 9q21.32    |                           | ✓     |         | (Wang, et al., 2020)                |
| <i>VRK1</i>    | 14q32.2    |                           | ✓     | ✓       | (Nguyen et al., 2015)               |
| <i>CAPN14</i>  | 2p23.1     |                           |       | ✓       | (Dekker et al., 2019)               |
| <i>CHRNA3</i>  | 15q25.1    |                           |       | ✓       | (Sabatelli et al., 2009)            |
| <i>CHRN4</i>   | 15q25.1    |                           |       | ✓       | (Sabatelli et al., 2009)            |
| <i>CNTF</i>    | 11q12.1    |                           |       | ✓       | (Laaksovirta et al., 2008)          |
| <i>CYLD</i>    | 16q12.1    |                           |       | ✓       | (Dobson-Stone et al., 2020)         |
| <i>DDX20</i>   | 1p13.2     |                           |       | ✓       | (Cacciottolo et al., 2019)          |
| <i>DYNC1H1</i> | 14q32.31   |                           |       | ✓       | (Scarlino et al., 2020b)            |
| <i>ELP3</i>    | 8p21.1     |                           |       | ✓       | (Bento-Abreu et al., 2018)          |
| <i>EWSR1</i>   | 22q12.2    |                           |       | ✓       | (Couthouis et al., 2012)            |
| <i>GARS1</i>   | 7p14.3     |                           |       | ✓       | (Corcia et al., 2019)               |
| <i>GLE1</i>    | 9q34.11    |                           |       | ✓       | (Kaneb et al., 2015)                |
| <i>MFN2</i>    | 1p36.22    |                           |       | ✓       | (Wang et al., 2018)                 |
| <i>MPZ</i>     | 1q23.3     |                           |       | ✓       | (Bisogni et al., 2022)              |
| <i>NIPA1</i>   | 15q11.2    |                           |       | ✓       | (Blauw, van Rheenen, et al., 2012b) |
| <i>PLEKHG5</i> | 1p36.31    |                           |       | ✓       | (Gonzalez-Quereda et al., 2021)     |

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|                |          |  |  |   |                         |
|----------------|----------|--|--|---|-------------------------|
| <i>PON1</i>    | 7q21.3   |  |  | ✓ | (Verde et al., 2019)    |
| <i>PON3</i>    | 7q21.3   |  |  | ✓ | (Saeed et al., 2006)    |
| <i>SCN11A</i>  | 3p22.2   |  |  | ✓ | (Castoro et al., 2018)  |
| <i>SLC52A3</i> | 20p13    |  |  | ✓ | (Johnson et al., 2012)  |
| <i>SYNE1</i>   | 6q25.2   |  |  | ✓ | (Naruse et al., 2020)   |
| <i>TRPV4</i>   | 12q24.11 |  |  | ✓ | (Pensato et al., 2020)  |
| <i>UNC13A</i>  | 19p13.11 |  |  | ✓ | (Diekstra et al., 2012) |

*Table A5. New additions and/or reclassifications in the ALSgeneScanner database. Breakdown of identified gene sources are as follows: 2 manual review, 16 ALSod, 9 ALSod and ClinVar, and 22 ClinVar.*



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**Chapter 5**

| <b>Country</b> | <b>Cases</b> | <b>Controls</b> | <b>Total</b> |
|----------------|--------------|-----------------|--------------|
| Belgium        | 561          | 89              | 650          |
| Netherlands    | 1854         | 1081            | 2935         |
| France         | 251          | 40              | 291          |
| Italy          | 55           | 0               | 55           |
| US             | 435          | 80              | 515          |
| UK             | 1445         | 453             | 1898         |
| Turkey         | 618          | 150             | 768          |
| Ireland        | 467          | 234             | 701          |
| Israel         | 105          | 0               | 105          |
| Portugal       | 53           | 19              | 72           |
| Sweden         | 204          | 112             | 316          |
| Switzerland    | 44           | 1               | 45           |
| Spain          | 377          | 175             | 552          |
| <b>Total</b>   | <b>6469</b>  | <b>2434</b>     | <b>8903</b>  |

*Table A6. Breakdown of Project MinE samples used for variant screening and burden analysis by country of sample collection.*

| Reference                 | Study Type   | Discovery Method      | Genetic Technology | Population (Country)                                     | Sample Groups   | Sex (M:F (Ratio))  | Age (years (SD or range))                 | Diagnostic Criteria                              |
|---------------------------|--------------|-----------------------|--------------------|--|---|--|---|--|
| (Figlewicz et al., 1994)  | Case-Control | Candidate Gene/Region | PCR                | France and America                                       | Case: 356 SALS<br>Control: 306 neurologically healthy unrelated individuals   | -  | -   | Definite ALS (El Escorial)                       |
| (Vechio et al., 1996)     | Case-Control | Candidate Gene/Region | PCR-SSCP           | -  | Case: 100 FALS + 75 SALS<br>Control: 100 unrelated individuals  | -  | -   | -  |
| (Tomkins et al., 1998)    | Case-Control | Candidate Gene/Region | PCR                | UK   | Case: 164 ALS<br>Control: 207 age-matched unrelated individuals   | -  | -   | -  |
| (Al-Chalabi et al., 1999) | Case-Control | Candidate Gene/Region | PCR-SSCP           | UK and Scandinavia (Denmark, Norway, Sweden and Finland) | Case: UK: 19 FALS + 188 SALS<br>Scandinavia: 59 FALS + 264 SALS<br>Control: UK: 219 age, sex and ethnicity-matched individuals<br>Scandinavia: 228 age, sex and ethnicity-matched individuals | UK SALS: 109:79 (1.38)<br>Scandinavian Cases: 194:129 (1.50) | UK SALS: 55.2<br>Scandinavian Cases: 61.5 | -  |
| (Garcia et al., 2006)     | Case-Control | Candidate Gene/Region | PCR                | America  | Case: 100 FALS + 100 SALS<br>Control: 100 neurologically healthy individuals  | -  | -   | -  |
| (Daoud et al., 2011)      | Case-Control | Gene Panel            | PCR                | France and Canada  | Case: 80 FALS + 110 SALS<br>Control: 190 neurologically healthy individuals   | 104:86 (1.21)  | 55.4 ± 13.1                               | Definite or probable ALS (El Escorial)           |
| (Couthouis et al., 2014)  | Case-Control | Gene Panel            | WES                | America  | Case: 242 SALS<br>Control: 29 age-matched individuals   | 131:111 (1.18)   | 60 (44-82)                                | Definite, probable or possible ALS (El Escorial) |

|                          |              |               |              |                   |  |  |   |   |
|--------------------------|--------------|---------------|--------------|-------------------|--|--|---|---|
| (Nakamura et al., 2016)  | Case-Control | Gene Panel    | WES + PCR    | Japan             | Case: 39 FALS + 469 SALS<br>Control: 191 neurologically healthy individuals                            | 298:210<br>(1.42)                                | 62.1 (53.5-68.4)                        | Definite, probable, probable laboratory-supported or possible ALS (EI Escorial) |
| (Krüger et al., 2016)    | Case         | Gene Panel    | NGS          | Germany           | Case: 80 ALS   | 44:36 (1.22)                                     | 60.1 (29-88)                            | -   |
| (Pang et al., 2017)      | Case-Control | Gene Panel    | WGS + WES    | China (Hong-Kong) | Case: 8 FALS + 46 SALS<br>Control: 699 volunteer individuals   | FALS: 3:5<br>(0.60)<br>SALS: 28:18<br>(1.56)     | FALS: 41.4 ± 8.71<br>SALS: 58.1 ± 13.45 | Definite, probable or probable laboratory-supported ALS (EI Escorial)           |
| (Morgan et al., 2017)    | Case-Control | Gene Panel    | WES + PCR    | UK                | Case: 131 FALS + 995 SALS<br>Control: 613 neurologically healthy age and ethnicity-matched individuals | FALS: 67:64<br>(1.05)<br>SALS: 567:428<br>(1.32) | FALS: 56 (24-85)<br>SALS: 61 (25-88)    | -   |
| (Nishiyama et al., 2017) | Case         | Gene Panel    | WES + Sanger | Japan             | 51 FALS  | -  | -                                       | EI Escorial   |
| (Garton et al., 2017)    | Case         | Variant Panel | WES          | Australia         | 120 ALS  | 75:45 (1.67)                                     | 61 ± 10.1                               | Definite or probable ALS (revised EI Escorial)                                  |
| (Muller et al., 2018)    | Case         | Gene Panel    | WES + PCR    | Germany           | 171 FALS   | -  | -                                       | EI Escorial   |
| (H. Zhang et al., 2018)  | Case-Control | Gene Panel    | WES + Sanger | China             | Case: 311 SALS<br>Control: 200 neurologically healthy individuals                                      | 199:112<br>(1.78)                                | 51.92 ± 10.8                            | Definite, probable, probable laboratory-supported or possible ALS (EI Escorial) |

|                              |              |                       |              |            |  |   |  |   |
|------------------------------|--------------|-----------------------|--------------|------------|--|---|--|---|
| (Z.-J. Liu et al., 2019)     | Case         | Gene Panel            | WES          | China      | 24 FALS + 21 early-onset SALS                                      | FALS: 13:11 (1.18)<br>SALS: 13:8 (1.63) | FALS: 40.3 ± 14.8<br>SALS: 30.7 ± 11.5 | EI Escorial   |
| (Tripolszki et al., 2019)    | Case         | Gene Panel            | WES          | Hungary    | 107 ALS  | 45:62 (0.73)                            | 60 (30-79)                             | EI Escorial + Awaji-Shima   |
| (W. Chen et al., 2020)       | Case         | Gene Panel            | WES + Sanger | China      | 268 ALS  | 160:108 (1.48)                          | 52.1 ± 10.4                            | Definite or probable ALS (EI Escorial)  |
| (F. Lin et al., 2021)        | Case-Control | Candidate Gene/Region | PCR          | China      | Case: 671 SALS<br>Control: 1787 neurologically healthy individuals | 410:261 (1.57)                          | 53.45 ± 9.96                           | EI Escorial   |
| (Giguët-Valard et al., 2021) | Case Report  | Whole Genome          | WES          | Martinique | 5 related FALS   | -                                       | -                                      | -   |
| (Shepherd et al., 2021)      | Case         | Gene Panel            | WES          | UK         | 7 FALS + 93 SALS   | 54:46 (1.17)                            | 60.4 (22-87)                           | Definite, probable, probable laboratory-supported or possible ALS (revised EI Escorial) |
| (McCann et al., 2021)        | Case         | Variant Panel         | WGS          | Australia  | 616 SALS   | 346:221 (1.57)                          | 60 ± 12                                | Definite or probable ALS (EI Escorial)  |

*Table A7. Summary characteristics of all included studies identified from the systematic review. All case-control studies (12) proceeded to the meta-analysis stage. FALS = familial ALS, SALS = sporadic ALS, WES = whole exome sequencing, WGS = whole genome sequencing, PCR = polymerase chain reaction, NGS = next-generation sequencing, PCR-SSCP = polymerase chain reaction-single-strand conformation polymorphism.*

| Variant Name<br>(HGVS Protein<br>Notation) | Domain     | rsID         | SIFT<br>Prediction | PolyPhen<br>Prediction | Case<br>Frequency | Control<br>Frequency | gnomAD v2.1.1<br>non-neuro<br>Frequency | Other Carried<br>Variants | Statistical<br>Analysis Results    | References                |
|--|------------|--------------|--------------------|------------------------|-------------------|----------------------|---|---------------------------|------------------------------------|---------------------------|
| E459Gfs*7                                  | Tail (E)   | rs59297913   | Deleterious        | Benign                 | 1/171             | -                    | N/A                                     | -                         | -                                  | (Muller et al., 2018)     |
| A528_P561del                               | Tail (KSP) | rs2063061681 | -                  | -                      | 1/356             | 0/306                | N/A                                     | -                         | -                                  | (Figlewicz et al., 1994)  |
| A652_K657del                               | Tail (KSP) | rs147489453  | -                  | -                      | 55/371            | 106/711              | 0.8726                                  | -                         | OR 0.98 (95% CI 0.77-1.26); p=0.89 | (F. Lin et al., 2021)     |
| E658_K665del                               | Tail (KSP) | rs1183993443 | -                  | -                      | 1/207             | 0/219                | 0.01947                                 | -                         | -                                  | (Al-Chalabi et al., 1999) |
|  |            |              |                    |                        | 2/371             | 6/711                | 0.02722                                 | -                         | OR 0.64 (95% CI 0.13-3.17); p=0.72 | (F. Lin et al., 2021)     |
| E664_P669del                               | Tail (KSP) | rs1317619836 | -                  | -                      | 1/207             | 1/219                | 0.0005205                               | -                         | -                                  | (Al-Chalabi et al., 1999) |
| A686_K699del                               | Tail (KSP) | -            | -                  | -                      | 2/323             | 1/228                | N/A                                     | -                         | -                                  | (Al-Chalabi et al., 1999) |
| S752_K757del                               | Tail (KSP) | rs570663492  | -                  | -                      | 1/323             | 2/228                | 0.0003574                               | -                         | -                                  | (Al-Chalabi et al., 1999) |
|  |            |              |                    |                        | 1/616             | -                    |   | OPTN M98K                 | -                                  | (McCann et al., 2021)     |
|  |            |              |                    |                        | 56/371            | 102/711              | 0.1138                                  | -                         | OR 1.07 (95% CI 0.83-1.37); p=0.61 | (F. Lin et al., 2021)     |
| K790del                                    | Tail (KSP) | rs59551486   | -                  | -                      | 4/356             | 0/306                | 0.001226                                | -                         | -                                  | (Figlewicz et al., 1994)  |

|                           |               |              |             |                   |        |       |            |           |                                     |                           |
|---------------------------|---------------|--------------|-------------|-------------------|--------|-------|------------|-----------|-------------------------------------|---------------------------|
|                           |               |              |             |                   | 1/1126 | 2/613 |            | -         | -                                   | (Morgan et al., 2017)     |
| K857del                   | Tail (KEP)    | rs762969612  | -           | -                 | 1/171  | -     | 0.00002324 | -         | -                                   | (Muller et al., 2018)     |
| S704_K731dup<br>(A708ins) | Tail (KSP)    | -            | -           | -                 | 1/164  | 0/209 | N/A        | -         | -                                   | (Tomkins et al., 1998)    |
| A40V                      | Head          | rs1474351396 | Tolerated   | Benign            | 1/185  | 1/190 | 0          | -         | -                                   | (Daoud et al., 2011)      |
| A90V                      | Head          | rs61556467   | Tolerated   | Benign            | 1/100  | 0/100 | 0.0005063  | -         | -                                   | (Garcia et al., 2006)     |
|                           |               |              |             |                   | 1/185  | -     |            | -         | -                                   | (Daoud et al., 2011)      |
| R148P                     | Rod (Coil 1B) | -            | Deleterious | Damaging          | 1/107  | -     | N/A        | -         | -                                   | (Tripolszki et al., 2019) |
| E152D                     | Rod (Coil 1B) | rs774792100  | Tolerated   | Benign            | 3/268  | -     | 0.003991   | -         | -                                   | (W. Chen et al., 2020)    |
|                           |               |              |             |                   | 1/371  | 1/711 |            | -         | OR 1.92 (95% CI 0.12-30.70); p=0.76 | (F. Lin et al., 2021)     |
| Q171H                     | Rod (Coil 1B) | -            | -           | -                 | 1/371  | 0/711 | N/A        | -         | OR Inf (95% CI Na-Inf); p=0.34      | (F. Lin et al., 2021)     |
| D187N                     | Rod (Coil 1B) | rs1372062630 | Deleterious | Probably Damaging | 1/469  | 0/191 | 0          | SOD1 L39V | -                                   | (Nakamura et al., 2016)   |
|                           |               |              |             |                   | 1/51   | -     | 0          | -         | -                                   | (Nishiyama et al., 2017)  |

|       |                                     |              |             |                   |       |       |            |             |                                |                           |
|-------|-------------------------------------|--------------|-------------|-------------------|-------|-------|------------|-------------|--------------------------------|---------------------------|
| R192P | Rod (Coil 1B)                       | rs2063001424 | Deleterious | -                 | 1/242 | 0/129 | N/A        | -           | -                              | (Couthouis et al., 2014)  |
| A203P | Rod (Coil 1B)                       | -            | Tolerated   | Possibly Damaging | 1/51  | -     | N/A        | SETX C1554G | -                              | (Nishiyama et al., 2017)  |
| G249S | Rod (linker between Coil 1B and 2A) | rs60825978   | Tolerated   | Benign            | 1/100 | 0/100 | 0.007444   | -           | -                              | (Garcia et al., 2006)     |
|       |                                     |              |             |                   | 1/268 | -     | 0.0305     | -           | -                              | (W. Chen et al., 2020)    |
|       |                                     |              |             |                   | 3/371 | 8/711 | -          | -           | (F. Lin et al., 2021)          |                           |
| S285R | Rod (Coil 2A)                       | rs1479105421 | Deleterious | Benign            | 1/469 | 0/191 | 0.0005071  | -           | -                              | (Nakamura et al., 2016)   |
|       |                                     |              |             |                   | 1/51  | -     | -          | -           | (Nishiyama et al., 2017)       |                           |
| A314V | Rod (Coil 2B)                       | rs539511579  | Deleterious | Probably Damaging | 1/371 | 0/711 | 0.0002238  | -           | OR Inf (95% CI Na-Inf); p=0.34 | (F. Lin et al., 2021)     |
| T338I | Rod (Coil 2B)                       | rs774252076  | Deleterious | Damaging          | 2/107 | -     | 0.00003355 | -           | -                              | (Tripolszki et al., 2019) |
| R346H | Rod (Coil 2B)                       | rs1401155915 | Tolerated   | Possibly Damaging | 1/186 | 0/190 | 0          | -           | -                              | (Daoud et al., 2011)      |
| R352S | Rod (Coil 2B)                       | rs149955255  | Deleterious | Possibly Damaging | 2/200 | 2/100 | 0.003516   | -           | -                              | (Garcia et al., 2006)     |
| A380T | Rod (Coil 2B)                       | rs201416955  | Tolerated   | Possibly Damaging | 1/100 | 0/100 | 0.00001939 | -           | -                              | (Garcia et al., 2006)     |
|       |                                     |              |             |                   | 2/311 | 0/200 | 0.005275   | OPTN R545Q  | -                              | (H. Zhang et al., 2018)   |

|       |               |              |             |                   |          |         |            |  |                                    |                           |
|-------|---------------|--------------|-------------|-------------------|----------|---------|------------|--|------------------------------------|---------------------------|
|       |               |              |             |                   | 2/268    | -       |            | -                                      | -                                  | (W. Chen et al., 2020)    |
|       |               |              |             |                   | 3/371    | 8/711   |            | -                                      | OR 0.72 (95% CI 0.19-2.71); p=0.76 | (F. Lin et al., 2021)     |
| A400V | Rod (Coil 2B) | rs757021413  | Deleterious | Probably Damaging | 51/190   | -       | N/A        | -                                      | -                                  | (Daoud et al., 2011)      |
| R412Q | Rod (Coil 2B) | rs763701610  | Deleterious | Possibly Damaging | 1/51     | -       | 0.00005584 | ITPR2 A612T, FUS c.-37C>T, ALS2 I1373M | -                                  | (Krüger et al., 2016)     |
| E460K | Tail (E)      | -            | -           | -                 | 20/100   | 8/100   | N/A        | -                                      | -                                  | (Vechio et al., 1996)     |
| E463K | Tail (E)      | rs59371099   | Deleterious | Probably Damaging | 32/180   | -       | 0.09682    | -                                      | -                                  | (Daoud et al., 2011)      |
|       |               |              |             |                   | 173/1126 | 109/613 |            | -                                      | -                                  | (Morgan et al., 2017)     |
| E491K | Tail (E)      | -            | -           | -                 | 1/268    | -       | N/A        | -                                      | -                                  | (W. Chen et al., 2020)    |
| P505L | Tail (E)      | rs1414968372 | Deleterious | Benign            | 1/107    | -       | N/A        | GRN C335R                              | -                                  | (Tripolszki et al., 2019) |
| P512S | Tail (E)      | -            | -           | -                 | 1/371    | 0/711   | N/A        | -                                      | OR Inf (95% CI Na-Inf); p=0.34     | (F. Lin et al., 2021)     |
| E597D | Tail (KSP)    | rs753850528  | Tolerated   | Benign            | 1/311    | 0/200   | 0.0002236  | -                                      | -                                  | (H. Zhang et al., 2018)   |
| P615L | Tail (KSP)    | rs5763269    | Deleterious | Possibly Damaging | 55/175   | 27/100  | 0.196      | -                                      | -                                  | (Vechio et al., 1996)     |



|       |            |              |             |                   |          |         |            |                 |                                    |                              |
|-------|------------|--------------|-------------|-------------------|----------|---------|------------|-----------------|------------------------------------|------------------------------|
|       |            |              |             |                   | 84/188   | -       | 0.2131     | -               | -                                  | (Daoud et al., 2011)         |
|       |            |              |             |                   | 414/1126 | 205/613 |            | -               | -                                  | (Morgan et al., 2017)        |
|       |            |              |             |                   | 30/371   | 66/711  | 0.07552    | -               | OR 0.84 (95% CI 0.61-1.16); p=0.30 | (F. Lin et al., 2021)        |
| T642M | Tail (KSP) | rs117258406  | Tolerated   | Benign            | 1/46     | 18/699  | 0.008416   | SPG11<br>L1982S | OR 0.78 (95% CI 0.02-5.19); p=1.00 | (Pang et al., 2017)          |
|       |            |              |             |                   | 4/311    | 0/200   |            | -               | -                                  | (H. Zhang et al., 2018)      |
|       |            |              |             |                   | 4/268    | -       |            | -               | -                                  | (W. Chen et al., 2020)       |
|       |            |              |             |                   | 4/371    | 5/711   |            | -               | -                                  | (F. Lin et al., 2021)        |
| K647N | Tail (KSP) | rs200634512  | Deleterious | Possibly Damaging | 1/5      | -       | 0.000358   | -               | -                                  | (Giguet-Valard et al., 2021) |
| V670E | Tail (KSP) | rs190692435  | Tolerated   | Possibly Damaging | 2/371    | 5/711   | 0.02705    | -               | OR 0.77 (95% CI 0.15-3.96); p=1.00 | (F. Lin et al., 2021)        |
| A672E | Tail (KSP) | rs775497149  | Tolerated   | Benign            | 1/371    | 5/711   | 0.02376    | -               | OR 0.38 (95% CI 0.05-3.28); p=0.67 | (F. Lin et al., 2021)        |
| V726L | Tail (KSP) | rs1051285707 | Tolerated   | Benign            | 1/120    | -       | 0.00003891 | -               | -                                  | (Garton et al., 2017)        |
| P777L | Tail (KSP) | rs199748453  | Deleterious | Probably Damaging | 1/100    | -       | 0.00005831 | ALS2 T293I      | -                                  | (Shepherd et al., 2021)      |
| S787R | Tail (KSP) | rs568759161  | Deleterious | Probably Damaging | 2/268    | -       | 0.002405   | -               | -                                  | (W. Chen et al., 2020)       |

|       |            |             |             |                      |          |         |            |   |  |                            |
|-------|------------|-------------|-------------|----------------------|----------|---------|------------|---|--|----------------------------|
|       |            |             |             |                      | 9/671    | 2/1787  |            | - | Discovery: OR<br>9.64 (95% CI<br>1.12-82.67);<br>p=0.02<br>Replication: OR<br>14.43 (95% CI<br>1.61-129.40);<br>p=0.009<br>Combined: OR<br>12.06 (95% CI<br>2.60-55.88);<br>p=0.0003 | (F. Lin et al.,<br>2021)   |
| A805E | Tail (KSP) | -           | -           | -                    | 80/100   | -       | N/A        | - | -  | (Vechio et al.,<br>1996)   |
| E805A | Tail (KSP) | rs165602    | Deleterious | Possibly<br>Damaging | 45/176   | -       | 0.1551     | - | -  | (Daoud et al.,<br>2011)    |
|       |            |             |             |                      | 309/1126 | 152/613 | 0.04673    | - | -  | (Morgan et al.,<br>2017)   |
|       |            |             |             |                      | 10/371   | 30/711  |            | - | -  | (F. Lin et al.,<br>2021)   |
| P848S | Tail (KEP) | -           | -           | -                    | 2/268    | -       | N/A        | - | (W. Chen et<br>al., 2020)  |                            |
| K857R | Tail (KEP) | rs747689406 | Deleterious | Possibly<br>Damaging | 1/311    | 0/200   | 0.00007522 | - | -  | (H. Zhang et<br>al., 2018) |
| K867N | Tail (KEP) | rs138156220 | Deleterious | Probably<br>Damaging | 1/182    | 0/190   | 0          | - | -  | (Daoud et al.,<br>2011)    |

|         |               |              |             |                   |        |        |            |              |                                     |                              |
|---------|---------------|--------------|-------------|-------------------|--------|--------|------------|--------------|-------------------------------------|------------------------------|
|         |               |              |             |                   | 1/5    | -      | 0          | SOD1 G93V    | -                                   | (Giguet-Valard et al., 2021) |
| E868K   | Tail (KEP)    | rs1295979036 | Tolerated   | Probably Damaging | 1/45   | -      | 0          | -            | -                                   | (Z.-J. Liu et al., 2019)     |
| T905I   | Tail (KEP)    | rs202199780  | Tolerated   | Benign            | 2/268  | -      | 0.001673   | -            | -                                   | (W. Chen et al., 2020)       |
| K917E   | Tail (KEP)    | -            | Deleterious | Possibly Damaging | 1/311  | 0/200  | 0          | CHMP2B A138T | -                                   | (H. Zhang et al., 2018)      |
| E918G   | Tail (KEP)    | rs189881592  | Deleterious | Possibly Damaging | 1/186  | 0/190  | 0          | -            | -                                   | (Daoud et al., 2011)         |
|         |               |              |             |                   | 1/311  | 0/200  | 0.003143   | -            | -                                   | (H. Zhang et al., 2018)      |
|         |               |              |             |                   | 2/268  | -      |            | -            | -                                   | (W. Chen et al., 2020)       |
|         |               |              |             |                   | 2/371  | 2/711  |            | -            | OR 1.92 (95% CI 0.27-13.65); p=0.61 | (F. Lin et al., 2021)        |
| Q117Ter | Rod (Coil 1A) | rs1317368575 | -           | -                 | 1/371  | 0/711  | 0.00009524 | -            | OR Inf (95% CI Na-Inf); p=0.34      | (F. Lin et al., 2021)        |
| L158L   | Rod (Coil 1B) | rs1002065392 | -           | -                 | 1/75   | 1/50   | 0          | -            | -                                   | (Vechio et al., 1996)        |
| L349L   | Rod (Coil 2B) | rs1269206770 | -           | -                 | 1/186  | -      | N/A        | -            | -                                   | (Daoud et al., 2011)         |
| A400A   | Rod (Coil 2B) | rs165734     | -           | -                 | 10/371 | 30/711 | 0.1807     | -            | -                                   | (F. Lin et al., 2021)        |

|       |               |             |   |   |                           |                       |          |   |   |                       |
|-------|---------------|-------------|---|---|---------------------------|-----------------------|----------|---|---|-----------------------|
| A401A | Rod (Coil 2B) | -           | - | - | 2x lower than in controls | 2x higher than in ALS | N/A      | - | - | (Vechio et al., 1996) |
| S580S | Tail (KSP)    | rs114263951 | - | - | 5/188                     | -                     | 0.01183  | - | - | (Daoud et al., 2011)  |
| A744A | Tail (KSP)    | rs165923    | - | - | 104/185                   | -                     | 0.7855   | - | - | (Daoud et al., 2011)  |
| D919D | Tail (KEP)    | rs56200920  | - | - | 1/186                     | -                     | 0.005927 | - | - | (Daoud et al., 2011)  |
|       |               |             |   |   | 2/371                     | 10/711                | 0.01124  | - | - | (F. Lin et al., 2021) |
| V928V | Tail (KEP)    | rs165625    | - | - | 149/186                   | -                     | 0.7856   | - | - | (Daoud et al., 2011)  |
|       |               |             |   |   | 30/371                    | 67/711                | 0.9238   | - | - | (F. Lin et al., 2021) |

*Table A8. Variant characteristics of all included records identified from the systematic review. All variants supported by case-control studies (34) were subject to subgroup-level meta-analysis, with 8 going forward to variant-level meta-analysis as the mutation was supported by at least 2 case-control studies. N/A values represent instances where the variant was not present in the population-specific gnomAD non-neuro database.*

| Variant                   | Start    | End      | Ref  | Alt |
|---------------------------|----------|----------|--|-----|
| E459Gfs*7                 | 29885004 | 29885004 | GAACA  | G   |
| A528_P561del              | 29885211 | 29885211 | GCTGAGGCCAAGTCCCCAGAGAAGGAGGAAGCAAATCCCCAGCCGAAGTCAAGTCCCCTGAGAAGGCC                 | G   |
| A652_K657del              | 29885576 | 29885576 | TGAGAAGGCCAAGTCCCC   | T   |
| E658_K665del              | 29885580 | 29885580 | AAGGCCAAGTCCCCAGAGAAGGAAG  | A   |
| E664_P669del              | 29885604 | 29885604 | GAGGCCAAGTCCCCTGAGA  | G   |
| A686_K699del              | 29885609 | 29885609 | CAAGTCCCCTGAGAAGGCCAAGTCCCCAGTGAAGGCAGAAGCA  | C   |
| S752_K757del              | 29885858 | 29885858 | AGCTAAGTCCCCAGAGAAG  | A   |
| K790del                   | 29885996 | 29885996 | CAAG   | C   |
| K857del                   | 29886192 | 29886192 | GAGA   | G   |
| S704_K731dup<br>(A708ins) | 29885709 | 29885709 | GCCAAGTCCCCAGTGAAGGAAGAAGCAAAGTCCCCTGAGAAGGCCAAGTCCCCAGTGAAGGAAGAAGCAAAGTCCCCTGAGAAG | G   |
| A40V                      | 29876370 | 29876370 | C  | T   |
| A90V                      | 29876520 | 29876520 | C  | T   |
| R148P                     | 29876694 | 29876694 | G  | C   |
| E152D                     | 29876707 | 29876707 | G  | C   |
| Q171H                     | 29876764 | 29876764 | G  | C   |
| D187N                     | 29876810 | 29876810 | G  | A   |
| R192P                     | 29876826 | 29876826 | G  | C   |
| A203P                     | 29876858 | 29876858 | G  | C   |
| G249S                     | 29876996 | 29876996 | G  | A   |
| S285R                     | 29877106 | 29877106 | C  | A   |
| A314V                     | 29879421 | 29879421 | C  | T   |
| T338I                     | 29879493 | 29879493 | C  | T   |
| R346H                     | 29879517 | 29879517 | G  | A   |
| R352S                     | 29879534 | 29879534 | C  | A   |
| A380T                     | 29881766 | 29881766 | G  | A   |
| A400V                     | 29881827 | 29881827 | C  | T   |
| R412Q                     | 29884864 | 29884864 | G  | A   |

|         |          |          |   |   |
|---------|----------|----------|---|---|
| E460K   | -        | -        | - | - |
| E463K   | 29885016 | 29885016 | G | A |
| E491K   | 29885100 | 29885100 | G | A |
| P505L   | 29885143 | 29885143 | C | T |
| P512S   | 29885163 | 29885163 | C | T |
| E597D   | 29885420 | 29885420 | G | C |
| P615L   | 29885473 | 29885473 | C | T |
| T642M   | 29885554 | 29885554 | C | T |
| K647N   | 29885570 | 29885570 | G | C |
| V670E   | 29885638 | 29885638 | T | A |
| A672E   | 29885644 | 29885644 | C | A |
| V726L   | 29885805 | 29885805 | G | C |
| P777L   | 29885959 | 29885959 | C | T |
| S787R   | 29885990 | 29885990 | C | G |
| A805E   | 29886043 | 29886043 | C | A |
| E805A   | 29886043 | 29886043 | A | C |
| P848S   | 29886171 | 29886171 | C | T |
| K857R   | 29886199 | 29886199 | A | G |
| K867N   | 29886230 | 29886230 | G | T |
| E868K   | 29886231 | 29886231 | G | A |
| T905I   | 29886343 | 29886343 | C | T |
| K917E   | 29886378 | 29886378 | A | G |
| E918G   | 29886382 | 29886382 | A | G |
| Q117Ter | 29876600 | 29876600 | C | T |
| L158L   | 29876725 | 29876725 | G | A |
| L349L   | 29879527 | 29879527 | G | T |
| A400A   | 29881828 | 29881828 | C | T |
| A401A   | -        | -        | - | - |
| S580S   | 29885369 | 29885369 | C | T |

|       |          |          |   |   |
|-------|----------|----------|---|---|
| A744A | 29885861 | 29885861 | T | C |
| D919D | 29886386 | 29886386 | C | T |
| V928V | 29886413 | 29886413 | A | G |

Table A9. Genomic coordinates and base pair substitutions (hg19) of all variants identified from the systematic review.

| Variant      | No. Studies | N Cases | N Controls | Fixed OR (95% CI; p-value) | Random OR (95% CI; p-value) | Heterogeneity (Q statistic; p-value) | Heterogeneity (I-squared) | Publication Bias (Egger t statistic; p-value) | Publication Bias (Harbord t statistic; p-value) |
|--------------|-------------|---------|------------|----------------------------|-----------------------------|--------------------------------------|---------------------------|---|---|
| G249S        | 2           | 471     | 811        | 0.91 (0.28-2.94; 0.87)     | 0.89 (0.26-3.03; 0.85)      | 0.66 (0.42)                          | 0%                        | N/A   | N/A   |
| A380T        | 3           | 782     | 1011       | 1.12 (0.39-3.21; 0.83)     | 1.06 (0.34-3.33; 0.92)      | 1.26 (0.53)                          | 0%                        | 12.17; <b>0.05</b>                            | 5.01; 0.13                                      |
| P615L        | 3           | 1672    | 1424       | 1.11 (0.93-1.33; 0.24)     | 1.11 (0.93-1.33; 0.24)      | 1.54 (0.46)                          | 0%                        | -0.46; 0.73                                   | -0.46; 0.73                                     |
| T642M        | 3           | 728     | 1610       | 1.71 (0.66-4.42; 0.27)     | 1.56 (0.55-4.39; 0.40)      | 1.14 (0.57)                          | 0%                        | 0.56; 0.67                                    | 0.35; 0.79                                      |
| E658_K665del | 2           | 578     | 930        | 0.91 (0.24-3.45; 0.88)     | 0.88 (0.21-3.70; 0.86)      | 0.78 (0.38)                          | 0%                        | N/A   | N/A   |
| S752_K757del | 2           | 694     | 939        | 1.03 (0.73-1.47; 0.85)     | 1.04 (0.73-1.47; 0.84)      | 0.80 (0.37)                          | 0%                        | N/A   | N/A   |
| K790del      | 2           | 1482    | 919        | 1.56 (0.37-6.64; 0.55)     | 1.31 (0.05-35.02; 0.87)     | 3.03 (0.08)                          | <b>67%</b>                | N/A   | N/A   |
| E805A        | 2           | 1497    | 1324       | 1.08 (0.88-1.34; 0.46)     | 0.94 (0.54-1.64; 0.83)      | 2.40 (0.12)                          | <b>58%</b>                | N/A   | N/A   |
| E918G        | 3           | 868     | 1101       | 2.16 (0.49-9.46; 0.31)     | 2.13 (0.48-9.40; 0.32)      | 0.06 (0.97)                          | 0%                        | 0.78; 0.58                                    | 4.18; 0.15                                      |

Table A10. Results of the variant-level meta-analysis. N/A values represent instances where publication bias could not be calculated as the minimum number of studies used for calculation was not reached.

| Start    | End      | Ref | Alt | Variant Type | VEP Impact | Exon | Intron | HGVS.c   | HGVS.p      | rsID         |
|----------|----------|-----|-----|--------------|------------|------|--------|----------|-------------|--------------|
| 29876227 | 29876227 | C   | G   | 5' UTR       | Modifier   | 1    | -      | c.-25C>G | -           | -            |
| 29876229 | 29876229 | G   | A   | 5' UTR       | Modifier   | 1    | -      | c.-23G>A | -           | rs1280164847 |
| 29876235 | 29876235 | G   | C   | 5' UTR       | Modifier   | 1    | -      | c.-17G>C | -           | -            |
| 29876236 | 29876236 | C   | A   | 5' UTR       | Modifier   | 1    | -      | c.-16C>A | -           | rs996402317  |
| 29876272 | 29876272 | G   | A   | Synonymous   | Low        | 1    | -      | c.21G>A  | p.Ala7Ala   | rs192350983  |
| 29876298 | 29876298 | C   | A   | Missense     | Moderate   | 1    | -      | c.47C>A  | p.Ala16Glu  | rs1468605569 |
| 29876336 | 29876336 | G   | T   | Missense     | Moderate   | 1    | -      | c.85G>T  | p.Ala29Ser  | rs752311867  |
| 29876338 | 29876338 | C   | T   | Synonymous   | Low        | 1    | -      | c.87C>T  | p.Ala29Ala  | -            |
| 29876348 | 29876348 | G   | A   | Missense     | Moderate   | 1    | -      | c.97G>A  | p.Gly33Ser  | -            |
| 29876392 | 29876392 | C   | T   | Synonymous   | Low        | 1    | -      | c.141C>T | p.Phe47Phe  | rs780966618  |
| 29876395 | 29876395 | C   | G   | Missense     | Moderate   | 1    | -      | c.144C>G | p.His48Gln  | rs1325065979 |
| 29876404 | 29876404 | A   | G   | Synonymous   | Low        | 1    | -      | c.153A>G | p.Thr51Thr  | rs755886692  |
| 29876410 | 29876410 | G   | A   | Synonymous   | Low        | 1    | -      | c.159G>A | p.Thr53Thr  | rs1205368020 |
| 29876416 | 29876416 | G   | A   | Synonymous   | Low        | 1    | -      | c.165G>A | p.Val55Val  | rs897546803  |
| 29876473 | 29876473 | C   | T   | Synonymous   | Low        | 1    | -      | c.222C>T | p.Thr74Thr  | rs1413495861 |
| 29876520 | 29876520 | C   | T   | Missense     | Moderate   | 1    | -      | c.269C>T | p.Ala90Val  | rs61556467   |
| 29876529 | 29876529 | C   | T   | Missense     | Moderate   | 1    | -      | c.278C>T | p.Thr93Ile  | rs751160327  |
| 29876552 | 29876552 | C   | T   | Synonymous   | Low        | 1    | -      | c.301C>T | p.Leu101Leu | rs1231899865 |
| 29876555 | 29876555 | C   | T   | Stop Gained  | High       | 1    | -      | c.304C>T | p.Gln102Ter | rs948554818  |
| 29876609 | 29876609 | G   | A   | Missense     | Moderate   | 1    | -      | c.358G>A | p.Ala120Thr | rs1386911340 |
| 29876620 | 29876620 | C   | T   | Synonymous   | Low        | 1    | -      | c.369C>T | p.Arg123Arg | rs768460278  |
| 29876632 | 29876632 | C   | G   | Synonymous   | Low        | 1    | -      | c.381C>G | p.Gly127Gly | rs760591823  |
| 29876649 | 29876649 | G   | A   | Missense     | Moderate   | 1    | -      | c.398G>A | p.Arg133Gln | rs997535105  |
| 29876660 | 29876660 | G   | T   | Missense     | Moderate   | 1    | -      | c.409G>T | p.Ala137Ser | rs754799725  |
| 29876668 | 29876668 | C   | G   | Synonymous   | Low        | 1    | -      | c.417C>G | p.Arg139Arg | rs912176188  |
| 29876699 | 29876699 | G   | A   | Missense     | Moderate   | 1    | -      | c.448G>A | p.Val150Ile | rs769162779  |
| 29876744 | 29876744 | G   | A   | Missense     | Moderate   | 1    | -      | c.493G>A | p.Gly165Ser | -            |
| 29876747 | 29876747 | C   | T   | Stop Gained  | High       | 1    | -      | c.496C>T | p.Gln166Ter | -            |
| 29876754 | 29876754 | G   | T   | Missense     | Moderate   | 1    | -      | c.503G>T | p.Arg168Leu | rs1009899708 |
| 29876756 | 29876756 | C   | T   | Synonymous   | Low        | 1    | -      | c.505C>T | p.Leu169Leu | rs1277092292 |
| 29876761 | 29876761 | G   | A   | Synonymous   | Low        | 1    | -      | c.510G>A | p.Glu170Glu | rs1208767813 |
| 29876765 | 29876765 | G   | A   | Missense     | Moderate   | 1    | -      | c.514G>A | p.Glu172Lys | rs1176398662 |



|          |          |           |   |                        |          |   |   |              |                    |              |
|----------|----------|-----------|---|------------------------|----------|---|---|--------------|--------------------|--------------|
| 29876777 | 29876777 | G         | A | Missense               | Moderate | 1 | - | c.526G>A     | p.Glu176Lys        | rs1422942222 |
| 29876800 | 29876800 | G         | A | Synonymous             | Low      | 1 | - | c.549G>A     | p.Gln183Gln        | -            |
| 29876834 | 29876834 | G         | A | Missense               | Moderate | 1 | - | c.583G>A     | p.Ala195Thr        | rs1273011909 |
| 29876842 | 29876842 | G         | C | Synonymous             | Low      | 1 | - | c.591G>C     | p.Ala197Ala        | rs1459116357 |
| 29876845 | 29876845 | G         | A | Synonymous             | Low      | 1 | - | c.594G>A     | p.Ala198Ala        | rs748478910  |
| 29876857 | 29876857 | CGCGCGCTG | - | Frameshift<br>Deletion | High     | 1 | - | c.606_613del | p.Ala203ArgfsTer74 | -            |
| 29876866 | 29876866 | C         | T | Synonymous             | Low      | 1 | - | c.615C>T     | p.Phe205Phe        | rs1301849129 |
| 29876878 | 29876878 | C         | G | Synonymous             | Low      | 1 | - | c.627C>G     | p.Ala209Ala        | rs562497163  |
| 29876927 | 29876927 | G         | A | Missense               | Moderate | 1 | - | c.676G>A     | p.Glu226Lys        | -            |
| 29876952 | 29876952 | A         | C | Missense               | Moderate | 1 | - | c.701A>C     | p.His234Pro        | -            |
| 29876955 | 29876955 | A         | T | Missense               | Moderate | 1 | - | c.704A>T     | p.Gln235Leu        | -            |
| 29876977 | 29876977 | C         | G | Synonymous             | Low      | 1 | - | c.726C>G     | p.Leu242Leu        | rs560344725  |
| 29876978 | 29876978 | G         | A | Missense               | Moderate | 1 | - | c.727G>A     | p.Gly243Ser        | rs548521745  |
| 29876983 | 29876983 | G         | A | Synonymous             | Low      | 1 | - | c.732G>A     | p.Gln244Gln        | rs527475764  |
| 29876996 | 29876996 | G         | A | Missense               | Moderate | 1 | - | c.745G>A     | p.Gly249Ser        | rs60825978   |
| 29877028 | 29877028 | G         | T | Synonymous             | Low      | 1 | - | c.777G>T     | p.Thr259Thr        | rs915610438  |
| 29877033 | 29877033 | A         | G | Missense               | Moderate | 1 | - | c.782A>G     | p.Asp261Gly        | rs768531339  |
| 29877061 | 29877061 | G         | C | Synonymous             | Low      | 1 | - | c.810G>C     | p.Ala270Ala        | rs201868609  |
| 29877094 | 29877094 | C         | G | Missense               | Moderate | 1 | - | c.843C>G     | p.His281Gln        | rs1267522365 |
| 29877099 | 29877099 | T         | C | Missense               | Moderate | 1 | - | c.848T>C     | p.Val283Ala        | -            |
| 29877102 | 29877102 | A         | G | Missense               | Moderate | 1 | - | c.851A>G     | p.Gln284Arg        | rs746595090  |
| 29877107 | 29877107 | A         | G | Missense               | Moderate | 1 | - | c.856A>G     | p.Thr286Ala        | rs770443491  |
| 29877109 | 29877109 | G         | C | Synonymous             | Low      | 1 | - | c.858G>C     | p.Thr286Thr        | rs1477253596 |
| 29877142 | 29877142 | G         | A | Intronic               | Low      | - | 1 | c.883+8G>A   | -                  | rs1191279791 |
| 29877150 | 29877150 | G         | A | Intronic               | Modifier | - | 1 | c.883+16G>A  | -                  | rs534281794  |
| 29877158 | 29877158 | G         | C | Intronic               | Modifier | - | 1 | c.883+24G>C  | -                  | rs1359878602 |
| 29877205 | 29877205 | C         | G | Intronic               | Modifier | - | 1 | c.883+71C>G  | -                  | rs1474258062 |
| 29877208 | 29877208 | A         | G | Intronic               | Modifier | - | 1 | c.883+74A>G  | -                  | -            |
| 29877222 | 29877222 | G         | A | Intronic               | Modifier | - | 1 | c.883+88G>A  | -                  | rs567088364  |
| 29877234 | 29877234 | A         | G | Intronic               | Modifier | - | 1 | c.883+100A>G | -                  | -            |
| 29877239 | 29877239 | C         | T | Intronic               | Modifier | - | 1 | c.883+105C>T | -                  | rs1414146401 |
| 29877256 | 29877256 | C         | T | Intronic               | Modifier | - | 1 | c.883+122C>T | -                  | rs534144890  |
| 29877263 | 29877263 | A         | G | Intronic               | Modifier | - | 1 | c.883+129A>G | -                  | rs138081293  |

|          |          |    |                           |          |          |   |   |                          |   |              |
|----------|----------|----|---------------------------|----------|----------|---|---|--------------------------|---|--------------|
| 29877317 | 29877317 | C  | T                         | Intronic | Modifier | - | 1 | c.883+183C>T             | - | -            |
| 29877321 | 29877321 | A  | G                         | Intronic | Modifier | - | 1 | c.883+187A>G             | - | rs367951665  |
| 29877324 | 29877324 | C  | T                         | Intronic | Modifier | - | 1 | c.883+190C>T             | - | -            |
| 29877343 | 29877343 | C  | T                         | Intronic | Modifier | - | 1 | c.883+209C>T             | - | rs1373636600 |
| 29877344 | 29877344 | C  | T                         | Intronic | Modifier | - | 1 | c.883+210C>T             | - | rs573999650  |
| 29877346 | 29877346 | C  | G                         | Intronic | Modifier | - | 1 | c.883+212C>G             | - | -            |
| 29877367 | 29877367 | G  | A                         | Intronic | Modifier | - | 1 | c.883+233G>A             | - | rs56083406   |
| 29877370 | 29877370 | C  | T                         | Intronic | Modifier | - | 1 | c.883+236C>T             | - | -            |
| 29877386 | 29877386 | C  | T                         | Intronic | Modifier | - | 1 | c.883+252C>T             | - | -            |
| 29877417 | 29877417 | C  | T                         | Intronic | Modifier | - | 1 | c.883+283C>T             | - | rs165607     |
| 29877432 | 29877432 | C  | T                         | Intronic | Modifier | - | 1 | c.883+298C>T             | - | rs556602600  |
| 29877437 | 29877437 | C  | CGTCAAGAAAA<br>AAACAAGTTT | Intronic | Modifier | - | 1 | c.883+305_883<br>+325dup | - | rs760534140  |
| 29877441 | 29877441 | C  | G                         | Intronic | Modifier | - | 1 | c.883+307C>G             | - | rs73407035   |
| 29877444 | 29877444 | G  | A                         | Intronic | Modifier | - | 1 | c.883+317dup             | - | rs763994664  |
| 29877448 | 29877448 | A  | G                         | Intronic | Modifier | - | 1 | c.883+314A>G             | - | -            |
| 29877475 | 29877475 | G  | A                         | Intronic | Modifier | - | 1 | c.883+341G>A             | - | rs576631246  |
| 29877541 | 29877541 | G  | C                         | Intronic | Modifier | - | 1 | c.883+407G>C             | - | -            |
| 29877545 | 29877545 | A  | G                         | Intronic | Modifier | - | 1 | c.883+411A>G             | - | rs75956622   |
| 29877557 | 29877557 | C  | T                         | Intronic | Modifier | - | 1 | c.883+423C>T             | - | rs165697     |
| 29877565 | 29877565 | A  | G                         | Intronic | Modifier | - | 1 | c.883+431A>G             | - | rs165865     |
| 29877581 | 29877581 | T  | A                         | Intronic | Modifier | - | 1 | c.883+447T>A             | - | rs188853358  |
| 29877587 | 29877587 | C  | T                         | Intronic | Modifier | - | 1 | c.883+453C>T             | - | rs144739005  |
| 29877592 | 29877592 | C  | A                         | Intronic | Modifier | - | 1 | c.883+458C>A             | - | rs1218743924 |
| 29877620 | 29877620 | T  | A                         | Intronic | Modifier | - | 1 | c.883+486T>A             | - | -            |
| 29877624 | 29877624 | C  | T                         | Intronic | Modifier | - | 1 | c.883+490C>T             | - | rs79658766   |
| 29877625 | 29877625 | A  | G                         | Intronic | Modifier | - | 1 | c.883+491A>G             | - | rs165821     |
| 29877656 | 29877656 | AC | -                         | Intronic | Modifier | - | 1 | c.883+522del             | - | rs1168824251 |
| 29877657 | 29877657 | G  | C                         | Intronic | Modifier | - | 1 | c.883+523G>C             | - | rs78580989   |
| 29877693 | 29877693 | C  | A                         | Intronic | Modifier | - | 1 | c.883+559C>A             | - | -            |
| 29877699 | 29877699 | G  | A                         | Intronic | Modifier | - | 1 | c.883+565G>A             | - | rs780172669  |
| 29877700 | 29877700 | G  | A                         | Intronic | Modifier | - | 1 | c.883+566G>A             | - | -            |
| 29877710 | 29877710 | C  | T                         | Intronic | Modifier | - | 1 | c.883+576C>T             | - | -            |
| 29877715 | 29877715 | G  | A                         | Intronic | Modifier | - | 1 | c.883+581G>A             | - | -            |

|          |          |                                 |      |          |          |   |   |                           |   |              |
|----------|----------|---------------------------------|------|----------|----------|---|---|---------------------------|---|--------------|
| 29877716 | 29877716 | T                               | G    | Intronic | Modifier | - | 1 | c.883+582T>G              | - | -            |
| 29877803 | 29877803 | A                               | G    | Intronic | Modifier | - | 1 | c.883+669A>G              | - | -            |
| 29877809 | 29877809 | G                               | A    | Intronic | Modifier | - | 1 | c.883+675G>A              | - | rs1187445478 |
| 29877855 | 29877855 | G                               | T    | Intronic | Modifier | - | 1 | c.883+721G>T              | - | -            |
| 29877860 | 29877860 | G                               | T    | Intronic | Modifier | - | 1 | c.883+726G>T              | - | rs73881537   |
| 29877874 | 29877874 | C                               | G    | Intronic | Modifier | - | 1 | c.883+740C>G              | - | -            |
| 29877877 | 29877877 | C                               | TGCA | Intronic | Modifier | - | 1 | c.883+744_883<br>+747dup  | - | rs1265330728 |
| 29877882 | 29877882 | G                               | A    | Intronic | Modifier | - | 1 | c.883+748G>A              | - | rs561113494  |
| 29877893 | 29877893 | A                               | G    | Intronic | Modifier | - | 1 | c.883+759A>G              | - | -            |
| 29877907 | 29877907 | T                               | G    | Intronic | Modifier | - | 1 | c.883+773T>G              | - | -            |
| 29877961 | 29877961 | G                               | C    | Intronic | Modifier | - | 1 | c.883+827G>C              | - | -            |
| 29877979 | 29877979 | C                               | T    | Intronic | Modifier | - | 1 | c.883+845C>T              | - | -            |
| 29877999 | 29877999 | ACTGT                           | -    | Intronic | Modifier | - | 1 | c.883+866_883<br>+869del  | - | rs1359000475 |
| 29878010 | 29878010 | CTT                             | -    | Intronic | Modifier | - | 1 | c.883+876_883<br>+877del  | - | rs1341072419 |
| 29878010 | 29878010 | T                               | C    | Intronic | Modifier | - | 1 | c.883+876T>C              | - | rs563803182  |
| 29878026 | 29878026 | TGAGA                           | -    | Intronic | Modifier | - | 1 | c.883+894_883<br>+897del  | - | rs918545488  |
| 29878039 | 29878039 | G                               | T    | Intronic | Modifier | - | 1 | c.883+905G>T              | - | rs747959620  |
| 29878057 | 29878057 | A                               | G    | Intronic | Modifier | - | 1 | c.883+923A>G              | - | -            |
| 29878068 | 29878068 | A                               | T    | Intronic | Modifier | - | 1 | c.883+934A>T              | - | -            |
| 29878168 | 29878168 | C                               | T    | Intronic | Modifier | - | 1 | c.883+1034C>T             | - | rs577782932  |
| 29878198 | 29878198 | T                               | C    | Intronic | Modifier | - | 1 | c.883+1068dup             | - | rs543584318  |
| 29878200 | 29878200 | C                               | T    | Intronic | Modifier | - | 1 | c.883+1066C>T             | - | rs1018018710 |
| 29878201 | 29878201 | C                               | T    | Intronic | Modifier | - | 1 | c.883+1067C>T             | - | rs115007285  |
| 29878318 | 29878318 | G                               | A    | Intronic | Modifier | - | 1 | c.884-1046G>A             | - | rs137916245  |
| 29878328 | 29878328 | G                               | A    | Intronic | Modifier | - | 1 | c.884-1036G>A             | - | rs776842833  |
| 29878367 | 29878367 | C                               | G    | Intronic | Modifier | - | 1 | c.884-997C>G              | - | rs980795548  |
| 29878435 | 29878435 | AGGTTTCCTGG<br>GAACCACGAGC<br>G | -    | Intronic | Modifier | - | 1 | c.884-946_884-<br>925del  | - | -            |
| 29878445 | 29878445 | C                               | G    | Intronic | Modifier | - | 1 | c.884-914dup              | - | rs148457788  |
| 29878448 | 29878448 | G                               | A    | Intronic | Modifier | - | 1 | c.884-916_884-<br>915insA | - | rs59399758   |

|          |          |     |   |          |          |   |   |                      |   |              |
|----------|----------|-----|---|----------|----------|---|---|----------------------|---|--------------|
| 29878450 | 29878450 | G   | C | Intronic | Modifier | - | 1 | c.884-914G>C         | - | -            |
| 29878452 | 29878452 | C   | G | Intronic | Modifier | - | 1 | c.884-912C>G         | - | rs759563670  |
| 29878481 | 29878481 | A   | G | Intronic | Modifier | - | 1 | c.884-883A>G         | - | rs114042882  |
| 29878483 | 29878483 | G   | A | Intronic | Modifier | - | 1 | c.884-881G>A         | - | rs995319069  |
| 29878525 | 29878525 | C   | T | Intronic | Modifier | - | 1 | c.884-839C>T         | - | rs982635274  |
| 29878581 | 29878581 | G   | A | Intronic | Modifier | - | 1 | c.884-783G>A         | - | -            |
| 29878583 | 29878583 | C   | T | Intronic | Modifier | - | 1 | c.884-781C>T         | - | -            |
| 29878629 | 29878629 | G   | A | Intronic | Modifier | - | 1 | c.884-735G>A         | - | rs990302434  |
| 29878670 | 29878670 | T   | C | Intronic | Modifier | - | 1 | c.884-694T>C         | - | rs114681751  |
| 29878698 | 29878698 | A   | G | Intronic | Modifier | - | 1 | c.884-666A>G         | - | -            |
| 29878709 | 29878709 | C   | T | Intronic | Modifier | - | 1 | c.884-655C>T         | - | rs1050867473 |
| 29878820 | 29878820 | T   | C | Intronic | Modifier | - | 1 | c.884-544T>C         | - | -            |
| 29878865 | 29878865 | G   | A | Intronic | Modifier | - | 1 | c.884-499G>A         | - | rs60499988   |
| 29878869 | 29878869 | C   | T | Intronic | Modifier | - | 1 | c.884-495C>T         | - | rs1268750543 |
| 29878874 | 29878874 | G   | A | Intronic | Modifier | - | 1 | c.884-490G>A         | - | -            |
| 29878890 | 29878890 | C   | T | Intronic | Modifier | - | 1 | c.884-474C>T         | - | -            |
| 29878894 | 29878894 | A   | C | Intronic | Modifier | - | 1 | c.884-470A>C         | - | -            |
| 29878930 | 29878930 | G   | T | Intronic | Modifier | - | 1 | c.884-434G>T         | - | rs1046802224 |
| 29878947 | 29878947 | T   | C | Intronic | Modifier | - | 1 | c.884-417T>C         | - | rs957592448  |
| 29878961 | 29878961 | CAT | - | Intronic | Modifier | - | 1 | c.884-404_884-403del | - | rs1482065911 |
| 29878995 | 29878995 | C   | T | Intronic | Modifier | - | 1 | c.884-369C>T         | - | rs762182598  |
| 29879010 | 29879010 | C   | T | Intronic | Modifier | - | 1 | c.884-354C>T         | - | rs1012822803 |
| 29879022 | 29879022 | C   | A | Intronic | Modifier | - | 1 | c.884-342C>A         | - | rs143372377  |
| 29879036 | 29879036 | G   | A | Intronic | Modifier | - | 1 | c.884-328G>A         | - | rs942354319  |
| 29879044 | 29879044 | C   | T | Intronic | Modifier | - | 1 | c.884-320C>T         | - | rs1039764937 |
| 29879072 | 29879072 | G   | A | Intronic | Modifier | - | 1 | c.884-292G>A         | - | rs577074185  |
| 29879079 | 29879079 | G   | A | Intronic | Modifier | - | 1 | c.884-285G>A         | - | rs949238939  |
| 29879211 | 29879211 | C   | T | Intronic | Modifier | - | 1 | c.884-153C>T         | - | rs1249661164 |
| 29879212 | 29879212 | G   | A | Intronic | Modifier | - | 1 | c.884-152G>A         | - | rs1456261265 |
| 29879229 | 29879229 | C   | T | Intronic | Modifier | - | 1 | c.884-135C>T         | - | rs562037652  |
| 29879246 | 29879246 | C   | T | Intronic | Modifier | - | 1 | c.884-118C>T         | - | -            |
| 29879247 | 29879247 | G   | A | Intronic | Modifier | - | 1 | c.884-117G>A         | - | rs112005621  |
| 29879251 | 29879251 | G   | A | Intronic | Modifier | - | 1 | c.884-113G>A         | - | rs1176098439 |

|          |          |     |                     |                       |          |   |   |                      |                    |              |
|----------|----------|-----|---------------------|-----------------------|----------|---|---|----------------------|--------------------|--------------|
| 29879252 | 29879252 | C   | T                   | Intronic              | Modifier | - | 1 | c.884-112C>T         | -                  | rs1359134672 |
| 29879264 | 29879264 | CT  | -                   | Intronic              | Modifier | - | 1 | c.884-100del         | -                  | -            |
| 29879264 | 29879264 | T   | A                   | Intronic              | Modifier | - | 1 | c.884-100_884-99insA | -                  | rs1291058402 |
| 29879281 | 29879281 | AAG | -                   | Intronic              | Modifier | - | 1 | c.884-83_884-82del   | -                  | rs1295712746 |
| 29879281 | 29879281 | AG  | -                   | Intronic              | Modifier | - | 1 | c.884-83del          | -                  | -            |
| 29879308 | 29879308 | C   | T                   | Intronic              | Modifier | - | 1 | c.884-56C>T          | -                  | rs1019810165 |
| 29879343 | 29879343 | C   | T                   | Intronic              | Modifier | - | 1 | c.884-21C>T          | -                  | rs1482031249 |
| 29879383 | 29879383 | G   | A                   | Synonymous            | Low      | 2 | - | c.903G>A             | p.Ser301Ser        | rs781291855  |
| 29879402 | 29879402 | A   | CAGACGCTATG<br>CGCT | In-frame<br>Insertion | Moderate | 2 | - | c.926_940dup         | p.Asp309_Ser313dup | rs1380569251 |
| 29879421 | 29879421 | C   | T                   | Missense              | Moderate | 2 | - | c.941C>T             | p.Ala314Val        | rs539511579  |
| 29879444 | 29879444 | C   | T                   | Missense              | Moderate | 2 | - | c.964C>T             | p.Arg322Trp        | rs778265423  |
| 29879483 | 29879483 | C   | G                   | Missense              | Moderate | 2 | - | c.1003C>G            | p.Leu335Val        | -            |
| 29879516 | 29879516 | C   | T                   | Missense              | Moderate | 2 | - | c.1036C>T            | p.Arg346Cys        | rs139219355  |
| 29879518 | 29879518 | C   | G                   | Synonymous            | Low      | 2 | - | c.1038C>G            | p.Arg346Arg        | rs377262654  |
| 29879524 | 29879524 | G   | C                   | Missense              | Moderate | 2 | - | c.1044G>C            | p.Glu348Asp        | rs1475562664 |
| 29879535 | 29879535 | G   | A                   | Missense              | Moderate | 2 | - | c.1055G>A            | p.Arg352His        | rs750088241  |
| 29879545 | 29879545 | C   | T                   | Synonymous            | Low      | 2 | - | c.1065C>T            | p.Ala355Ala        | rs144040465  |
| 29879559 | 29879559 | A   | G                   | Missense              | Moderate | 2 | - | c.1079A>G            | p.Tyr360Cys        | rs768679590  |
| 29879570 | 29879570 | CA  | -                   | Intronic              | Low      | - | 2 | c.1083+7del          | -                  | -            |
| 29879592 | 29879592 | C   | G                   | Intronic              | Modifier | - | 2 | c.1083+29C>G         | -                  | rs1357430644 |
| 29879601 | 29879601 | C   | T                   | Intronic              | Modifier | - | 2 | c.1083+38C>T         | -                  | rs1020522395 |
| 29879604 | 29879604 | A   | G                   | Intronic              | Modifier | - | 2 | c.1083+41A>G         | -                  | rs371191443  |
| 29879646 | 29879646 | G   | T                   | Intronic              | Modifier | - | 2 | c.1083+83G>T         | -                  | rs570932481  |
| 29879653 | 29879653 | T   | C                   | Intronic              | Modifier | - | 2 | c.1083+90T>C         | -                  | -            |
| 29879659 | 29879659 | A   | C                   | Intronic              | Modifier | - | 2 | c.1083+96A>C         | -                  | rs558830358  |
| 29879661 | 29879661 | A   | T                   | Intronic              | Modifier | - | 2 | c.1083+98A>T         | -                  | rs775797988  |
| 29879662 | 29879662 | T   | C                   | Intronic              | Modifier | - | 2 | c.1083+99T>C         | -                  | rs1004871512 |
| 29879671 | 29879671 | T   | C                   | Intronic              | Modifier | - | 2 | c.1083+108T>C        | -                  | rs747239243  |
| 29879693 | 29879693 | CT  | -                   | Intronic              | Modifier | - | 2 | c.1083+132del        | -                  | -            |
| 29879695 | 29879695 | T   | C                   | Intronic              | Modifier | - | 2 | c.1083+132T>C        | -                  | rs1403096338 |
| 29879745 | 29879745 | C   | G                   | Intronic              | Modifier | - | 2 | c.1083+182C>G        | -                  | rs77685295   |
| 29879753 | 29879753 | C   | T                   | Intronic              | Modifier | - | 2 | c.1083+190C>T        | -                  | -            |

|          |          |           |          |          |          |   |   |                                |   |              |
|----------|----------|-----------|----------|----------|----------|---|---|--------------------------------|---|--------------|
| 29879754 | 29879754 | C         | T        | Intronic | Modifier | - | 2 | c.1083+191C>T                  | - | rs114811985  |
| 29879817 | 29879817 | GATAGACTT | -        | Intronic | Modifier | - | 2 | c.1083+247_1083+254del         | - | -            |
| 29879828 | 29879828 | A         | TTTATTTT | Intronic | Modifier | - | 2 | c.1083+272_1083+273insTTTTATTT | - | -            |
| 29879841 | 29879841 | TTTATTAT  | A        | Intronic | Modifier | - | 2 | c.1083+270_1083+278delinsA     | - | -            |
| 29879844 | 29879844 | A         | TTTTTTTT | Intronic | Modifier | - | 2 | c.1083+284_1083+285insTTTTTTTT | - | -            |
| 29879847 | 29879847 | T         | TGAG     | Intronic | Modifier | - | 2 | c.1083+284_1083+285insTGA<br>G | - | -            |
| 29879853 | 29879853 | T         | TTATTTAC | Intronic | Modifier | - | 2 | c.1083+292_1083+293insATTTACTT | - | rs1342137926 |
| 29879888 | 29879888 | G         | T        | Intronic | Modifier | - | 2 | c.1083+325G>T                  | - | -            |
| 29879914 | 29879914 | C         | T        | Intronic | Modifier | - | 2 | c.1083+351C>T                  | - | -            |
| 29879917 | 29879917 | C         | A        | Intronic | Modifier | - | 2 | c.1083+354C>A                  | - | rs34915139   |
| 29879923 | 29879923 | C         | T        | Intronic | Modifier | - | 2 | c.1083+360C>T                  | - | -            |
| 29879943 | 29879943 | A         | G        | Intronic | Modifier | - | 2 | c.1083+380A>G                  | - | rs969772763  |
| 29879946 | 29879946 | TTC       | -        | Intronic | Modifier | - | 2 | c.1083+384_1083+385del         | - | -            |
| 29879948 | 29879948 | C         | T        | Intronic | Modifier | - | 2 | c.1083+385C>T                  | - | rs761560241  |
| 29879963 | 29879963 | C         | T        | Intronic | Modifier | - | 2 | c.1083+400C>T                  | - | rs903216611  |
| 29879970 | 29879970 | C         | T        | Intronic | Modifier | - | 2 | c.1083+407C>T                  | - | rs369540636  |
| 29879979 | 29879979 | C         | T        | Intronic | Modifier | - | 2 | c.1083+416C>T                  | - | rs899973194  |
| 29879984 | 29879984 | G         | A        | Intronic | Modifier | - | 2 | c.1083+421G>A                  | - | rs988563535  |
| 29880013 | 29880013 | A         | G        | Intronic | Modifier | - | 2 | c.1083+450A>G                  | - | rs545472872  |
| 29880049 | 29880049 | G         | A        | Intronic | Modifier | - | 2 | c.1083+486G>A                  | - | rs8136014    |
| 29880091 | 29880091 | A         | G        | Intronic | Modifier | - | 2 | c.1083+528A>G                  | - | rs1003956839 |
| 29880114 | 29880114 | C         | T        | Intronic | Modifier | - | 2 | c.1083+551C>T                  | - | -            |
| 29880119 | 29880119 | G         | T        | Intronic | Modifier | - | 2 | c.1083+556G>T                  | - | -            |
| 29880128 | 29880128 | C         | T        | Intronic | Modifier | - | 2 | c.1083+565C>T                  | - | rs148546902  |
| 29880129 | 29880129 | G         | A        | Intronic | Modifier | - | 2 | c.1083+566G>A                  | - | rs868328509  |
| 29880141 | 29880141 | A         | AGAGAT   | Intronic | Modifier | - | 2 | c.1083+580_1083+585dup         | - | rs1321513053 |

|          |          |       |   |          |          |   |   |                                  |   |              |
|----------|----------|-------|---|----------|----------|---|---|----------------------------------|---|--------------|
| 29880155 | 29880155 | TA    | - | Intronic | Modifier | - | 2 | c.1083+594del                    | - | -            |
| 29880167 | 29880167 | T     | C | Intronic | Modifier | - | 2 | c.1083+604T>C                    | - | rs778934270  |
| 29880187 | 29880187 | C     | T | Intronic | Modifier | - | 2 | c.1083+624C>T                    | - | rs959441263  |
| 29880193 | 29880193 | G     | T | Intronic | Modifier | - | 2 | c.1083+630G>T                    | - | -            |
| 29880194 | 29880194 | G     | A | Intronic | Modifier | - | 2 | c.1083+631G>A                    | - | rs117259769  |
| 29880211 | 29880211 | C     | T | Intronic | Modifier | - | 2 | c.1083+648C>T                    | - | rs77580710   |
| 29880233 | 29880233 | T     | C | Intronic | Modifier | - | 2 | c.1083+670T>C                    | - | rs1458642140 |
| 29880260 | 29880260 | C     | T | Intronic | Modifier | - | 2 | c.1083+697C>T                    | - | rs537568541  |
| 29880261 | 29880261 | G     | A | Intronic | Modifier | - | 2 | c.1083+698G>A                    | - | rs57986874   |
| 29880277 | 29880277 | A     | G | Intronic | Modifier | - | 2 | c.1083+714A>G                    | - | rs189299986  |
| 29880346 | 29880346 | C     | T | Intronic | Modifier | - | 2 | c.1083+783C>T                    | - | rs552866413  |
| 29880382 | 29880382 | A     | C | Intronic | Modifier | - | 2 | c.1083+819A>C                    | - | -            |
| 29880386 | 29880386 | T     | C | Intronic | Modifier | - | 2 | c.1083+823T>C                    | - | rs556568863  |
| 29880400 | 29880400 | G     | A | Intronic | Modifier | - | 2 | c.1083+837G>A                    | - | rs1451269879 |
| 29880445 | 29880445 | A     | G | Intronic | Modifier | - | 2 | c.1083+882A>G                    | - | rs572804768  |
| 29880458 | 29880458 | G     | T | Intronic | Modifier | - | 2 | c.1083+895G>T                    | - | rs924730895  |
| 29880492 | 29880492 | A     | G | Intronic | Modifier | - | 2 | c.1083+929A>G                    | - | rs151051572  |
| 29880502 | 29880502 | G     | A | Intronic | Modifier | - | 2 | c.1083+939G>A                    | - | rs2240634    |
| 29880528 | 29880528 | G     | A | Intronic | Modifier | - | 2 | c.1083+965G>A                    | - | rs563717409  |
| 29880580 | 29880580 | G     | C | Intronic | Modifier | - | 2 | c.1083+1017G><br>C               | - | -            |
| 29880585 | 29880585 | G     | A | Intronic | Modifier | - | 2 | c.1083+1022G><br>A               | - | rs543290585  |
| 29880591 | 29880591 | G     | A | Intronic | Modifier | - | 2 | c.1083+1028G><br>A               | - | rs1366926907 |
| 29880621 | 29880621 | C     | T | Intronic | Modifier | - | 2 | c.1083+1058C><br>T               | - | rs534776514  |
| 29880630 | 29880630 | G     | A | Intronic | Modifier | - | 2 | c.1083+1067G><br>A               | - | rs1019218040 |
| 29880652 | 29880652 | T     | A | Intronic | Modifier | - | 2 | c.1084-1053dup                   | - | rs773168247  |
| 29880653 | 29880653 | A     | T | Intronic | Modifier | - | 2 | c.1084-1059A>T                   | - | rs965488701  |
| 29880662 | 29880662 | A     | T | Intronic | Modifier | - | 2 | c.1084-1050A>T                   | - | rs180872873  |
| 29880665 | 29880665 | TAAAA | - | Intronic | Modifier | - | 2 | c.1084-<br>1047_1084-<br>1044del | - | rs1273203992 |
| 29880692 | 29880692 | C     | T | Intronic | Modifier | - | 2 | c.1084-<br>1020C>T               | - | -            |

|          |          |     |      |          |          |   |   |                        |   |              |
|----------|----------|-----|------|----------|----------|---|---|------------------------|---|--------------|
| 29880693 | 29880693 | C   | G    | Intronic | Modifier | - | 2 | c.1084-1019C>G         | - | rs567894563  |
| 29880694 | 29880694 | T   | C    | Intronic | Modifier | - | 2 | c.1084-1018T>C         | - | rs984314659  |
| 29880705 | 29880705 | C   | G    | Intronic | Modifier | - | 2 | c.1084-1007C>G         | - | rs760470586  |
| 29880759 | 29880759 | G   | A    | Intronic | Modifier | - | 2 | c.1084-953G>A          | - | -            |
| 29880765 | 29880765 | T   | C    | Intronic | Modifier | - | 2 | c.1084-947T>C          | - | rs939108695  |
| 29880766 | 29880766 | CTG | -    | Intronic | Modifier | - | 2 | c.1084-945_1084-944del | - | rs770692971  |
| 29880766 | 29880766 | G   | A    | Intronic | Modifier | - | 2 | c.1084-946G>A          | - | rs114456709  |
| 29880787 | 29880787 | G   | A    | Intronic | Modifier | - | 2 | c.1084-925G>A          | - | -            |
| 29880800 | 29880800 | G   | A    | Intronic | Modifier | - | 2 | c.1084-912G>A          | - | rs1010587199 |
| 29880804 | 29880804 | G   | C    | Intronic | Modifier | - | 2 | c.1084-908G>C          | - | rs573878341  |
| 29880814 | 29880814 | C   | T    | Intronic | Modifier | - | 2 | c.1084-898C>T          | - | rs868582729  |
| 29880823 | 29880823 | T   | G    | Intronic | Modifier | - | 2 | c.1084-889T>G          | - | -            |
| 29880856 | 29880856 | C   | T    | Intronic | Modifier | - | 2 | c.1084-856C>T          | - | rs1366171508 |
| 29880884 | 29880884 | C   | G    | Intronic | Modifier | - | 2 | c.1084-828C>G          | - | rs566334659  |
| 29880907 | 29880907 | T   | C    | Intronic | Modifier | - | 2 | c.1084-805T>C          | - | rs931732579  |
| 29880914 | 29880914 | T   | C    | Intronic | Modifier | - | 2 | c.1084-798T>C          | - | rs5763264    |
| 29880916 | 29880916 | C   | T    | Intronic | Modifier | - | 2 | c.1084-796C>T          | - | rs553558060  |
| 29880942 | 29880942 | G   | A    | Intronic | Modifier | - | 2 | c.1084-770G>A          | - | -            |
| 29880948 | 29880948 | T   | G    | Intronic | Modifier | - | 2 | c.1084-764T>G          | - | -            |
| 29880977 | 29880977 | C   | T    | Intronic | Modifier | - | 2 | c.1084-735C>T          | - | rs1181856343 |
| 29880990 | 29880990 | A   | C    | Intronic | Modifier | - | 2 | c.1084-722A>C          | - | -            |
| 29881010 | 29881010 | A   | G    | Intronic | Modifier | - | 2 | c.1084-702A>G          | - | rs1319767449 |
| 29881149 | 29881149 | T   | C    | Intronic | Modifier | - | 2 | c.1084-563T>C          | - | -            |
| 29881150 | 29881150 | G   | GTAT | Intronic | Modifier | - | 2 | c.1084-560_1084-557dup | - | rs1286429529 |
| 29881162 | 29881162 | G   | A    | Intronic | Modifier | - | 2 | c.1084-550G>A          | - | -            |
| 29881176 | 29881176 | C   | T    | Intronic | Modifier | - | 2 | c.1084-536C>T          | - | rs559654353  |
| 29881195 | 29881195 | A   | G    | Intronic | Modifier | - | 2 | c.1084-517A>G          | - | rs913417474  |
| 29881212 | 29881212 | C   | T    | Intronic | Modifier | - | 2 | c.1084-500C>T          | - | -            |
| 29881214 | 29881214 | C   | T    | Intronic | Modifier | - | 2 | c.1084-498C>T          | - | rs2240635    |



|          |          |   |   |            |          |   |   |               |             |              |
|----------|----------|---|---|------------|----------|---|---|---------------|-------------|--------------|
| 29881237 | 29881237 | A | G | Intronic   | Modifier | - | 2 | c.1084-475A>G | -           | rs142119901  |
| 29881265 | 29881265 | T | C | Intronic   | Modifier | - | 2 | c.1084-447T>C | -           | rs1040695377 |
| 29881277 | 29881277 | A | G | Intronic   | Modifier | - | 2 | c.1084-435A>G | -           | -            |
| 29881292 | 29881292 | A | T | Intronic   | Modifier | - | 2 | c.1084-420A>T | -           | -            |
| 29881333 | 29881333 | C | G | Intronic   | Modifier | - | 2 | c.1084-379C>G | -           | -            |
| 29881340 | 29881340 | C | T | Intronic   | Modifier | - | 2 | c.1084-372C>T | -           | rs1303062643 |
| 29881369 | 29881369 | G | A | Intronic   | Modifier | - | 2 | c.1084-343G>A | -           | rs534920944  |
| 29881378 | 29881378 | C | T | Intronic   | Modifier | - | 2 | c.1084-334C>T | -           | rs555490349  |
| 29881388 | 29881388 | G | A | Intronic   | Modifier | - | 2 | c.1084-324G>A | -           | rs138583539  |
| 29881405 | 29881405 | T | C | Intronic   | Modifier | - | 2 | c.1084-307T>C | -           | -            |
| 29881459 | 29881459 | G | A | Intronic   | Modifier | - | 2 | c.1084-253G>A | -           | rs946441565  |
| 29881461 | 29881461 | A | G | Intronic   | Modifier | - | 2 | c.1084-251A>G | -           | rs12484008   |
| 29881468 | 29881468 | G | A | Intronic   | Modifier | - | 2 | c.1084-244G>A | -           | rs3815335    |
| 29881537 | 29881537 | C | T | Intronic   | Modifier | - | 2 | c.1084-175C>T | -           | rs78248741   |
| 29881559 | 29881559 | A | G | Intronic   | Modifier | - | 2 | c.1084-153A>G | -           | -            |
| 29881622 | 29881622 | G | A | Intronic   | Modifier | - | 2 | c.1084-90G>A  | -           | rs368599359  |
| 29881633 | 29881633 | G | A | Intronic   | Modifier | - | 2 | c.1084-79G>A  | -           | rs533283887  |
| 29881645 | 29881645 | G | A | Intronic   | Modifier | - | 2 | c.1084-67G>A  | -           | rs551382175  |
| 29881673 | 29881673 | A | G | Intronic   | Modifier | - | 2 | c.1084-39A>G  | -           | rs755841191  |
| 29881683 | 29881683 | A | G | Intronic   | Modifier | - | 2 | c.1084-29A>G  | -           | -            |
| 29881703 | 29881703 | C | T | Intronic   | Low      | - | 2 | c.1084-9C>T   | -           | -            |
| 29881704 | 29881704 | C | G | Intronic   | Low      | - | 2 | c.1084-8C>G   | -           | -            |
| 29881727 | 29881727 | C | T | Synonymous | Low      | 3 | - | c.1099C>T     | p.Leu367Leu | -            |
| 29881776 | 29881776 | G | A | Missense   | Moderate | 3 | - | c.1148G>A     | p.Arg383Gln | rs377149236  |
| 29881797 | 29881797 | A | C | Missense   | Moderate | 3 | - | c.1169A>C     | p.Asn390Thr | rs148653339  |
| 29881810 | 29881810 | T | G | Synonymous | Low      | 3 | - | c.1182T>G     | p.Ala394Ala | rs1033200120 |
| 29881828 | 29881828 | C | T | Synonymous | Low      | 3 | - | c.1200C>T     | p.Ala400Ala | rs165734     |
| 29881854 | 29881854 | T | C | Intronic   | Modifier | - | 3 | c.1208+18T>C  | -           | -            |
| 29881868 | 29881868 | G | A | Intronic   | Modifier | - | 3 | c.1208+32G>A  | -           | -            |
| 29881884 | 29881884 | G | A | Intronic   | Modifier | - | 3 | c.1208+48G>A  | -           | rs4823040    |
| 29881885 | 29881885 | C | T | Intronic   | Modifier | - | 3 | c.1208+49C>T  | -           | rs540168753  |
| 29881890 | 29881890 | C | T | Intronic   | Modifier | - | 3 | c.1208+54C>T  | -           | rs114903253  |
| 29881907 | 29881907 | C | G | Intronic   | Modifier | - | 3 | c.1208+71C>G  | -           | rs1187543862 |
| 29881962 | 29881962 | C | T | Intronic   | Modifier | - | 3 | c.1208+126C>T | -           | rs1031194111 |

|          |          |       |   |          |          |   |   |                             |   |              |
|----------|----------|-------|---|----------|----------|---|---|-----------------------------|---|--------------|
| 29881963 | 29881963 | G     | A | Intronic | Modifier | - | 3 | c.1208+127G>A               | - | rs937910485  |
| 29881990 | 29881990 | C     | T | Intronic | Modifier | - | 3 | c.1208+154C>T               | - | rs1466417517 |
| 29882005 | 29882005 | C     | A | Intronic | Modifier | - | 3 | c.1208+169C>A               | - | rs1056424058 |
| 29882071 | 29882071 | G     | A | Intronic | Modifier | - | 3 | c.1208+235G>A               | - | rs779090983  |
| 29882082 | 29882082 | A     | G | Intronic | Modifier | - | 3 | c.1208+246A>G               | - | -            |
| 29882092 | 29882092 | C     | T | Intronic | Modifier | - | 3 | c.1208+256C>T               | - | rs897689341  |
| 29882110 | 29882110 | C     | T | Intronic | Modifier | - | 3 | c.1208+274C>T               | - | rs1012266468 |
| 29882111 | 29882111 | G     | A | Intronic | Modifier | - | 3 | c.1208+275G>A               | - | rs28525662   |
| 29882150 | 29882150 | C     | T | Intronic | Modifier | - | 3 | c.1208+314C>T               | - | rs1177767322 |
| 29882157 | 29882157 | G     | A | Intronic | Modifier | - | 3 | c.1208+321G>A               | - | rs147136515  |
| 29882183 | 29882183 | T     | A | Intronic | Modifier | - | 3 | c.1208+347_12<br>08+348insA | - | rs111690803  |
| 29882184 | 29882184 | T     | A | Intronic | Modifier | - | 3 | c.1208+348T>A               | - | rs190911251  |
| 29882187 | 29882187 | T     | A | Intronic | Modifier | - | 3 | c.1208+351T>A               | - | rs375863529  |
| 29882247 | 29882247 | C     | G | Intronic | Modifier | - | 3 | c.1208+411C>G               | - | rs143316545  |
| 29882294 | 29882294 | G     | A | Intronic | Modifier | - | 3 | c.1208+458G>A               | - | rs5997481    |
| 29882303 | 29882303 | C     | T | Intronic | Modifier | - | 3 | c.1208+467C>T               | - | -            |
| 29882324 | 29882324 | A     | G | Intronic | Modifier | - | 3 | c.1208+488A>G               | - | rs6006162    |
| 29882326 | 29882326 | G     | C | Intronic | Modifier | - | 3 | c.1208+490G>C               | - | rs903889822  |
| 29882328 | 29882328 | T     | A | Intronic | Modifier | - | 3 | c.1208+492T>A               | - | -            |
| 29882386 | 29882386 | G     | C | Intronic | Modifier | - | 3 | c.1208+550G>C               | - | -            |
| 29882403 | 29882403 | T     | C | Intronic | Modifier | - | 3 | c.1208+567T>C               | - | rs1319062352 |
| 29882443 | 29882443 | G     | A | Intronic | Modifier | - | 3 | c.1208+607G>A               | - | rs188013725  |
| 29882460 | 29882460 | C     | T | Intronic | Modifier | - | 3 | c.1208+624C>T               | - | rs555368787  |
| 29882484 | 29882484 | T     | A | Intronic | Modifier | - | 3 | c.1208+648T>A               | - | -            |
| 29882489 | 29882489 | T     | A | Intronic | Modifier | - | 3 | c.1208+653T>A               | - | rs752352485  |
| 29882500 | 29882500 | A     | T | Intronic | Modifier | - | 3 | c.1208+664A>T               | - | rs1240145238 |
| 29882506 | 29882506 | G     | T | Intronic | Modifier | - | 3 | c.1208+671dup               | - | -            |
| 29882508 | 29882508 | TC    | - | Intronic | Modifier | - | 3 | c.1208+672del               | - | rs527873265  |
| 29882530 | 29882530 | TTTTG | - | Intronic | Modifier | - | 3 | c.1208+691_12<br>08+694del  | - | rs1198608745 |
| 29882546 | 29882546 | C     | T | Intronic | Modifier | - | 3 | c.1208+710C>T               | - | rs757583792  |
| 29882555 | 29882555 | A     | T | Intronic | Modifier | - | 3 | c.1208+719A>T               | - | rs193062610  |
| 29882556 | 29882556 | G     | A | Intronic | Modifier | - | 3 | c.1208+720G>A               | - | rs963017814  |

|          |          |    |   |          |          |   |   |                    |   |              |
|----------|----------|----|---|----------|----------|---|---|--------------------|---|--------------|
| 29882569 | 29882569 | C  | T | Intronic | Modifier | - | 3 | c.1208+733C>T      | - | rs1231911858 |
| 29882571 | 29882571 | AG | - | Intronic | Modifier | - | 3 | c.1208+735del      | - | -            |
| 29882573 | 29882573 | A  | C | Intronic | Modifier | - | 3 | c.1208+737A>C      | - | rs780861559  |
| 29882580 | 29882580 | C  | T | Intronic | Modifier | - | 3 | c.1208+744C>T      | - | rs1392375542 |
| 29882630 | 29882630 | G  | A | Intronic | Modifier | - | 3 | c.1208+794G>A      | - | rs747407223  |
| 29882664 | 29882664 | A  | G | Intronic | Modifier | - | 3 | c.1208+828A>G      | - | -            |
| 29882687 | 29882687 | T  | A | Intronic | Modifier | - | 3 | c.1208+851T>A      | - | rs150888215  |
| 29882693 | 29882693 | G  | A | Intronic | Modifier | - | 3 | c.1208+857G>A      | - | rs531344127  |
| 29882694 | 29882694 | T  | G | Intronic | Modifier | - | 3 | c.1208+858T>G      | - | -            |
| 29882713 | 29882713 | T  | C | Intronic | Modifier | - | 3 | c.1208+877T>C      | - | -            |
| 29882715 | 29882715 | T  | C | Intronic | Modifier | - | 3 | c.1208+879T>C      | - | -            |
| 29882738 | 29882738 | C  | T | Intronic | Modifier | - | 3 | c.1208+902C>T      | - | -            |
| 29882754 | 29882754 | C  | T | Intronic | Modifier | - | 3 | c.1208+918C>T      | - | rs1051929078 |
| 29882755 | 29882755 | G  | A | Intronic | Modifier | - | 3 | c.1208+919G>A      | - | rs139362410  |
| 29882760 | 29882760 | C  | T | Intronic | Modifier | - | 3 | c.1208+924C>T      | - | rs551722146  |
| 29882791 | 29882791 | C  | A | Intronic | Modifier | - | 3 | c.1208+955C>A      | - | rs537125677  |
| 29882794 | 29882794 | G  | A | Intronic | Modifier | - | 3 | c.1208+958G>A      | - | rs1026424254 |
| 29882813 | 29882813 | A  | G | Intronic | Modifier | - | 3 | c.1208+977A>G      | - | rs1299918179 |
| 29882830 | 29882830 | C  | T | Intronic | Modifier | - | 3 | c.1208+994C>T      | - | rs556908766  |
| 29882838 | 29882838 | C  | A | Intronic | Modifier | - | 3 | c.1208+1002C><br>A | - | rs187342281  |
| 29882849 | 29882849 | G  | T | Intronic | Modifier | - | 3 | c.1208+1013G><br>T | - | rs980830606  |
| 29882850 | 29882850 | A  | C | Intronic | Modifier | - | 3 | c.1208+1014A><br>C | - | rs925373768  |
| 29882857 | 29882857 | C  | T | Intronic | Modifier | - | 3 | c.1208+1021C><br>T | - | rs936782201  |
| 29882864 | 29882864 | A  | G | Intronic | Modifier | - | 3 | c.1208+1028A><br>G | - | rs913923260  |
| 29882865 | 29882865 | G  | A | Intronic | Modifier | - | 3 | c.1208+1029G><br>A | - | rs1205303005 |
| 29882882 | 29882882 | C  | T | Intronic | Modifier | - | 3 | c.1208+1046C><br>T | - | rs764790044  |
| 29882902 | 29882902 | C  | T | Intronic | Modifier | - | 3 | c.1208+1066C><br>T | - | -            |
| 29882915 | 29882915 | G  | C | Intronic | Modifier | - | 3 | c.1208+1079G><br>C | - | rs1486110150 |

|          |          |       |     |          |          |   |   |                                     |   |              |
|----------|----------|-------|-----|----------|----------|---|---|-------------------------------------|---|--------------|
| 29882945 | 29882945 | A     | G   | Intronic | Modifier | - | 3 | c.1208+1109A><br>G                  | - | rs150023132  |
| 29882967 | 29882967 | T     | G   | Intronic | Modifier | - | 3 | c.1208+1131T><br>G                  | - | -            |
| 29882973 | 29882973 | C     | T   | Intronic | Modifier | - | 3 | c.1208+1137C><br>T                  | - | rs165899     |
| 29882976 | 29882976 | C     | G   | Intronic | Modifier | - | 3 | c.1208+1140C><br>G                  | - | rs542818912  |
| 29883007 | 29883007 | A     | T   | Intronic | Modifier | - | 3 | c.1208+1171A><br>T                  | - | -            |
| 29883018 | 29883018 | A     | G   | Intronic | Modifier | - | 3 | c.1208+1182A><br>G                  | - | rs573136532  |
| 29883076 | 29883076 | C     | T   | Intronic | Modifier | - | 3 | c.1208+1240C><br>T                  | - | rs553734179  |
| 29883087 | 29883087 | A     | T   | Intronic | Modifier | - | 3 | c.1208+1251A><br>T                  | - | rs1304338716 |
| 29883094 | 29883094 | CA    | -   | Intronic | Modifier | - | 3 | c.1208+1258del                      | - | -            |
| 29883123 | 29883123 | TAGTC | -   | Intronic | Modifier | - | 3 | c.1208+1287_1<br>208+1290del        | - | rs362061     |
| 29883162 | 29883162 | C     | G   | Intronic | Modifier | - | 3 | c.1208+1326C><br>G                  | - | -            |
| 29883164 | 29883164 | G     | T   | Intronic | Modifier | - | 3 | c.1208+1328G><br>T                  | - | rs561170932  |
| 29883165 | 29883165 | G     | C   | Intronic | Modifier | - | 3 | c.1208+1329G><br>C                  | - | -            |
| 29883208 | 29883208 | T     | C   | Intronic | Modifier | - | 3 | c.1208+1372T><br>C                  | - | rs1201391625 |
| 29883254 | 29883254 | G     | T   | Intronic | Modifier | - | 3 | c.1208+1418G><br>T                  | - | -            |
| 29883316 | 29883316 | C     | G   | Intronic | Modifier | - | 3 | c.1208+1480C><br>G                  | - | -            |
| 29883346 | 29883346 | G     | A   | Intronic | Modifier | - | 3 | c.1209-<br>1492G>A                  | - | rs189670956  |
| 29883380 | 29883380 | G     | A   | Intronic | Modifier | - | 3 | c.1209-<br>1458G>A                  | - | -            |
| 29883413 | 29883413 | G     | C   | Intronic | Modifier | - | 3 | c.1209-<br>1425G>C                  | - | -            |
| 29883466 | 29883466 | A     | AAG | Intronic | Modifier | - | 3 | c.1209-<br>1370_1209-<br>1369insGAA | - | rs1285972523 |

|          |          |       |   |          |          |   |   |                          |   |              |
|----------|----------|-------|---|----------|----------|---|---|--------------------------|---|--------------|
| 29883513 | 29883513 | C     | T | Intronic | Modifier | - | 3 | c.1209-1325C>T           | - | rs1030352345 |
| 29883524 | 29883524 | C     | T | Intronic | Modifier | - | 3 | c.1209-1314C>T           | - | rs750190295  |
| 29883525 | 29883525 | G     | A | Intronic | Modifier | - | 3 | c.1209-1313G>A           | - | rs950766752  |
| 29883530 | 29883530 | A     | T | Intronic | Modifier | - | 3 | c.1209-1308A>T           | - | -            |
| 29883561 | 29883561 | C     | T | Intronic | Modifier | - | 3 | c.1209-1277C>T           | - | -            |
| 29883568 | 29883568 | C     | T | Intronic | Modifier | - | 3 | c.1209-1270C>T           | - | -            |
| 29883576 | 29883576 | G     | A | Intronic | Modifier | - | 3 | c.1209-1262G>A           | - | rs373486863  |
| 29883630 | 29883630 | TAAC  | - | Intronic | Modifier | - | 3 | c.1209-1203_1209-1201del | - | rs916778818  |
| 29883635 | 29883635 | A     | C | Intronic | Modifier | - | 3 | c.1209-1203A>C           | - | rs1418123505 |
| 29883636 | 29883636 | C     | A | Intronic | Modifier | - | 3 | c.1209-1202C>A           | - | rs1164703398 |
| 29883648 | 29883648 | A     | C | Intronic | Modifier | - | 3 | c.1209-1190A>C           | - | -            |
| 29883658 | 29883658 | C     | T | Intronic | Modifier | - | 3 | c.1209-1180C>T           | - | rs1281070945 |
| 29883659 | 29883659 | G     | A | Intronic | Modifier | - | 3 | c.1209-1179G>A           | - | rs143625327  |
| 29883662 | 29883662 | C     | T | Intronic | Modifier | - | 3 | c.1209-1176C>T           | - | rs1334347932 |
| 29883710 | 29883710 | C     | G | Intronic | Modifier | - | 3 | c.1209-1128C>G           | - | -            |
| 29883714 | 29883714 | G     | A | Intronic | Modifier | - | 3 | c.1209-1124G>A           | - | rs998962613  |
| 29883772 | 29883772 | CACTT | - | Intronic | Modifier | - | 3 | c.1209-1066_1209-1063del | - | rs362231     |
| 29883787 | 29883787 | A     | G | Intronic | Modifier | - | 3 | c.1209-1051A>G           | - | rs901063529  |
| 29883797 | 29883797 | G     | A | Intronic | Modifier | - | 3 | c.1209-1041G>A           | - | rs571615682  |
| 29883810 | 29883810 | A     | C | Intronic | Modifier | - | 3 | c.1209-1028A>C           | - | -            |
| 29883836 | 29883836 | C     | T | Intronic | Modifier | - | 3 | c.1209-1002C>T           | - | rs781731242  |
| 29883842 | 29883842 | G     | T | Intronic | Modifier | - | 3 | c.1209-996G>T            | - | rs563602777  |

|          |          |           |   |          |          |   |   |                        |   |              |
|----------|----------|-----------|---|----------|----------|---|---|------------------------|---|--------------|
| 29883892 | 29883892 | G         | T | Intronic | Modifier | - | 3 | c.1209-946G>T          | - | rs174650     |
| 29883923 | 29883923 | G         | A | Intronic | Modifier | - | 3 | c.1209-915G>A          | - | -            |
| 29883942 | 29883942 | A         | T | Intronic | Modifier | - | 3 | c.1209-896A>T          | - | -            |
| 29883945 | 29883945 | A         | C | Intronic | Modifier | - | 3 | c.1209-893A>C          | - | -            |
| 29883958 | 29883958 | A         | C | Intronic | Modifier | - | 3 | c.1209-880A>C          | - | rs80091782   |
| 29884011 | 29884011 | C         | T | Intronic | Modifier | - | 3 | c.1209-827C>T          | - | rs555103444  |
| 29884027 | 29884027 | G         | A | Intronic | Modifier | - | 3 | c.1209-811G>A          | - | rs769503095  |
| 29884037 | 29884037 | C         | T | Intronic | Modifier | - | 3 | c.1209-801C>T          | - | -            |
| 29884047 | 29884047 | C         | T | Intronic | Modifier | - | 3 | c.1209-791C>T          | - | -            |
| 29884073 | 29884073 | C         | T | Intronic | Modifier | - | 3 | c.1209-765C>T          | - | rs141161567  |
| 29884123 | 29884123 | G         | A | Intronic | Modifier | - | 3 | c.1209-715G>A          | - | rs566071826  |
| 29884131 | 29884131 | C         | T | Intronic | Modifier | - | 3 | c.1209-707C>T          | - | rs528754360  |
| 29884181 | 29884181 | C         | T | Intronic | Modifier | - | 3 | c.1209-657C>T          | - | rs567502217  |
| 29884182 | 29884182 | G         | A | Intronic | Modifier | - | 3 | c.1209-656G>A          | - | rs185791469  |
| 29884208 | 29884208 | C         | T | Intronic | Modifier | - | 3 | c.1209-630C>T          | - | rs377340059  |
| 29884226 | 29884226 | G         | A | Intronic | Modifier | - | 3 | c.1209-612G>A          | - | rs1432228295 |
| 29884229 | 29884229 | CGTGCGCCT | - | Intronic | Modifier | - | 3 | c.1209-614_1209-607del | - | -            |
| 29884231 | 29884231 | T         | C | Intronic | Modifier | - | 3 | c.1209-607T>C          | - | rs956995883  |
| 29884235 | 29884235 | C         | T | Intronic | Modifier | - | 3 | c.1209-603C>T          | - | rs971572887  |
| 29884278 | 29884278 | G         | A | Intronic | Modifier | - | 3 | c.1209-560G>A          | - | rs935759554  |
| 29884285 | 29884285 | T         | G | Intronic | Modifier | - | 3 | c.1209-553T>G          | - | rs571203555  |
| 29884367 | 29884367 | G         | A | Intronic | Modifier | - | 3 | c.1209-471G>A          | - | rs536728781  |
| 29884432 | 29884432 | T         | C | Intronic | Modifier | - | 3 | c.1209-406T>C          | - | -            |
| 29884485 | 29884485 | T         | C | Intronic | Modifier | - | 3 | c.1209-353T>C          | - | rs6006163    |
| 29884509 | 29884509 | G         | T | Intronic | Modifier | - | 3 | c.1209-329G>T          | - | rs760318118  |
| 29884520 | 29884520 | T         | C | Intronic | Modifier | - | 3 | c.1209-318T>C          | - | rs886441058  |
| 29884567 | 29884567 | C         | T | Intronic | Modifier | - | 3 | c.1209-271C>T          | - | rs165624     |
| 29884574 | 29884574 | A         | G | Intronic | Modifier | - | 3 | c.1209-264A>G          | - | -            |
| 29884575 | 29884575 | G         | T | Intronic | Modifier | - | 3 | c.1209-263G>T          | - | rs181661746  |
| 29884599 | 29884599 | C         | T | Intronic | Modifier | - | 3 | c.1209-239C>T          | - | -            |
| 29884603 | 29884603 | A         | G | Intronic | Modifier | - | 3 | c.1209-235A>G          | - | rs557043300  |
| 29884612 | 29884612 | A         | T | Intronic | Modifier | - | 3 | c.1209-226A>T          | - | rs1022377385 |

|          |          |   |        |                       |          |   |   |                |                        |              |
|----------|----------|---|--------|-----------------------|----------|---|---|----------------|------------------------|--------------|
| 29884639 | 29884639 | C   | T      | Intronic              | Modifier | - | 3 | c.1209-199C>T  | -                      | rs541500423  |
| 29884640 | 29884640 | G   | A      | Intronic              | Modifier | - | 3 | c.1209-198G>A  | -                      | rs912855297  |
| 29884643 | 29884643 | G   | T      | Intronic              | Modifier | - | 3 | c.1209-195G>T  | -                      | rs751682286  |
| 29884650 | 29884650 | T   | C      | Intronic              | Modifier | - | 3 | c.1209-188T>C  | -                      | rs982583256  |
| 29884712 | 29884712 | T   | G      | Intronic              | Modifier | - | 3 | c.1209-126T>G  | -                      | rs1323270119 |
| 29884734 | 29884734 | C   | T      | Intronic              | Modifier | - | 3 | c.1209-104C>T  | -                      | rs565596168  |
| 29884736 | 29884736 | C   | G      | Intronic              | Modifier | - | 3 | c.1209-102C>G  | -                      | rs1039501899 |
| 29884799 | 29884799 | C   | T      | Intronic              | Modifier | - | 3 | c.1209-39C>T   | -                      | rs376487122  |
| 29884804 | 29884804 | GT  | -      | Intronic              | Modifier | - | 3 | c.1209-32del   | -                      | rs1427581204 |
| 29884809 | 29884809 | A   | G      | Intronic              | Modifier | - | 3 | c.1209-29A>G   | -                      | rs746250651  |
| 29884814 | 29884814 | T   | C      | Intronic              | Modifier | - | 3 | c.1209-24T>C   | -                      | rs770018275  |
| 29884817 | 29884817 | G   | A      | Intronic              | Modifier | - | 3 | c.1209-21G>A   | -                      | rs201134753  |
| 29884869 | 29884869 | G   | A      | Missense              | Moderate | 4 | - | c.1240G>A      | p.Gly414Ser            | -            |
| 29884881 | 29884881 | A   | G      | Missense              | Moderate | 4 | - | c.1252A>G      | p.Ile418Val            | rs751075628  |
| 29884939 | 29884939 | A   | G      | Missense              | Moderate | 4 | - | c.1310A>G      | p.Lys437Arg            | rs1602971285 |
| 29884940 | 29884940 | G   | T      | Missense              | Moderate | 4 | - | c.1311G>T      | p.Lys437Asn            | -            |
| 29884950 | 29884950 | G   | A      | Missense              | Moderate | 4 | - | c.1321G>A      | p.Glu441Lys            | rs145061116  |
| 29884976 | 29884976 | G   | C      | Missense              | Moderate | 4 | - | c.1347G>C      | p.Lys449Asn            | rs199932977  |
| 29885016 | 29885016 | G   | A      | Missense              | Moderate | 4 | - | c.1387G>A      | p.Glu463Lys            | rs59371099   |
| 29885058 | 29885058 | G   | C      | Missense              | Moderate | 4 | - | c.1429G>C      | p.Glu477Gln            | -            |
| 29885075 | 29885075 | G   | A      | Synonymous            | Low      | 4 | - | c.1446G>A      | p.Glu482Glu            | rs5997482    |
| 29885120 | 29885120 | TGAAGAAGAGG<br>AGGCAGAAGGG<br>GGA                       | -      | In-frame<br>Deletion  | Moderate | 4 | - | c.1476_1499del | p.Glu493_Glu500de<br>l | rs748774766  |
| 29885127 | 29885127 | G   | AAACAA | In-frame<br>Insertion | Moderate | 4 | - | c.1500_1505dup | p.Thr501_Lys502du<br>p | rs576586746  |
| 29885164 | 29885164 | C   | G      | Missense              | Moderate | 4 | - | c.1535C>G      | p.Pro512Arg            | -            |
| 29885198 | 29885198 | G   | C      | Missense              | Moderate | 4 | - | c.1569G>C      | p.Glu523Asp            | rs138278265  |
| 29885202 | 29885202 | A   | G      | Missense              | Moderate | 4 | - | c.1573A>G      | p.Lys525Glu            | rs751816018  |
| 29885204 | 29885204 | G   | C      | Missense              | Moderate | 4 | - | c.1575G>C      | p.Lys525Asn            | rs149183166  |
| 29885255 | 29885255 | C   | T      | Synonymous            | Low      | 4 | - | c.1626C>T      | p.Ala542Ala            | rs747901802  |
| 29885260 | 29885260 | CCAAGTCCCCA<br>GAGAAGGAGGA<br>AGCAAAATCCC<br>CAGCCGAAGT | -      | In-frame<br>Deletion  | Moderate | 4 | - | c.1599_1640del | p.Glu536_Lys549de<br>l | rs1353196821 |

|          |          |  |  |                    |          |   |   |   |   |              |
|----------|----------|--|--|--------------------|----------|---|---|---|---|--------------|
| 29885308 | 29885308 | C  | T  | Missense           | Moderate | 4 | - | c.1679C>T   | p.Ser560Leu   | rs750569231  |
| 29885311 | 29885311 | C  | T  | Missense           | Moderate | 4 | - | c.1682C>T   | p.Pro561Leu   | rs548556825  |
| 29885313 | 29885313 | C  | G  | Missense           | Moderate | 4 | - | c.1684C>G   | p.Pro562Ala   | rs530872313  |
| 29885369 | 29885369 | C  | T  | Synonymous         | Low      | 4 | - | c.1740C>T   | p.Ser580Ser   | rs114263951  |
| 29885378 | 29885378 | G  | GAA  | In-frame Insertion | Moderate | 4 | - | c.1750_1751ins AAG  | p.Lys583_Ala584ins Glu  | -            |
| 29885383 | 29885383 | A  | G  | Missense           | Moderate | 4 | - | c.1754A>G   | p.Lys585Arg   | -            |
| 29885386 | 29885386 | C  | T  | Missense           | Moderate | 4 | - | c.1757C>T   | p.Ser586Phe   | -            |
| 29885403 | 29885403 | G  | T  | Missense           | Moderate | 4 | - | c.1774G>T   | p.Ala592Ser   | rs768529407  |
| 29885412 | 29885412 | C  | T  | Missense           | Moderate | 4 | - | c.1783C>T   | p.Pro595Ser   | rs6006165    |
| 29885423 | 29885423 | AAAGTCACCCGG CTGAGGCC                          | -  | In-frame Deletion  | Moderate | 4 | - | c.1782_1799del  | p.Ala596_Pro601del  | -            |
| 29885425 | 29885425 | A  | C  | Missense           | Moderate | 4 | - | c.1796A>C   | p.Lys599Thr   | rs1403224343 |
| 29885436 | 29885436 | A  | AGGCCAAGTCC CCAGCGAAGGA AGAAGCAAAGT CCCC GGCTG | In-frame Insertion | Moderate | 4 | - | c.1822_1823ins CGAAGGAAGA AGCAAAGTCC CCGGCTGAGG CCAAGTCCCC AG | p.Pro607_Val608ins AlaLysGluGluAlaLysSerProAlaGluAlaLysSerPro | -            |
| 29885438 | 29885438 | G  | GAA  | In-frame Insertion | Moderate | 4 | - | c.1810_1811ins AAG  | p.Lys603_Ala604ins Glu  | -            |
| 29885462 | 29885462 | A  | G  | Synonymous         | Low      | 4 | - | c.1833A>G   | p.Glu611Glu   | rs1196681707 |
| 29885475 | 29885475 | G  | C  | Missense           | Moderate | 4 | - | c.1846G>C   | p.Ala616Pro   | rs1398309477 |
| 29885508 | 29885508 | A  | C  | Missense           | Moderate | 4 | - | c.1879A>C   | p.Lys627Gln   | rs1353842666 |
| 29885554 | 29885554 | C  | T  | Missense           | Moderate | 4 | - | c.1925C>T   | p.Thr642Met   | rs117258406  |
| 29885556 | 29885556 | CCAGCTGAGGT CAAGTCCCCGG AAAAGGCCAAG TCTCCAACGA | -  | In-frame Deletion  | Moderate | 4 | - | c.1886_1927del  | p.Pro629_Lys643del insGln                                     | -            |
| 29885558 | 29885558 | AGCTGAGGTCA AGTCCCCGGAA AAGGCCAAGTC TCCAACGAAG | -  | In-frame Deletion  | Moderate | 4 | - | c.1889_1930del  | p.Ala630_Lys643del  | -            |
| 29885564 | 29885564 | GGTCAAGTCCC CGGAAAAGGCC AAGTCTCCAAC GAAGGAGGAA | -  | In-frame Deletion  | Moderate | 4 | - | c.1895_1936del  | p.Val632_Glu645del  | -            |
| 29885564 | 29885564 | A  | GCAAAGTCCCC TGAGAAG                            | In-frame Insertion | Moderate | 4 | - | c.1938_1955dup  | p.Ala652_Lys657dup  | -            |



|          |          |   |                        |                         |          |   |   |  |  |              |
|----------|----------|---|------------------------|-------------------------|----------|---|---|--|--|--------------|
| 29885570 | 29885570 | G   | C                      | Missense                | Moderate | 4 | - | c.1941G>C                                | p.Lys647Asn                                  | rs200634512  |
| 29885571 | 29885571 | T   | CCCCTGAGAAG<br>GCCAAGG | In-frame<br>Insertion   | Moderate | 4 | - | c.1959_1960ins<br>GCCCTGAGA<br>AGGCCAAG  | p.Lys653_Ser654in<br>sAlaProGluLysAlaL<br>ys | -            |
| 29885576 | 29885576 | GGAAAAGGCCA<br>AGTCTCCAACG<br>AAGGAGGAAGC<br>AAAGTCCCCT | -                      | In-frame<br>Deletion    | Moderate | 4 | - | c.1908_1949del                           | p.Thr642_Pro655de<br>l                       | -            |
| 29885582 | 29885582 | G   | GCCAAGTCCCC<br>TGAGAAC | In-frame<br>Insertion   | Moderate | 4 | - | c.1964_1965ins<br>TGAGAACGCC<br>AAGTCCCC | p.Glu656_Lys657in<br>sAsnAlaLysSerPro<br>Glu | -            |
| 29885585 | 29885585 | C   | AAGGCCCCAGA<br>GAAGGCA | In-frame<br>Insertion   | Moderate | 4 | - | c.1959_1960ins<br>GCCCCAGAGA<br>AGGCCAAG | p.Lys653_Ser654in<br>sAlaProGluLysAlaL<br>ys | -            |
| 29885599 | 29885599 | A   | GGACAAGGCC<br>CAGCGAC  | In-frame<br>Insertion   | Moderate | 4 | - | c.1973_1974ins<br>CAAGGCCCA<br>GCGACGGA  | p.Lys657_Glu658in<br>sAspLysAlaProAlaT<br>hr | -            |
| 29885601 | 29885601 | G   | CC                     | Frameshift<br>Insertion | High     | 4 | - | c.1972_1973ins<br>CC                     | p.Glu658AlafsTer14                           | rs1427435154 |
| 29885604 | 29885604 | AAGGCCAAGTC<br>CCCAGAGAAGG<br>AAG                       | -                      | In-frame<br>Deletion    | Moderate | 4 | - | c.1965_1988del                           | p.Glu658_Lys665de<br>l                       | rs267607533  |
| 29885604 | 29885604 | AAGGAAG   | -                      | In-frame<br>Deletion    | Moderate | 4 | - | c.1973_1978del                           | p.Glu658_Glu659de<br>l                       | rs149571560  |
| 29885622 | 29885622 | GAGGCCAAGTC<br>CCCTGAGA                                 | -                      | In-frame<br>Deletion    | Moderate | 4 | - | c.1989_2006del                           | p.Glu664_Pro669de<br>l                       | rs267607534  |
| 29885622 | 29885622 | A   | AGGGAG                 | In-frame<br>Insertion   | Moderate | 4 | - | c.1996_1997ins<br>GAGAGG                 | p.Lys665_Ala666ins<br>GlyGlu                 | -            |
| 29885640 | 29885640 | A   | C                      | Missense                | Moderate | 4 | - | c.2011A>C                                | p.Lys671Gln                                  | -            |
| 29885648 | 29885648 | A   | G                      | Synonymous              | Low      | 4 | - | c.2019A>G                                | p.Glu673Glu                                  | rs746048017  |
| 29885651 | 29885651 | A   | C                      | Synonymous              | Low      | 4 | - | c.2022A>C                                | p.Ala674Ala                                  | rs763507482  |
| 29885711 | 29885711 | C   | T                      | Synonymous              | Low      | 4 | - | c.2082C>T                                | p.Ala694Ala                                  | rs1452419487 |
| 29885736 | 29885736 | A   | C                      | Missense                | Moderate | 4 | - | c.2107A>C                                | p.Lys703Gln                                  | -            |
| 29885742 | 29885742 | C   | T                      | Missense                | Moderate | 4 | - | c.2113C>T                                | p.Pro705Ser                                  | rs770039871  |
| 29885783 | 29885783 | C   | T                      | Synonymous              | Low      | 4 | - | c.2154C>T                                | p.Ser718Ser                                  | rs772385634  |
| 29885819 | 29885819 | AAAGACCCCG<br>AGAAGGCCAAG<br>TCCCCAGTGAA<br>GGAAGAAGCT  | C                      | In-frame<br>Deletion    | Moderate | 4 | - | c.2190_2232deli<br>nsC                   | p.Thr732_Lys745de<br>l                       | -            |
| 29885835 | 29885835 | G   | T                      | Missense                | Moderate | 4 | - | c.2206G>T                                | p.Ala736Ser                                  | -            |

|          |          |   |   |                       |          |   |   |                        |                    |             |
|----------|----------|---|---|-----------------------|----------|---|---|------------------------|--------------------|-------------|
| 29885861 | 29885861 | AAAGACCCCG<br>AGAAGGCCAAG<br>TCCCCAGTGAA<br>GGAAGAAGCT  | C | In-frame<br>Deletion  | Moderate | 4 | - | c.2232_2274deli<br>nsC | p.Lys745_Ala758del | -           |
| 29885861 | 29885861 | CAAGTCCCCAG<br>TGAAGGAAGAA<br>GCT                       | - | In-frame<br>Deletion  | Moderate | 4 | - | c.2219_2242del         | p.Val740_Pro747del | rs778386609 |
| 29885870 | 29885870 | CGAGAAGGCCA<br>AGTCCCCAGTG<br>AAGGAAGAAGC<br>TAAGTCCCCA | - | In-frame<br>Deletion  | Moderate | 4 | - | c.2219_2260del         | p.Val740_Pro753del | -           |
| 29885884 | 29885884 | C   | T | Missense              | Moderate | 4 | - | c.2255C>T              | p.Ser752Phe        | -           |
| 29885913 | 29885913 | A   | G | Missense              | Moderate | 4 | - | c.2284A>G              | p.Lys762Glu        | -           |
| 29885939 | 29885939 | G   | A | Synonymous            | Low      | 4 | - | c.2310G>A              | p.Ala770Ala        | rs757096652 |
| 29885959 | 29885959 | C   | T | Missense              | Moderate | 4 | - | c.2330C>T              | p.Pro777Leu        | rs199748453 |
| 29885976 | 29885976 | G   | A | Missense              | Moderate | 4 | - | c.2347G>A              | p.Glu783Lys        | -           |
| 29885996 | 29885996 | CAAG  | - | In-frame<br>Deletion  | Moderate | 4 | - | c.2368_2370del         | p.Lys790del        | rs59551486  |
| 29886001 | 29886001 | A   | C | Missense              | Moderate | 4 | - | c.2372A>C              | p.Glu791Ala        | -           |
| 29886025 | 29886025 | C   | T | Missense              | Moderate | 4 | - | c.2396C>T              | p.Ala799Val        | rs375529650 |
| 29886026 | 29886026 | G   | A | Synonymous            | Low      | 4 | - | c.2397G>A              | p.Ala799Ala        | rs376035598 |
| 29886034 | 29886034 | C   | T | Missense              | Moderate | 4 | - | c.2405C>T              | p.Pro802Leu        | rs758520448 |
| 29886043 | 29886043 | A   | C | Missense              | Moderate | 4 | - | c.2414A>C              | p.Glu805Ala        | rs165602    |
| 29886044 | 29886044 | G   | A | Synonymous            | Low      | 4 | - | c.2415G>A              | p.Glu805Glu        | rs940285527 |
| 29886069 | 29886069 | A   | G | Missense              | Moderate | 4 | - | c.2440A>G              | p.Ile814Val        | rs748832999 |
| 29886072 | 29886072 | C   | A | Missense              | Moderate | 4 | - | c.2443C>A              | p.Pro815Thr        | -           |
| 29886088 | 29886088 | T   | C | Missense              | Moderate | 4 | - | c.2459T>C              | p.Val820Ala        | -           |
| 29886140 | 29886140 | G   | A | Synonymous            | Low      | 4 | - | c.2511G>A              | p.Glu837Glu        | rs751566708 |
| 29886147 | 29886147 | A   | G | Missense              | Moderate | 4 | - | c.2518A>G              | p.Lys840Glu        | rs750908593 |
| 29886189 | 29886189 | CAG   | - | Frameshift<br>Variant | High     | 4 | - | c.2561_2562del         | p.Glu854GlyfsTer37 | rs775700827 |
| 29886200 | 29886200 | G   | A | Synonymous            | Low      | 4 | - | c.2571G>A              | p.Lys857Lys        | rs145669735 |
| 29886230 | 29886230 | G   | T | Missense              | Moderate | 4 | - | c.2601G>T              | p.Lys867Asn        | rs138156220 |
| 29886253 | 29886253 | TGGA  | - | In-frame<br>Deletion  | Moderate | 4 | - | c.2626_2628del         | p.Glu876del        | rs768937935 |
| 29886268 | 29886268 | C   | T | Missense              | Moderate | 4 | - | c.2639C>T              | p.Pro880Leu        | rs756683695 |
| 29886275 | 29886275 | C   | T | Synonymous            | Low      | 4 | - | c.2646C>T              | p.Val882Val        | rs528790943 |

|          |          |     |   |                    |          |   |   |                |                   |              |
|----------|----------|-----|---|--------------------|----------|---|---|----------------|-------------------|--------------|
| 29886276 | 29886276 | G   | A | Missense           | Moderate | 4 | - | c.2647G>A      | p.Glu883Lys       | rs754121553  |
| 29886289 | 29886289 | A   | G | Missense           | Moderate | 4 | - | c.2660A>G      | p.Glu887Gly       | -            |
| 29886352 | 29886352 | A   | G | Missense           | Moderate | 4 | - | c.2723A>G      | p.Lys908Arg       | -            |
| 29886360 | 29886360 | C   | T | Missense           | Moderate | 4 | - | c.2731C>T      | p.Pro911Ser       | rs376751999  |
| 29886375 | 29886375 | G   | A | Missense           | Moderate | 4 | - | c.2746G>A      | p.Val916Met       | rs762057603  |
| 29886386 | 29886386 | C   | T | Synonymous         | Low      | 4 | - | c.2757C>T      | p.Asp919Asp       | rs56200920   |
| 29886400 | 29886400 | A   | C | Missense           | Moderate | 4 | - | c.2771A>C      | p.Glu924Ala       | rs199737170  |
| 29886413 | 29886413 | A   | G | Synonymous         | Low      | 4 | - | c.2784A>G      | p.Val928Val       | rs165625     |
| 29886415 | 29886415 | C   | A | Missense           | Moderate | 4 | - | c.2786C>A      | p.Ala929Asp       | -            |
| 29886478 | 29886478 | C   | T | Missense           | Moderate | 4 | - | c.2849C>T      | p.Ala950Val       | rs553629461  |
| 29886485 | 29886485 | G   | A | Synonymous         | Low      | 4 | - | c.2856G>A      | p.Pro952Pro       | rs147416824  |
| 29886498 | 29886498 | A   | G | Missense           | Moderate | 4 | - | c.2869A>G      | p.Thr957Ala       | rs760693353  |
| 29886509 | 29886509 | G   | T | Missense           | Moderate | 4 | - | c.2880G>T      | p.Glu960Asp       | rs372070551  |
| 29886517 | 29886517 | A   | G | Missense           | Moderate | 4 | - | c.2888A>G      | p.Lys963Arg       | rs1480895257 |
| 29886543 | 29886543 | CAG | - | Frameshift Variant | High     | 4 | - | c.2915_2916del | p.Glu972GlyfsTer7 | rs1346887118 |
| 29886635 | 29886635 | A   | G | Synonymous         | Low      | 4 | - | c.3006A>G      | p.Gln1002Gln      | rs768522862  |
| 29886673 | 29886673 | A   | G | Missense           | Moderate | 4 | - | c.3044A>G      | p.Lys1015Arg      | -            |
| 29886713 | 29886713 | C   | T | 3' UTR             | Modifier | 4 | - | c.*21C>T       |                   | rs191972471  |
| 29886714 | 29886714 | G   | A | 3' UTR             | Modifier | 4 | - | c.*22G>A       |                   | rs183499750  |
| 29886718 | 29886718 | C   | G | 3' UTR             | Modifier | 4 | - | c.*26C>G       |                   | rs374202245  |
| 29886726 | 29886726 | G   | A | 3' UTR             | Modifier | 4 | - | c.*34G>A       |                   | -            |
| 29886744 | 29886744 | G   | A | 3' UTR             | Modifier | 4 | - | c.*52G>A       |                   | rs766995345  |
| 29886758 | 29886758 | A   | G | 3' UTR             | Modifier | 4 | - | c.*66A>G       |                   | rs753770865  |
| 29886778 | 29886778 | T   | C | 3' UTR             | Modifier | 4 | - | c.*86T>C       |                   | rs1270308635 |
| 29886797 | 29886797 | GA  | - | 3' UTR             | Modifier | 4 | - | c.*106del      |                   | rs748195897  |
| 29886798 | 29886798 | A   | G | 3' UTR             | Modifier | 4 | - | c.*106A>G      |                   | rs771159816  |
| 29886815 | 29886815 | C   | T | 3' UTR             | Modifier | 4 | - | c.*123C>T      |                   | rs781167046  |
| 29886835 | 29886835 | A   | G | 3' UTR             | Modifier | 4 | - | c.*143A>G      |                   | rs1050302661 |
| 29886840 | 29886840 | AT  | - | 3' UTR             | Modifier | 4 | - | c.*150del      |                   | rs747501203  |
| 29886852 | 29886852 | A   | G | 3' UTR             | Modifier | 4 | - | c.*160A>G      |                   | -            |
| 29886893 | 29886893 | G   | T | 3' UTR             | Modifier | 4 | - | c.*201G>T      |                   | rs1061373    |
| 29886906 | 29886906 | C   | T | 3' UTR             | Modifier | 4 | - | c.*214C>T      |                   | rs533220152  |
| 29886907 | 29886907 | G   | A | 3' UTR             | Modifier | 4 | - | c.*215G>A      |                   | rs755046912  |

|          |          |     |   |        |          |   |   |                |  |              |
|----------|----------|-----|---|--------|----------|---|---|----------------|--|--------------|
| 29886909 | 29886909 | T   | C | 3' UTR | Modifier | 4 | - | c.*217T>C      |  | rs897216138  |
| 29887012 | 29887012 | T   | C | 3' UTR | Modifier | 4 | - | c.*320T>C      |  | rs192696400  |
| 29887018 | 29887018 | G   | A | 3' UTR | Modifier | 4 | - | c.*326G>A      |  | -            |
| 29887053 | 29887053 | G   | C | 3' UTR | Modifier | 4 | - | c.*361G>C      |  | rs185039421  |
| 29887072 | 29887072 | C   | T | 3' UTR | Modifier | 4 | - | c.*380C>T      |  | rs978569780  |
| 29887112 | 29887112 | TTC | - | 3' UTR | Modifier | 4 | - | c.*420_*421del |  | rs1490643558 |
| 29887148 | 29887148 | G   | A | 3' UTR | Modifier | 4 | - | c.*456G>A      |  | -            |
| 29887151 | 29887151 | C   | G | 3' UTR | Modifier | 4 | - | c.*459C>G      |  | rs540106485  |
| 29887182 | 29887182 | C   | T | 3' UTR | Modifier | 4 | - | c.*490C>T      |  | rs142042497  |
| 29887186 | 29887186 | G   | C | 3' UTR | Modifier | 4 | - | c.*494G>C      |  | rs710195     |
| 29887211 | 29887211 | C   | T | 3' UTR | Modifier | 4 | - | c.*519C>T      |  | rs911785075  |
| 29887212 | 29887212 | G   | A | 3' UTR | Modifier | 4 | - | c.*520G>A      |  | rs944633264  |
| 29887216 | 29887216 | T   | C | 3' UTR | Modifier | 4 | - | c.*524T>C      |  | rs1218993302 |
| 29887227 | 29887227 | G   | T | 3' UTR | Modifier | 4 | - | c.*535G>T      |  | rs772755733  |
| 29887238 | 29887238 | A   | G | 3' UTR | Modifier | 4 | - | c.*546A>G      |  | rs561850196  |
| 29887249 | 29887249 | G   | A | 3' UTR | Modifier | 4 | - | c.*557G>A      |  | rs1321602381 |
| 29887271 | 29887271 | A   | T | 3' UTR | Modifier | 4 | - | c.*579A>T      |  | -            |
| 29887315 | 29887315 | G   | C | 3' UTR | Modifier | 4 | - | c.*623G>C      |  | -            |

Table A11. Details of all of the 591 variants (hg19) identified in the Project MinE dataset. HGVS.c notation refers to the ENST00000310624.6 transcript. HGVS.p notation refers to the ENSP00000311997.6 protein transcript.

| Variant      | No. Studies | N Cases | N Controls | Fixed OR (95% CI; p-value) | Random OR (95% CI; p-value) | Heterogeneity (Q statistic; p-value) | Heterogeneity (I-squared) | Publication Bias (Egger t statistic; p-value) | Publication Bias (Harbord t statistic; p-value) |
|--------------|-------------|---------|------------|----------------------------|-----------------------------|--------------------------------------|---------------------------|---|---|
| A90V         | 2           | 6569    | 2534       | 2.45 (0.42-14.51; 0.32)    | 2.47 (0.42-14.47; 0.32)     | 0.02 (0.88)                          | 0%                        | N/A   | N/A   |
| G249S        | 3           | 6940    | 3245       | 1.10 (0.71-1.70; 0.68)     | 1.10 (0.70-1.70; 0.69)      | 0.79 (0.67)                          | 0%                        | 0.14; 0.91                                    | 0.40; 0.76                                      |
| A314V        | 2           | 6840    | 3145       | 2.61 (0.27-25.00; 0.41)    | 2.55 (0.26-24.53; 0.42)     | 0.50 (0.48)                          | 0%                        | N/A   | N/A   |
| E463K        | 2           | 7595    | 3047       | 0.95 (0.85-1.06; 0.36)     | 0.95 (0.85-1.06; 0.36)      | 1.01 (0.31)                          | 2%                        | N/A   | N/A   |
| T642M        | 4           | 7197    | 4044       | 1.39 (0.53-3.16; 0.56)     | 1.23 (0.46-3.28; 0.69)      | 3.29 (0.35)                          | 9%                        | -0.44; 0.71                                   | -1.21; 0.35                                     |
| E658_K665del | 3           | 7047    | 3364       | 0.68 (0.35-1.32; 0.25)     | 0.66 (0.34-1.29; 0.23)      | 0.96 (0.62)                          | 0%                        | 1.59; 0.36                                    | 2.58; 0.24                                      |
| E664_P669del | 2           | 6676    | 2653       | 1.22 (0.38-3.92; 0.74)     | 1.22 (0.38-3.93; 0.74)      | 0.01 (0.91)                          | 0%                        | N/A   | N/A   |
| K790del      | 3           | 7951    | 3353       | 0.60 (0.28-1.29; 0.19)     | 0.63 (0.13-3.01; 0.57)      | 3.97 (0.14)                          | <b>50%</b>                | 0.81; 0.57                                    | 0.55; 0.68                                      |
| E805A        | 3           | 7966    | 3758       | 1.01 (0.93-1.11; 0.76)     | 1.02 (0.93-1.11; 0.75)      | 2.89 (0.24)                          | 31%                       | N/A   | N/A   |
| K867N        | 2           | 6651    | 2624       | 1.94 (0.20-18.60; 0.57)    | 1.88 (0.20-18.15; 0.58)     | 0.20 (0.66)                          | 0%                        | N/A   | N/A   |

Table A12. Results of variant-level meta-analysis when including the Project MinE cohort as an additional study. Meta-analysis was repeated for 5 variants (G249S, T642M, E658\_K665del, K790del, E805A), and new meta-analysis was performed for 5 variants (A90V, A314V, E463K, E664\_P669del, K867N), who now have sufficient evidence to be included ( $\geq 2$  case-control studies). N/A values represent instances where publication bias could not be calculated as the minimum number of studies used for calculation was not reached.

| Variant      | Start    | End      | Ref     | Alt | SIFT                         | PolyPhen          | Total Frequency (Case/Control) |
|--------------|----------|----------|---------|-----|------------------------------|-------------------|--------------------------------|
| G414S        | 29884869 | 29884869 | G       | A   | Tolerated                    | Possibly Damaging | 1 (0/1)                        |
| K437R        | 29884939 | 29884939 | A       | G   | Deleterious                  | Probably Damaging | 1 (1/0)                        |
| K437N        | 29884940 | 29884940 | G       | T   | Deleterious                  | Probably Damaging | 1 (1/0)                        |
| E441K        | 29884950 | 29884950 | G       | A   | Deleterious                  | Probably Damaging | 1 (0/1)                        |
| K449N        | 29884976 | 29884976 | G       | C   | Deleterious                  | Probably Damaging | 1 (1/0)                        |
| E477Q        | 29885058 | 29885058 | G       | C   | Deleterious                  | Possibly Damaging | 1 (1/0)                        |
| P512R        | 29885164 | 29885164 | C       | G   | Deleterious                  | Possibly Damaging | 1 (1/0)                        |
| E523D        | 29885198 | 29885198 | G       | C   | Deleterious                  | Benign            | 1 (1/0)                        |
| K525E        | 29885202 | 29885202 | A       | G   | Deleterious                  | Benign            | 1 (1/0)                        |
| S560L        | 29885308 | 29885308 | C       | T   | Deleterious                  | Benign            | 1 (1/0)                        |
| P561L        | 29885311 | 29885311 | C       | T   | Deleterious                  | Benign            | 1 (1/0)                        |
| K585R        | 29885383 | 29885383 | A       | G   | Deleterious                  | Possibly Damaging | 2 (1/1)                        |
| S586F        | 29885386 | 29885386 | C       | T   | Deleterious                  | Benign            | 1 (0/1)                        |
| A592S        | 29885403 | 29885403 | G       | T   | Deleterious                  | Benign            | 2 (2/0)                        |
| K599T        | 29885425 | 29885425 | A       | C   | Deleterious                  | Probably Damaging | 1 (0/1)                        |
| K627Q        | 29885508 | 29885508 | A       | C   | Deleterious                  | Benign            | 1 (1/0)                        |
| K647N        | 29885570 | 29885570 | G       | C   | Deleterious (Low Confidence) | Possibly Damaging | 1 (1/0)                        |
| E658_E659del | 29885598 | 29885598 | AAGGAAG | A   | -                            | -                 | 36 (31/5)                      |
| E664_P669del | 29885604 | 29885604 | GAGGCCA | G   | -                            | -                 | 13 (10/3)                      |
| K671Q        | 29885640 | 29885640 | A       | C   | Deleterious (Low Confidence) | Possibly Damaging | 2 (1/1)                        |
| K703Q        | 29885736 | 29885736 | A       | C   | Deleterious (Low Confidence) | Probably Damaging | 1 (1/0)                        |
| P705S        | 29885742 | 29885742 | C       | T   | Deleterious (Low Confidence) | Probably Damaging | 1 (1/0)                        |
| A736S        | 29885835 | 29885835 | G       | T   | Deleterious (Low Confidence) | Benign            | 1 (1/0)                        |
| S752F        | 29885884 | 29885884 | C       | T   | Deleterious (Low Confidence) | Possibly Damaging | 1 (1/0)                        |
| P777L        | 29885959 | 29885959 | C       | T   | Deleterious (Low Confidence) | Probably Damaging | 1 (1/0)                        |
| K790del      | 29885996 | 29885996 | CAAG    | C   | -                            | -                 | 18 (9/9)                       |
| E791A        | 29886001 | 29886001 | A       | C   | Deleterious (Low Confidence) | Benign            | 1 (1/0)                        |

|        |          |          |   |   |                              |                   |         |
|--------|----------|----------|---|---|------------------------------|-------------------|---------|
| P802L  | 29886034 | 29886034 | C | T | Deleterious (Low Confidence) | Benign            | 1 (1/0) |
| K840E  | 29886147 | 29886147 | A | G | Tolerated (Low Confidence)   | Possibly Damaging | 1 (1/0) |
| K867N  | 29886230 | 29886230 | G | T | Deleterious (Low Confidence) | Probably Damaging | 1 (1/0) |
| P880L  | 29886268 | 29886268 | C | T | Deleterious (Low Confidence) | Benign            | 1 (1/0) |
| E883K  | 29886276 | 29886276 | G | A | Deleterious (Low Confidence) | Probably Damaging | 1 (1/0) |
| E887G  | 29886289 | 29886289 | A | G | Deleterious (Low Confidence) | Benign            | 1 (1/0) |
| K908R  | 29886352 | 29886352 | A | G | Deleterious (Low Confidence) | Benign            | 1 (1/0) |
| V916M  | 29886375 | 29886375 | G | A | Deleterious (Low Confidence) | Benign            | 4 (4/0) |
| E924A  | 29886400 | 29886400 | A | C | Deleterious (Low Confidence) | Benign            | 2 (2/0) |
| A929D  | 29886415 | 29886415 | C | A | Deleterious (Low Confidence) | Benign            | 1 (0/1) |
| A950V  | 29886478 | 29886478 | C | T | Deleterious (Low Confidence) | Probably Damaging | 2 (2/0) |
| K1015R | 29886673 | 29886673 | A | G | Deleterious (Low Confidence) | Benign            | 1 (1/0) |

*Table A13. Genomic coordinates (hg19) and pathogenicity prediction of the ultra-rare pathogenic missense and high-frequency rare in-frame deletion variants which were found to significantly increase the risk of ALS when performing burden analysis in the Project MinE dataset.*

## Chapter 6

| Gene ID         | Mean     | log2Fold Change (lfc) | lfcSE    | stat     | p-value  | p-value adjusted | weight   |
|-----------------|----------|-----------------------|----------|----------|----------|------------------|----------|
| ENSG00000084090 | 1721.952 | 0.242756              | 0.041782 | 5.810036 | 6.25E-09 | 0.000101         | 2.293762 |
| ENSG00000105887 | 2245.828 | 0.252967              | 0.046694 | 5.4175   | 6.04E-08 | 0.000448         | 2.492774 |
| ENSG00000143319 | 298.83   | -0.21298              | 0.04011  | -5.30991 | 1.10E-07 | 0.00046          | 1.995423 |
| ENSG00000125868 | 1916.511 | 0.346591              | 0.066092 | 5.244052 | 1.57E-07 | 0.00046          | 2.514347 |
| ENSG00000151229 | 1712.515 | 0.296613              | 0.057164 | 5.188791 | 2.12E-07 | 0.00046          | 2.295759 |
| ENSG00000164116 | 968.0289 | 0.32409               | 0.062948 | 5.148558 | 2.62E-07 | 0.00046          | 2.514347 |
| ENSG00000107758 | 2081.728 | 0.283809              | 0.055477 | 5.115808 | 3.12E-07 | 0.00046          | 2.583187 |
| ENSG00000135624 | 1176.327 | 0.252105              | 0.049392 | 5.104126 | 3.32E-07 | 0.00046          | 2.583187 |
| ENSG00000215114 | 785.4728 | 0.182654              | 0.035798 | 5.102296 | 3.36E-07 | 0.00046          | 2.293762 |
| ENSG00000266412 | 1772.36  | 0.212498              | 0.04176  | 5.088504 | 3.61E-07 | 0.00046          | 2.295759 |
| ENSG00000198728 | 1276.734 | -0.1693               | 0.033307 | -5.08293 | 3.72E-07 | 0.00046          | 2.295759 |
| ENSG00000173598 | 1129.096 | 0.284701              | 0.056138 | 5.071433 | 3.95E-07 | 0.00046          | 2.514347 |
| ENSG00000119801 | 1224.95  | 0.274382              | 0.054132 | 5.068781 | 4.00E-07 | 0.00046          | 2.514347 |
| ENSG00000259392 | 25.69186 | -0.63532              | 0.122442 | -5.18875 | 2.12E-07 | 0.00055          | 0.947688 |
| ENSG00000078687 | 1841.534 | -0.1989               | 0.03963  | -5.01895 | 5.20E-07 | 0.00055          | 2.456745 |
| ENSG00000103160 | 590.9191 | 0.249458              | 0.049912 | 4.997977 | 5.79E-07 | 0.000576         | 2.295759 |
| ENSG00000155096 | 1937.293 | 0.23596               | 0.047507 | 4.966812 | 6.81E-07 | 0.000576         | 2.295759 |
| ENSG00000091039 | 1869.347 | 0.222329              | 0.044784 | 4.96446  | 6.89E-07 | 0.000576         | 2.456745 |
| ENSG00000101558 | 2149.075 | 0.183109              | 0.036914 | 4.960451 | 7.03E-07 | 0.000576         | 2.456745 |
| ENSG00000144746 | 1332.314 | 0.29681               | 0.059881 | 4.956655 | 7.17E-07 | 0.000577         | 2.295759 |
| ENSG00000260230 | 3763.358 | 0.198697              | 0.040171 | 4.946289 | 7.56E-07 | 0.00058          | 2.295759 |
| ENSG00000185864 | 275.2925 | -0.40285              | 0.082249 | -4.898   | 9.68E-07 | 0.00062          | 2.025126 |
| ENSG00000155304 | 829.9333 | 0.275986              | 0.056347 | 4.897959 | 9.68E-07 | 0.00062          | 2.293762 |
| ENSG00000118432 | 1221.16  | 0.383092              | 0.078262 | 4.894973 | 9.83E-07 | 0.00062          | 2.225762 |
| ENSG00000100804 | 558.0857 | 0.285526              | 0.058359 | 4.892575 | 9.95E-07 | 0.00062          | 2.293762 |
| ENSG00000156136 | 265.4173 | 0.293191              | 0.060194 | 4.870728 | 1.11E-06 | 0.00062          | 2.225762 |
| ENSG00000100030 | 4643.508 | 0.214551              | 0.044133 | 4.861481 | 1.17E-06 | 0.00062          | 2.583187 |

|                 |          |          |  |          |          |          |          |          |
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| ENSG00000147044 | 801.0537 | 0.162133 |  | 0.033383 | 4.856746 | 1.19E-06 | 0.00062  | 2.514347 |
| ENSG00000140391 | 2222.775 | 0.230645 |  | 0.047496 | 4.856053 | 1.20E-06 | 0.00062  | 2.514347 |
| ENSG00000023734 | 918.7745 | 0.227714 |  | 0.046962 | 4.848882 | 1.24E-06 | 0.00062  | 2.225762 |
| ENSG00000169116 | 1622.504 | 0.317037 |  | 0.065421 | 4.84613  | 1.26E-06 | 0.00062  | 2.225762 |
| ENSG00000165672 | 710.933  | 0.279459 |  | 0.057687 | 4.844399 | 1.27E-06 | 0.00062  | 2.225762 |
| ENSG00000143612 | 1279.955 | 0.210298 |  | 0.043461 | 4.83883  | 1.31E-06 | 0.00062  | 2.514347 |
| ENSG00000106771 | 2464.576 | 0.203686 |  | 0.042129 | 4.834759 | 1.33E-06 | 0.00062  | 2.492774 |
| ENSG00000102753 | 747.1184 | 0.190268 |  | 0.039629 | 4.801229 | 1.58E-06 | 0.000726 | 2.293762 |
| ENSG00000115484 | 856.5296 | 0.25676  |  | 0.053554 | 4.79445  | 1.63E-06 | 0.00073  | 2.293762 |
| ENSG00000223599 | 56.31848 | -0.37378 |  | 0.075877 | -4.92618 | 8.39E-07 | 0.000739 | 1.023066 |
| ENSG00000176834 | 231.258  | -0.24426 |  | 0.051114 | -4.77881 | 1.76E-06 | 0.000739 | 2.225762 |
| ENSG00000100934 | 1091.095 | 0.257899 |  | 0.054028 | 4.773422 | 1.81E-06 | 0.000739 | 2.293762 |
| ENSG00000214193 | 519.0564 | -0.2849  |  | 0.059785 | -4.76539 | 1.88E-06 | 0.000739 | 2.29693  |
| ENSG00000061676 | 5108.546 | 0.212295 |  | 0.044697 | 4.749684 | 2.04E-06 | 0.000739 | 2.583187 |
| ENSG00000085662 | 486.9222 | 0.219263 |  | 0.046254 | 4.740455 | 2.13E-06 | 0.000787 | 2.29693  |
| ENSG00000132341 | 1591.055 | 0.257585 |  | 0.054514 | 4.725089 | 2.30E-06 | 0.000787 | 2.514347 |
| ENSG00000169018 | 2219.018 | 0.218945 |  | 0.046425 | 4.716132 | 2.40E-06 | 0.000787 | 2.514347 |
| ENSG00000067560 | 1859.156 | 0.169361 |  | 0.035957 | 4.710065 | 2.48E-06 | 0.000787 | 2.583187 |
| ENSG00000182220 | 1515.18  | 0.278711 |  | 0.059072 | 4.718169 | 2.38E-06 | 0.00083  | 2.295759 |
| ENSG00000232931 | 1204.536 | -0.31348 |  | 0.066491 | -4.71457 | 2.42E-06 | 0.00083  | 2.293762 |
| ENSG00000188803 | 411.0558 | -0.47584 |  | 0.101163 | -4.70365 | 2.56E-06 | 0.000848 | 2.225762 |
| ENSG00000078140 | 1452.7   | 0.188588 |  | 0.04013  | 4.699484 | 2.61E-06 | 0.000848 | 2.293762 |
| ENSG00000124486 | 3834.897 | 0.179042 |  | 0.038208 | 4.686052 | 2.79E-06 | 0.000848 | 2.456745 |
| ENSG00000083720 | 1440.696 | 0.277057 |  | 0.059097 | 4.688184 | 2.76E-06 | 0.00087  | 2.295759 |
| ENSG00000206149 | 577.4827 | -0.3456  |  | 0.073684 | -4.69025 | 2.73E-06 | 0.000871 | 2.225762 |
| ENSG00000249673 | 259.7063 | -0.27728 |  | 0.058918 | -4.70614 | 2.52E-06 | 0.000879 | 1.977088 |
| ENSG00000146433 | 1143.316 | 0.187559 |  | 0.040124 | 4.674533 | 2.95E-06 | 0.000879 | 2.293762 |
| ENSG00000120265 | 1260.131 | 0.329445 |  | 0.070501 | 4.672925 | 2.97E-06 | 0.000896 | 2.225762 |
| ENSG00000119446 | 381.1576 | 0.216776 |  | 0.046507 | 4.661176 | 3.14E-06 | 0.000903 | 2.295759 |
| ENSG00000082458 | 1344.287 | 0.220027 |  | 0.047407 | 4.641254 | 3.46E-06 | 0.000957 | 2.225762 |



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| ENSG00000071073 | 1232.949 | 0.248443 | 0.053581 | 4.636771 | 3.54E-06 | 0.000957 | 2.295759 |
| ENSG00000108924 | 2666.586 | 0.227575 | 0.049168 | 4.628525 | 3.68E-06 | 0.000957 | 2.492774 |
| ENSG00000163630 | 900.3796 | 0.451432 | 0.09754  | 4.628151 | 3.69E-06 | 0.000957 | 2.225762 |
| ENSG00000102401 | 1089.287 | 0.241552 | 0.052307 | 4.618003 | 3.87E-06 | 0.000957 | 2.295759 |
| ENSG00000165934 | 776.0951 | 0.154109 | 0.033437 | 4.608993 | 4.05E-06 | 0.000957 | 2.295759 |
| ENSG00000050165 | 6409.342 | 0.253925 | 0.055153 | 4.603973 | 4.15E-06 | 0.000957 | 2.583187 |
| ENSG00000184408 | 736.6054 | 0.231484 | 0.050281 | 4.603779 | 4.15E-06 | 0.000957 | 2.514347 |
| ENSG00000132294 | 2570.606 | 0.238936 | 0.052007 | 4.59427  | 4.34E-06 | 0.000957 | 2.514347 |
| ENSG00000123836 | 1089.718 | 0.361735 | 0.078788 | 4.591261 | 4.41E-06 | 0.000957 | 2.583187 |
| ENSG00000119414 | 851.3815 | 0.191817 | 0.041779 | 4.591183 | 4.41E-06 | 0.000957 | 2.514347 |
| ENSG00000113595 | 1187.221 | 0.239731 | 0.052279 | 4.585612 | 4.53E-06 | 0.000957 | 2.583187 |
| ENSG00000164032 | 442.6725 | 0.328643 | 0.071014 | 4.627869 | 3.69E-06 | 0.000984 | 1.995423 |
| ENSG00000159674 | 121.7896 | -0.44379 | 0.096327 | -4.60708 | 4.08E-06 | 0.000984 | 2.189833 |
| ENSG00000187094 | 1116.395 | 0.351872 | 0.076947 | 4.572933 | 4.81E-06 | 0.000995 | 2.514347 |
| ENSG00000090447 | 162.5607 | -0.2996  | 0.065045 | -4.60594 | 4.11E-06 | 0.001011 | 1.995423 |
| ENSG00000072135 | 439.2264 | -0.22441 | 0.048903 | -4.58892 | 4.46E-06 | 0.001011 | 2.225762 |
| ENSG00000072401 | 202.8735 | 0.253116 | 0.055218 | 4.583934 | 4.56E-06 | 0.001011 | 2.295759 |
| ENSG00000123091 | 2889.178 | 0.192521 | 0.042243 | 4.557514 | 5.18E-06 | 0.001011 | 2.456745 |
| ENSG00000205339 | 1937.275 | 0.189092 | 0.041519 | 4.554354 | 5.25E-06 | 0.001011 | 2.583187 |
| ENSG00000101966 | 1304.978 | 0.127584 | 0.028042 | 4.54968  | 5.37E-06 | 0.001011 | 2.583187 |
| ENSG00000113575 | 1663.785 | 0.242499 | 0.053335 | 4.546686 | 5.45E-06 | 0.001027 | 2.514347 |
| ENSG00000198668 | 26595.52 | 0.196944 | 0.043385 | 4.539412 | 5.64E-06 | 0.001058 | 2.492774 |
| ENSG00000047597 | 280.2855 | 0.31585  | 0.06916  | 4.566967 | 4.95E-06 | 0.001062 | 2.025126 |
| ENSG00000115839 | 1371.386 | 0.169783 | 0.037351 | 4.54555  | 5.48E-06 | 0.001062 | 2.295759 |
| ENSG00000115091 | 1250.743 | 0.211337 | 0.046522 | 4.542727 | 5.55E-06 | 0.001062 | 2.295759 |
| ENSG00000065154 | 1522.94  | 0.300507 | 0.066429 | 4.523765 | 6.07E-06 | 0.001062 | 2.583187 |
| ENSG00000006007 | 803.6137 | 0.217806 | 0.048171 | 4.521542 | 6.14E-06 | 0.001062 | 2.514347 |
| ENSG00000159459 | 1293.831 | 0.14561  | 0.032215 | 4.519931 | 6.19E-06 | 0.001062 | 2.583187 |
| ENSG00000237887 | 61.35785 | -0.36966 | 0.078593 | -4.70352 | 2.56E-06 | 0.001074 | 0.989117 |
| ENSG00000164841 | 195.5155 | 0.294075 | 0.064865 | 4.533674 | 5.80E-06 | 0.001074 | 2.295759 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000136750 | 986.8132 | 0.536389 | 0.118435 | 4.528995 | 5.93E-06 | 0.001074 | 2.293762 |
| ENSG00000162378 | 2402.099 | 0.20499  | 0.045417 | 4.51353  | 6.38E-06 | 0.001074 | 2.456745 |
| ENSG00000196950 | 2588.512 | 0.321057 | 0.071207 | 4.508788 | 6.52E-06 | 0.001074 | 2.492774 |
| ENSG00000165434 | 2862.022 | 0.380763 | 0.084462 | 4.508115 | 6.54E-06 | 0.001081 | 2.456745 |
| ENSG00000178974 | 924.8954 | 0.210421 | 0.046865 | 4.489915 | 7.13E-06 | 0.001108 | 2.583187 |
| ENSG00000102471 | 1659.68  | 0.295537 | 0.065494 | 4.512437 | 6.41E-06 | 0.001109 | 2.295759 |
| ENSG00000171867 | 6006.938 | 0.238464 | 0.053181 | 4.483986 | 7.33E-06 | 0.001115 | 2.583187 |
| ENSG00000168283 | 445.7878 | 0.242222 | 0.053692 | 4.511307 | 6.44E-06 | 0.00112  | 2.225762 |
| ENSG00000196792 | 713.0654 | 0.140627 | 0.031254 | 4.499494 | 6.81E-06 | 0.00112  | 2.295759 |
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| ENSG00000142686 | 1415.688 | 0.27173  | 0.060679 | 4.478135 | 7.53E-06 | 0.00112  | 2.583187 |
| ENSG00000001561 | 892.7404 | 0.290946 | 0.064744 | 4.493827 | 7.00E-06 | 0.001138 | 2.293762 |
| ENSG00000182481 | 350.5815 | 0.297752 | 0.065927 | 4.516398 | 6.29E-06 | 0.001206 | 1.918337 |
| ENSG00000198791 | 1289.091 | 0.211858 | 0.047529 | 4.457471 | 8.29E-06 | 0.001206 | 2.514347 |
| ENSG00000163950 | 327.2803 | 0.215807 | 0.048098 | 4.486808 | 7.23E-06 | 0.001232 | 1.977088 |
| ENSG00000125386 | 877.1625 | -0.16944 | 0.037914 | -4.46901 | 7.86E-06 | 0.001232 | 2.225762 |
| ENSG00000005812 | 679.7816 | 0.182184 | 0.040775 | 4.468002 | 7.90E-06 | 0.001232 | 2.293762 |
| ENSG00000197006 | 778.5986 | 0.223899 | 0.050184 | 4.461524 | 8.14E-06 | 0.001232 | 2.293762 |
| ENSG00000109929 | 1460.464 | 0.224821 | 0.050421 | 4.458894 | 8.24E-06 | 0.001232 | 2.225762 |
| ENSG00000064726 | 1213.656 | 0.231767 | 0.05204  | 4.453595 | 8.44E-06 | 0.001232 | 2.293762 |
| ENSG00000186432 | 1430.525 | 0.179137 | 0.040323 | 4.44257  | 8.89E-06 | 0.001232 | 2.583187 |
| ENSG00000113013 | 2771.068 | 0.18897  | 0.042551 | 4.440976 | 8.96E-06 | 0.001232 | 2.456745 |
| ENSG00000069849 | 594.2952 | 0.3056   | 0.068841 | 4.439239 | 9.03E-06 | 0.001232 | 2.583187 |
| ENSG00000134852 | 1624.373 | 0.16173  | 0.036482 | 4.43317  | 9.29E-06 | 0.001232 | 2.514347 |
| ENSG00000150768 | 541.71   | 0.216098 | 0.048634 | 4.443386 | 8.86E-06 | 0.00126  | 2.29693  |
| ENSG00000166546 | 145.2804 | -0.34369 | 0.077408 | -4.44001 | 9.00E-06 | 0.00126  | 2.338927 |
| ENSG00000117153 | 607.4601 | 0.213935 | 0.048169 | 4.441335 | 8.94E-06 | 0.001302 | 2.225762 |
| ENSG00000131236 | 1471.002 | 0.21652  | 0.048809 | 4.436052 | 9.16E-06 | 0.001311 | 2.225762 |
| ENSG00000128989 | 4827.841 | 0.23519  | 0.053332 | 4.40994  | 1.03E-05 | 0.001311 | 2.514347 |
| ENSG00000145428 | 237.8568 | 0.280781 | 0.063369 | 4.430861 | 9.39E-06 | 0.001331 | 2.225762 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000117410 | 782.5546 | 0.252665 | 0.057483 | 4.395482 | 1.11E-05 | 0.001339 | 2.583187 |
| ENSG00000180096 | 87.6     | -0.33522 | 0.073737 | -4.54612 | 5.46E-06 | 0.001352 | 1.182918 |
| ENSG00000240707 | 89.22004 | -0.57742 | 0.127032 | -4.54547 | 5.48E-06 | 0.001352 | 1.182918 |
| ENSG00000165832 | 449.2055 | 0.285777 | 0.064484 | 4.431714 | 9.35E-06 | 0.001352 | 1.995423 |
| ENSG00000198563 | 671.2974 | -0.1861  | 0.042134 | -4.41687 | 1.00E-05 | 0.001352 | 2.225762 |
| ENSG00000153914 | 1261.815 | 0.138242 | 0.031344 | 4.410421 | 1.03E-05 | 0.001352 | 2.295759 |
| ENSG00000230989 | 850.7762 | 0.216527 | 0.049252 | 4.396293 | 1.10E-05 | 0.001352 | 2.514347 |
| ENSG00000156976 | 6187.731 | 0.305338 | 0.069524 | 4.391831 | 1.12E-05 | 0.001352 | 2.456745 |
| ENSG00000104723 | 713.2545 | 0.245677 | 0.055995 | 4.387455 | 1.15E-05 | 0.001352 | 2.514347 |
| ENSG00000152332 | 2975.992 | 0.252967 | 0.05775  | 4.380418 | 1.18E-05 | 0.001352 | 2.583187 |
| ENSG00000177565 | 2658.079 | 0.171843 | 0.039265 | 4.376431 | 1.21E-05 | 0.001352 | 2.583187 |
| ENSG00000132824 | 2836.276 | 0.203458 | 0.046529 | 4.372681 | 1.23E-05 | 0.001361 | 2.583187 |
| ENSG00000185291 | 229.6775 | -0.36118 | 0.081336 | -4.4406  | 8.97E-06 | 0.001365 | 1.867169 |
| ENSG00000186369 | 208.7862 | 0.362565 | 0.081955 | 4.423957 | 9.69E-06 | 0.001366 | 1.995423 |
| ENSG00000139192 | 144.4407 | -0.25954 | 0.05884  | -4.41098 | 1.03E-05 | 0.001366 | 2.108016 |
| ENSG00000090905 | 2591.282 | -0.13369 | 0.030616 | -4.36676 | 1.26E-05 | 0.001393 | 2.514347 |
| ENSG00000187676 | 331.966  | 0.24811  | 0.056311 | 4.406088 | 1.05E-05 | 0.001433 | 2.025126 |
| ENSG00000281649 | 752.8293 | 0.181562 | 0.041505 | 4.374504 | 1.22E-05 | 0.001451 | 2.295759 |
| ENSG00000061918 | 1619.662 | 0.289209 | 0.066154 | 4.371768 | 1.23E-05 | 0.001459 | 2.293762 |
| ENSG00000205133 | 507.4931 | 0.225617 | 0.051678 | 4.365827 | 1.27E-05 | 0.001472 | 2.29693  |
| ENSG00000157540 | 2260.297 | 0.115259 | 0.026515 | 4.346886 | 1.38E-05 | 0.001472 | 2.492774 |
| ENSG00000164091 | 1610.608 | 0.144629 | 0.033298 | 4.343422 | 1.40E-05 | 0.001472 | 2.514347 |
| ENSG00000128245 | 5117.523 | 0.318034 | 0.073249 | 4.341829 | 1.41E-05 | 0.001472 | 2.583187 |
| ENSG00000072315 | 457.7623 | 0.292016 | 0.066848 | 4.368372 | 1.25E-05 | 0.001473 | 2.225762 |
| ENSG00000141759 | 476.1458 | 0.176428 | 0.040471 | 4.359334 | 1.30E-05 | 0.001478 | 2.295759 |
| ENSG00000151465 | 296.0594 | 0.237544 | 0.054199 | 4.382808 | 1.17E-05 | 0.001489 | 1.977088 |
| ENSG00000009844 | 539.1262 | 0.237336 | 0.054435 | 4.359989 | 1.30E-05 | 0.001489 | 2.225762 |
| ENSG00000134294 | 2330.114 | 0.380781 | 0.087434 | 4.355078 | 1.33E-05 | 0.001489 | 2.295759 |
| ENSG00000164211 | 601.4825 | 0.312503 | 0.071803 | 4.352223 | 1.35E-05 | 0.001489 | 2.295759 |
| ENSG00000125755 | 1311.732 | -0.1862  | 0.042792 | -4.35126 | 1.35E-05 | 0.001489 | 2.295759 |

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| ENSG00000183196 | 399.6358 | 0.412814 | 0.09447  | 4.369787 | 1.24E-05 | 0.001495 | 2.025126 |
| ENSG00000185163 | 592.2894 | -0.21359 | 0.049092 | -4.35076 | 1.36E-05 | 0.001495 | 2.225762 |
| ENSG00000187957 | 1452.574 | 0.276327 | 0.063538 | 4.349017 | 1.37E-05 | 0.001495 | 2.225762 |
| ENSG00000143155 | 546.6117 | 0.224282 | 0.051651 | 4.342258 | 1.41E-05 | 0.001495 | 2.293762 |
| ENSG00000163536 | 2169.723 | 0.377276 | 0.087189 | 4.327091 | 1.51E-05 | 0.001495 | 2.456745 |
| ENSG00000176155 | 1095.888 | -0.27023 | 0.062279 | -4.33905 | 1.43E-05 | 0.001506 | 2.293762 |
| ENSG00000113638 | 746.248  | 0.207654 | 0.047893 | 4.335766 | 1.45E-05 | 0.001518 | 2.295759 |
| ENSG00000091527 | 1100.537 | 0.209885 | 0.048402 | 4.336313 | 1.45E-05 | 0.001551 | 2.225762 |
| ENSG00000236670 | 29.08773 | -0.49583 | 0.109462 | -4.52967 | 5.91E-06 | 0.001636 | 0.848718 |
| ENSG00000151893 | 1299.275 | 0.13783  | 0.031889 | 4.32221  | 1.54E-05 | 0.001636 | 2.225762 |
| ENSG00000151458 | 658.1073 | 0.216885 | 0.050216 | 4.319064 | 1.57E-05 | 0.001636 | 2.225762 |
| ENSG00000126858 | 1042.219 | 0.175743 | 0.04074  | 4.313798 | 1.60E-05 | 0.001636 | 2.293762 |
| ENSG00000135835 | 351.5175 | -0.25833 | 0.059547 | -4.33824 | 1.44E-05 | 0.001638 | 1.995423 |
| ENSG00000178104 | 3886.383 | 0.183278 | 0.042736 | 4.288584 | 1.80E-05 | 0.001638 | 2.492774 |
| ENSG00000119900 | 2808.354 | 0.24199  | 0.056441 | 4.287497 | 1.81E-05 | 0.001638 | 2.514347 |
| ENSG00000117450 | 763.6182 | 0.247153 | 0.057662 | 4.286227 | 1.82E-05 | 0.001638 | 2.514347 |
| ENSG00000121579 | 976.8994 | 0.172714 | 0.040165 | 4.300094 | 1.71E-05 | 0.001666 | 2.295759 |
| ENSG00000162980 | 530.0916 | 0.200728 | 0.046681 | 4.300003 | 1.71E-05 | 0.001666 | 2.295759 |
| ENSG00000179456 | 1933.673 | 0.200591 | 0.04688  | 4.27885  | 1.88E-05 | 0.001702 | 2.456745 |
| ENSG00000091073 | 95.41358 | -0.33966 | 0.077981 | -4.35573 | 1.33E-05 | 0.001726 | 1.695647 |
| ENSG00000134278 | 1499.98  | 0.1537   | 0.036013 | 4.267874 | 1.97E-05 | 0.001726 | 2.514347 |
| ENSG00000173915 | 400.3349 | 0.34234  | 0.079165 | 4.324373 | 1.53E-05 | 0.001743 | 1.918337 |
| ENSG00000012660 | 773.2433 | 0.25722  | 0.060396 | 4.258871 | 2.05E-05 | 0.001776 | 2.514347 |
| ENSG00000180817 | 1082.016 | 0.277453 | 0.064864 | 4.277437 | 1.89E-05 | 0.001779 | 2.295759 |
| ENSG00000068366 | 1187.617 | 0.260978 | 0.061449 | 4.247084 | 2.17E-05 | 0.00185  | 2.514347 |
| ENSG00000102024 | 753.0453 | 0.269489 | 0.063209 | 4.263479 | 2.01E-05 | 0.001871 | 2.295759 |
| ENSG00000005893 | 3113.607 | 0.323039 | 0.076262 | 4.235925 | 2.28E-05 | 0.001871 | 2.583187 |
| ENSG00000224531 | 1148.43  | 0.208708 | 0.049006 | 4.258831 | 2.05E-05 | 0.001916 | 2.225762 |
| ENSG00000143889 | 654.9022 | 0.156105 | 0.036696 | 4.254035 | 2.10E-05 | 0.001916 | 2.295759 |
| ENSG00000147676 | 509.977  | 0.323532 | 0.076074 | 4.252874 | 2.11E-05 | 0.001916 | 2.295759 |

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| ENSG00000213639 | 2044.897 | 0.186834 | 0.044089 | 4.237668 | 2.26E-05 | 0.001916 | 2.456745 |
| ENSG00000176953 | 387.4917 | -0.16305 | 0.038359 | -4.25063 | 2.13E-05 | 0.001957 | 2.225762 |
| ENSG00000139684 | 523.3045 | 0.232384 | 0.054674 | 4.250367 | 2.13E-05 | 0.001957 | 2.225762 |
| ENSG00000162368 | 1003.171 | 0.221678 | 0.052217 | 4.245361 | 2.18E-05 | 0.001957 | 2.293762 |
| ENSG00000121775 | 135.1546 | -0.23265 | 0.054744 | -4.24975 | 2.14E-05 | 0.001979 | 2.189833 |
| ENSG00000103978 | 399.1491 | 0.212212 | 0.049986 | 4.245397 | 2.18E-05 | 0.001979 | 2.225762 |
| ENSG00000023330 | 585.2115 | 0.222756 | 0.052617 | 4.233529 | 2.30E-05 | 0.002014 | 2.293762 |
| ENSG00000104327 | 232.363  | 0.453369 | 0.106545 | 4.255204 | 2.09E-05 | 0.002057 | 2.025126 |
| ENSG00000133703 | 822.3711 | 0.159649 | 0.037715 | 4.233076 | 2.31E-05 | 0.002057 | 2.225762 |
| ENSG00000175920 | 103.7361 | -0.51173 | 0.116866 | -4.37879 | 1.19E-05 | 0.002063 | 1.142898 |
| ENSG00000116151 | 272.569  | -0.22055 | 0.052243 | -4.22167 | 2.42E-05 | 0.002071 | 2.295759 |
| ENSG00000156642 | 2659.277 | 0.216887 | 0.05161  | 4.202399 | 2.64E-05 | 0.002071 | 2.492774 |
| ENSG00000130856 | 1010.246 | -0.11903 | 0.028223 | -4.21737 | 2.47E-05 | 0.00209  | 2.295759 |
| ENSG00000156261 | 754.0756 | 0.218627 | 0.051848 | 4.216699 | 2.48E-05 | 0.00209  | 2.293762 |
| ENSG00000116106 | 2993.512 | 0.219887 | 0.052485 | 4.189515 | 2.80E-05 | 0.002158 | 2.492774 |
| ENSG00000165678 | 2406.201 | 0.264126 | 0.063102 | 4.185688 | 2.84E-05 | 0.002164 | 2.514347 |
| ENSG00000203930 | 8975.668 | -0.46151 | 0.109782 | -4.2039  | 2.62E-05 | 0.002176 | 2.295759 |
| ENSG00000147133 | 1265.067 | -0.17585 | 0.041842 | -4.20266 | 2.64E-05 | 0.002245 | 2.225762 |
| ENSG00000106459 | 328.3592 | -0.15978 | 0.037802 | -4.22679 | 2.37E-05 | 0.002248 | 1.977088 |
| ENSG00000075415 | 3102.255 | 0.188372 | 0.044916 | 4.193866 | 2.74E-05 | 0.002248 | 2.295759 |
| ENSG00000114841 | 1408.696 | -0.32385 | 0.077282 | -4.19055 | 2.78E-05 | 0.002263 | 2.293762 |
| ENSG00000197885 | 529.0499 | 0.224446 | 0.053582 | 4.188839 | 2.80E-05 | 0.002267 | 2.295759 |
| ENSG00000131730 | 203.7718 | -0.23559 | 0.05617  | -4.19421 | 2.74E-05 | 0.002272 | 2.225762 |
| ENSG00000166987 | 243.2017 | -0.28973 | 0.069113 | -4.19214 | 2.76E-05 | 0.002282 | 2.225762 |
| ENSG00000197062 | 372.0157 | -0.18909 | 0.045123 | -4.19045 | 2.78E-05 | 0.002287 | 2.225762 |
| ENSG00000112992 | 1740.211 | 0.167062 | 0.039903 | 4.186646 | 2.83E-05 | 0.002312 | 2.225762 |
| ENSG00000114316 | 832.3448 | -0.12295 | 0.029569 | -4.15802 | 3.21E-05 | 0.002312 | 2.514347 |
| ENSG00000104731 | 518.1874 | -0.22611 | 0.054162 | -4.17477 | 2.98E-05 | 0.002343 | 2.293762 |
| ENSG00000235244 | 460.132  | -0.24489 | 0.058402 | -4.19325 | 2.75E-05 | 0.002361 | 2.025126 |
| ENSG00000147649 | 1557.4   | 0.138696 | 0.033232 | 4.173611 | 3.00E-05 | 0.002361 | 2.225762 |

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| ENSG00000072415 | 1023.596 | 0.168272 | 0.040353 | 4.169998 | 3.05E-05 | 0.002361 | 2.225762 |
| ENSG00000141425 | 1813.145 | 0.18528  | 0.04445  | 4.168271 | 3.07E-05 | 0.002361 | 2.295759 |
| ENSG00000108984 | 663.2154 | 0.199888 | 0.047993 | 4.164928 | 3.11E-05 | 0.002361 | 2.295759 |
| ENSG00000266714 | 1253.155 | -0.27318 | 0.06564  | -4.16177 | 3.16E-05 | 0.002361 | 2.293762 |
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| ENSG00000108861 | 1965.722 | 0.193471 | 0.046551 | 4.15613  | 3.24E-05 | 0.002361 | 2.456745 |
| ENSG00000164754 | 2053.9   | 0.186343 | 0.045009 | 4.140122 | 3.47E-05 | 0.002361 | 2.514347 |
| ENSG00000198898 | 1163.712 | 0.279556 | 0.067595 | 4.135766 | 3.54E-05 | 0.002361 | 2.583187 |
| ENSG00000172795 | 1236.343 | 0.191215 | 0.046243 | 4.135006 | 3.55E-05 | 0.002361 | 2.583187 |
| ENSG00000261529 | 363.2345 | -0.30246 | 0.072305 | -4.18306 | 2.88E-05 | 0.002414 | 2.025126 |
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| ENSG00000101290 | 4205.339 | 0.143927 | 0.034816 | 4.133901 | 3.57E-05 | 0.002449 | 2.456745 |
| ENSG00000164823 | 378.2155 | 0.249975 | 0.059836 | 4.177642 | 2.95E-05 | 0.002479 | 1.995423 |
| ENSG00000145681 | 58.33947 | 0.521549 | 0.120678 | 4.32184  | 1.55E-05 | 0.002511 | 1.020896 |
| ENSG00000077721 | 374.2756 | 0.190767 | 0.046065 | 4.141237 | 3.45E-05 | 0.002511 | 2.295759 |
| ENSG00000163605 | 1082.561 | 0.22368  | 0.054391 | 4.112439 | 3.92E-05 | 0.002511 | 2.583187 |
| ENSG00000215301 | 3169.293 | 0.15801  | 0.038388 | 4.116149 | 3.85E-05 | 0.002549 | 2.492774 |
| ENSG00000111203 | 268.1501 | -0.21938 | 0.052725 | -4.16085 | 3.17E-05 | 0.002591 | 1.995423 |
| ENSG00000071894 | 889.1666 | -0.26552 | 0.064318 | -4.12823 | 3.66E-05 | 0.002591 | 2.295759 |
| ENSG00000117155 | 1876.853 | 0.180965 | 0.044115 | 4.102113 | 4.09E-05 | 0.002591 | 2.583187 |
| ENSG00000116127 | 2921.057 | -0.18857 | 0.045874 | -4.11054 | 3.95E-05 | 0.002603 | 2.456745 |
| ENSG00000056097 | 2298.68  | 0.160842 | 0.039239 | 4.099027 | 4.15E-05 | 0.002662 | 2.514347 |
| ENSG00000255182 | 55.33617 | -0.41345 | 0.096373 | -4.29015 | 1.79E-05 | 0.002732 | 1.044965 |
| ENSG00000156735 | 996.6696 | 0.187785 | 0.045893 | 4.091793 | 4.28E-05 | 0.002732 | 2.514347 |
| ENSG00000180089 | 28.11927 | -0.47238 | 0.109411 | -4.31745 | 1.58E-05 | 0.002758 | 0.911386 |
| ENSG00000092841 | 1190.496 | 0.26264  | 0.063935 | 4.107888 | 3.99E-05 | 0.002758 | 2.295759 |
| ENSG00000204305 | 51.82251 | -0.37591 | 0.087622 | -4.29007 | 1.79E-05 | 0.00276  | 1.020896 |
| ENSG00000147224 | 367.3749 | 0.238455 | 0.058088 | 4.105096 | 4.04E-05 | 0.00276  | 2.295759 |
| ENSG00000167615 | 3344.154 | -0.28544 | 0.070005 | -4.07741 | 4.55E-05 | 0.00276  | 2.583187 |
| ENSG00000168286 | 155.5578 | 0.250079 | 0.060694 | 4.120337 | 3.78E-05 | 0.002792 | 2.108016 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000147041 | 123.6408 | 0.42945  | 0.104608 | 4.105341 | 4.04E-05 | 0.002792 | 2.225762 |
| ENSG00000115944 | 750.1011 | 0.230231 | 0.056173 | 4.098626 | 4.16E-05 | 0.002792 | 2.295759 |
| ENSG00000105968 | 2827.646 | 0.140284 | 0.034376 | 4.080875 | 4.49E-05 | 0.002792 | 2.492774 |
| ENSG00000129128 | 1246.725 | 0.177279 | 0.043276 | 4.096509 | 4.19E-05 | 0.002803 | 2.293762 |
| ENSG00000131507 | 3960.19  | 0.233524 | 0.057454 | 4.064578 | 4.81E-05 | 0.002844 | 2.583187 |
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| ENSG00000109466 | 1184.258 | 0.211383 | 0.051778 | 4.082494 | 4.46E-05 | 0.002893 | 2.295759 |
| ENSG00000108946 | 3857.101 | 0.231734 | 0.056986 | 4.066545 | 4.77E-05 | 0.002893 | 2.456745 |
| ENSG00000117118 | 484.8721 | 0.215112 | 0.052712 | 4.080871 | 4.49E-05 | 0.002898 | 2.29693  |
| ENSG00000143195 | 1261.969 | 0.213239 | 0.052268 | 4.079735 | 4.51E-05 | 0.002902 | 2.295759 |
| ENSG00000224430 | 222.3238 | -0.26889 | 0.06518  | -4.12542 | 3.70E-05 | 0.002917 | 1.867169 |
| ENSG00000168843 | 304.7167 | 0.368193 | 0.089767 | 4.101633 | 4.10E-05 | 0.002986 | 1.995423 |
| ENSG00000155959 | 424.1295 | 0.297826 | 0.073097 | 4.07437  | 4.61E-05 | 0.002986 | 2.225762 |
| ENSG00000124209 | 1685.085 | 0.14589  | 0.036034 | 4.048726 | 5.15E-05 | 0.002986 | 2.514347 |
| ENSG00000111726 | 561.6383 | 0.269275 | 0.06664  | 4.040764 | 5.33E-05 | 0.002986 | 2.583187 |
| ENSG00000111775 | 541.2527 | 0.290668 | 0.071939 | 4.040486 | 5.33E-05 | 0.002986 | 2.583187 |
| ENSG00000141367 | 9459.708 | 0.233697 | 0.057859 | 4.039088 | 5.37E-05 | 0.002986 | 2.583187 |
| ENSG00000234771 | 159.5865 | -0.37065 | 0.090116 | -4.11308 | 3.90E-05 | 0.002994 | 1.867169 |
| ENSG00000170270 | 62.62337 | 0.34813  | 0.082214 | 4.234444 | 2.29E-05 | 0.00307  | 1.044965 |
| ENSG00000169330 | 141.828  | 0.283815 | 0.069168 | 4.103299 | 4.07E-05 | 0.00307  | 1.867169 |
| ENSG00000178397 | 250.6856 | 0.231668 | 0.056599 | 4.093108 | 4.26E-05 | 0.00307  | 1.977088 |
| ENSG00000174013 | 618.6006 | 0.210464 | 0.051886 | 4.056305 | 4.99E-05 | 0.00307  | 2.295759 |
| ENSG00000170606 | 2002.499 | 0.233589 | 0.05784  | 4.038563 | 5.38E-05 | 0.00307  | 2.456745 |
| ENSG00000166913 | 4791.695 | 0.22705  | 0.056275 | 4.034647 | 5.47E-05 | 0.00307  | 2.492774 |
| ENSG00000251474 | 324.9842 | -0.20498 | 0.050578 | -4.0528  | 5.06E-05 | 0.003073 | 2.295759 |
| ENSG00000144535 | 586.8259 | -0.1818  | 0.04522  | -4.02025 | 5.81E-05 | 0.003125 | 2.583187 |
| ENSG00000174695 | 1117.919 | 0.193439 | 0.047796 | 4.047167 | 5.18E-05 | 0.003127 | 2.293762 |

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| ENSG00000137040 | 769.413  | 0.243779 | 0.060251 | 4.046019 | 5.21E-05 | 0.003131 | 2.293762 |
| ENSG00000197956 | 510.6223 | 0.340978 | 0.084149 | 4.05208  | 5.08E-05 | 0.003132 | 2.225762 |
| ENSG00000117906 | 745.2869 | 0.195337 | 0.048311 | 4.043342 | 5.27E-05 | 0.003142 | 2.293762 |
| ENSG00000104290 | 2313.672 | 0.171804 | 0.042501 | 4.042328 | 5.29E-05 | 0.003142 | 2.295759 |
| ENSG00000088808 | 945.4137 | -0.14412 | 0.035908 | -4.01365 | 5.98E-05 | 0.003143 | 2.583187 |
| ENSG00000133731 | 543.9388 | 0.22794  | 0.056317 | 4.047421 | 5.18E-05 | 0.003148 | 2.225762 |
| ENSG00000169021 | 532.0929 | 0.281245 | 0.070176 | 4.007728 | 6.13E-05 | 0.00319  | 2.583187 |
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| ENSG00000196810 | 276.2497 | -0.17382 | 0.042752 | -4.06582 | 4.79E-05 | 0.003204 | 1.995423 |
| ENSG00000145817 | 421.2609 | 0.201004 | 0.049865 | 4.030938 | 5.56E-05 | 0.003204 | 2.295759 |
| ENSG00000155097 | 2860.051 | 0.209076 | 0.052115 | 4.01183  | 6.02E-05 | 0.003204 | 2.492774 |
| ENSG00000138757 | 2986.309 | 0.233664 | 0.058358 | 4.00399  | 6.23E-05 | 0.003204 | 2.583187 |
| ENSG00000176472 | 42.64008 | -0.35873 | 0.085207 | -4.2101  | 2.55E-05 | 0.003223 | 1.044965 |
| ENSG00000108468 | 622.7843 | 0.14608  | 0.036208 | 4.03447  | 5.47E-05 | 0.003227 | 2.225762 |
| ENSG00000146731 | 1012.825 | 0.189857 | 0.047147 | 4.026951 | 5.65E-05 | 0.003227 | 2.293762 |
| ENSG00000137166 | 334.8341 | -0.32245 | 0.079526 | -4.05463 | 5.02E-05 | 0.003237 | 2.025126 |
| ENSG00000186298 | 854.7299 | 0.216366 | 0.053679 | 4.030762 | 5.56E-05 | 0.003249 | 2.225762 |
| ENSG00000168386 | 325.8293 | 0.29699  | 0.07334  | 4.049487 | 5.13E-05 | 0.003262 | 2.025126 |
| ENSG00000138069 | 892.3629 | 0.157238 | 0.039375 | 3.993376 | 6.51E-05 | 0.003262 | 2.583187 |
| ENSG00000091656 | 941.5625 | -0.22339 | 0.055952 | -3.9926  | 6.54E-05 | 0.003262 | 2.583187 |
| ENSG00000128595 | 769.3107 | 0.198275 | 0.049341 | 4.018487 | 5.86E-05 | 0.003275 | 2.293762 |
| ENSG00000185900 | 1674.778 | 0.139859 | 0.034822 | 4.016362 | 5.91E-05 | 0.003291 | 2.295759 |
| ENSG00000136143 | 859.8065 | 0.277716 | 0.06907  | 4.020781 | 5.80E-05 | 0.003308 | 2.225762 |
| ENSG00000184277 | 625.8636 | 0.206768 | 0.051513 | 4.01389  | 5.97E-05 | 0.003308 | 2.295759 |
| ENSG00000125347 | 265.8363 | -0.27128 | 0.067112 | -4.04213 | 5.30E-05 | 0.003353 | 1.995423 |
| ENSG00000163913 | 614.8758 | -0.15622 | 0.039244 | -3.98074 | 6.87E-05 | 0.003353 | 2.583187 |
| ENSG00000260412 | 242.5287 | 0.331408 | 0.081992 | 4.041957 | 5.30E-05 | 0.003357 | 1.977088 |
| ENSG00000138698 | 1296.506 | 0.268521 | 0.067481 | 3.97919  | 6.92E-05 | 0.003357 | 2.583187 |
| ENSG00000116586 | 133.1525 | 0.246463 | 0.061255 | 4.023581 | 5.73E-05 | 0.003394 | 2.108016 |
| ENSG00000197363 | 282.6219 | -0.23944 | 0.059763 | -4.00647 | 6.16E-05 | 0.003421 | 2.225762 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000115762 | 2499.432 | 0.199615 | 0.05011  | 3.983537 | 6.79E-05 | 0.003421 | 2.456745 |
| ENSG00000101079 | 1936.273 | 0.249421 | 0.06266  | 3.980558 | 6.88E-05 | 0.003421 | 2.492774 |
| ENSG00000184923 | 59.5848  | -0.55043 | 0.131627 | -4.18176 | 2.89E-05 | 0.003446 | 1.023066 |
| ENSG00000144227 | 72.91984 | 0.523796 | 0.128842 | 4.065413 | 4.79E-05 | 0.003446 | 1.695647 |
| ENSG00000120645 | 1605.363 | -0.2804  | 0.070037 | -4.00361 | 6.24E-05 | 0.003446 | 2.225762 |
| ENSG00000114098 | 908.626  | 0.126184 | 0.031563 | 3.997807 | 6.39E-05 | 0.003446 | 2.225762 |
| ENSG00000196104 | 1085.698 | 0.335226 | 0.083893 | 3.995848 | 6.45E-05 | 0.003446 | 2.295759 |
| ENSG00000144827 | 495.149  | 0.216406 | 0.054228 | 3.990638 | 6.59E-05 | 0.003446 | 2.293762 |
| ENSG00000137409 | 3497.57  | 0.184455 | 0.04645  | 3.971063 | 7.16E-05 | 0.003446 | 2.514347 |
| ENSG00000118200 | 3852.292 | 0.144188 | 0.036315 | 3.970445 | 7.17E-05 | 0.003446 | 2.514347 |
| ENSG00000253719 | 2027.24  | 0.182295 | 0.045932 | 3.968833 | 7.22E-05 | 0.003446 | 2.514347 |
| ENSG00000164885 | 322.9828 | 0.269617 | 0.067588 | 3.989122 | 6.63E-05 | 0.003453 | 2.295759 |
| ENSG00000183978 | 273.3314 | 0.231329 | 0.058011 | 3.987666 | 6.67E-05 | 0.003464 | 2.295759 |
| ENSG00000070367 | 1373.586 | 0.136478 | 0.034179 | 3.993062 | 6.52E-05 | 0.003481 | 2.225762 |
| ENSG00000245248 | 91.95635 | -0.40626 | 0.098266 | -4.13432 | 3.56E-05 | 0.003496 | 1.182918 |
| ENSG00000050130 | 399.6782 | 0.212134 | 0.053283 | 3.981252 | 6.86E-05 | 0.003496 | 2.295759 |
| ENSG00000131398 | 947.8308 | -0.42838 | 0.107609 | -3.98087 | 6.87E-05 | 0.003496 | 2.295759 |
| ENSG00000015532 | 439.7108 | -0.18012 | 0.045262 | -3.97952 | 6.91E-05 | 0.003496 | 2.295759 |
| ENSG00000092148 | 3683.522 | 0.13078  | 0.032978 | 3.965633 | 7.32E-05 | 0.003496 | 2.456745 |
| ENSG00000112697 | 2870.565 | 0.164796 | 0.041579 | 3.963416 | 7.39E-05 | 0.003496 | 2.456745 |
| ENSG00000072657 | 837.5739 | 0.24768  | 0.062541 | 3.960249 | 7.49E-05 | 0.003496 | 2.514347 |
| ENSG00000113328 | 414.9993 | 0.237336 | 0.05916  | 4.011776 | 6.03E-05 | 0.003497 | 1.995423 |
| ENSG00000131697 | 634.022  | -0.21491 | 0.053933 | -3.98478 | 6.75E-05 | 0.003503 | 2.225762 |
| ENSG00000163964 | 340.5448 | 0.192558 | 0.04814  | 3.999945 | 6.34E-05 | 0.003589 | 2.025126 |
| ENSG00000109572 | 2333.27  | 0.17815  | 0.044865 | 3.970803 | 7.16E-05 | 0.003589 | 2.295759 |
| ENSG00000109158 | 1982.174 | 0.233386 | 0.059114 | 3.94806  | 7.88E-05 | 0.003615 | 2.492774 |
| ENSG00000100916 | 194.2834 | 0.23416  | 0.059043 | 3.965901 | 7.31E-05 | 0.003618 | 2.295759 |
| ENSG00000109971 | 13196.12 | 0.265413 | 0.067268 | 3.945614 | 7.96E-05 | 0.003618 | 2.492774 |
| ENSG00000129473 | 1750.933 | 0.161561 | 0.040965 | 3.943872 | 8.02E-05 | 0.003618 | 2.514347 |
| ENSG00000130590 | 92.80163 | -0.28429 | 0.06887  | -4.12786 | 3.66E-05 | 0.003629 | 1.136415 |

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| ENSG00000135387 | 2557.73  | 0.143646 | 0.036246 | 3.963143 | 7.40E-05 | 0.003629 | 2.295759 |
| ENSG00000132463 | 1400.93  | 0.153908 | 0.038851 | 3.961485 | 7.45E-05 | 0.003642 | 2.295759 |
| ENSG00000156467 | 1571.821 | 0.238937 | 0.060332 | 3.960387 | 7.48E-05 | 0.003642 | 2.295759 |
| ENSG00000122550 | 582.6146 | 0.151032 | 0.038146 | 3.959323 | 7.52E-05 | 0.003642 | 2.29693  |
| ENSG00000065559 | 2015.556 | 0.241482 | 0.061241 | 3.943159 | 8.04E-05 | 0.003642 | 2.456745 |
| ENSG00000234841 | 79.54185 | -0.33451 | 0.081399 | -4.10958 | 3.96E-05 | 0.003659 | 1.201846 |
| ENSG00000112996 | 1541.717 | 0.164948 | 0.041917 | 3.935077 | 8.32E-05 | 0.003659 | 2.514347 |
| ENSG00000175175 | 758.5276 | 0.2265   | 0.05757  | 3.934342 | 8.34E-05 | 0.003659 | 2.514347 |
| ENSG00000163541 | 525.3773 | 0.217084 | 0.054891 | 3.954824 | 7.66E-05 | 0.003671 | 2.293762 |
| ENSG00000065518 | 451.7737 | 0.234056 | 0.058752 | 3.983806 | 6.78E-05 | 0.003693 | 1.995423 |
| ENSG00000114999 | 1363.608 | 0.145858 | 0.036901 | 3.952693 | 7.73E-05 | 0.003693 | 2.293762 |
| ENSG00000180616 | 619.5128 | 0.283617 | 0.071787 | 3.950789 | 7.79E-05 | 0.003693 | 2.29693  |
| ENSG00000135002 | 536.4034 | 0.265309 | 0.067157 | 3.950595 | 7.80E-05 | 0.003693 | 2.295759 |
| ENSG00000183723 | 2430.915 | 0.167948 | 0.042833 | 3.921004 | 8.82E-05 | 0.003698 | 2.583187 |
| ENSG00000151135 | 357.9559 | 0.230034 | 0.057681 | 3.988055 | 6.66E-05 | 0.003701 | 1.918337 |
| ENSG00000184613 | 3551.456 | 0.298815 | 0.075708 | 3.946953 | 7.92E-05 | 0.003701 | 2.295759 |
| ENSG00000005249 | 1134.279 | 0.204265 | 0.051754 | 3.946886 | 7.92E-05 | 0.003701 | 2.293762 |
| ENSG00000149196 | 224.2876 | 0.208874 | 0.052944 | 3.945215 | 7.97E-05 | 0.003701 | 2.295759 |
| ENSG00000115419 | 3972.303 | 0.228094 | 0.0581   | 3.925904 | 8.64E-05 | 0.003701 | 2.492774 |
| ENSG00000197746 | 11666.22 | 0.193709 | 0.049458 | 3.916627 | 8.98E-05 | 0.003701 | 2.583187 |
| ENSG00000164983 | 720.4739 | 0.189858 | 0.048055 | 3.950837 | 7.79E-05 | 0.003711 | 2.225762 |
| ENSG00000109332 | 2648.828 | 0.153831 | 0.039297 | 3.914551 | 9.06E-05 | 0.003711 | 2.583187 |
| ENSG00000164603 | 266.8207 | 0.226873 | 0.057143 | 3.970242 | 7.18E-05 | 0.003724 | 2.025126 |
| ENSG00000166266 | 940.139  | 0.182153 | 0.046145 | 3.947389 | 7.90E-05 | 0.003724 | 2.225762 |
| ENSG00000174460 | 240.527  | 0.489478 | 0.12422  | 3.940411 | 8.13E-05 | 0.003724 | 2.295759 |
| ENSG00000164172 | 636.3239 | 0.237069 | 0.06018  | 3.93935  | 8.17E-05 | 0.003724 | 2.295759 |
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| ENSG00000101856 | 1041.355 | 0.278135 | 0.070667 | 3.935877 | 8.29E-05 | 0.003761 | 2.293762 |
| ENSG00000228274 | 74.06458 | -0.26518 | 0.066188 | -4.00645 | 6.16E-05 | 0.003762 | 1.695647 |
| ENSG00000100554 | 1168.134 | 0.224776 | 0.05754  | 3.906404 | 9.37E-05 | 0.003762 | 2.583187 |

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| ENSG00000142168 | 1970.887 | 0.225799 | 0.057448 | 3.930461 | 8.48E-05 | 0.003811 | 2.295759 |
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| ENSG00000211456 | 813.9484 | 0.165341 | 0.042334 | 3.905623 | 9.40E-05 | 0.003811 | 2.514347 |
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| ENSG00000122873 | 449.8242 | 0.269013 | 0.068003 | 3.955916 | 7.62E-05 | 0.003864 | 1.995423 |
| ENSG00000166073 | 407.5743 | 0.223847 | 0.057073 | 3.922087 | 8.78E-05 | 0.003864 | 2.295759 |
| ENSG00000163527 | 990.2214 | 0.171586 | 0.04375  | 3.921983 | 8.78E-05 | 0.003864 | 2.293762 |
| ENSG00000170091 | 1843.31  | 0.267062 | 0.068518 | 3.897713 | 9.71E-05 | 0.003886 | 2.514347 |
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| ENSG00000003096 | 96.0184  | 0.353702 | 0.086683 | 4.080405 | 4.50E-05 | 0.003949 | 1.136415 |
| ENSG00000078668 | 1076.964 | 0.24259  | 0.061873 | 3.920757 | 8.83E-05 | 0.003949 | 2.225762 |
| ENSG00000165943 | 2313.112 | 0.260694 | 0.067143 | 3.882652 | 0.000103 | 0.003972 | 2.583187 |
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| ENSG00000096384 | 10033.9  | 0.245754 | 0.062936 | 3.90484  | 9.43E-05 | 0.004044 | 2.295759 |
| ENSG00000105643 | 593.9657 | 0.316329 | 0.081021 | 3.904279 | 9.45E-05 | 0.004044 | 2.295759 |
| ENSG00000143222 | 297.2898 | 0.229684 | 0.058763 | 3.908639 | 9.28E-05 | 0.004086 | 2.225762 |
| ENSG00000175164 | 45.18917 | -0.51456 | 0.126012 | -4.08343 | 4.44E-05 | 0.004091 | 1.044965 |
| ENSG00000161896 | 115.2135 | 0.636817 | 0.163626 | 3.891902 | 9.95E-05 | 0.004091 | 2.338927 |
| ENSG00000118058 | 4061.709 | -0.12415 | 0.031995 | -3.88037 | 0.000104 | 0.004091 | 2.456745 |
| ENSG00000134308 | 2552.793 | 0.19357  | 0.049899 | 3.879253 | 0.000105 | 0.004091 | 2.492774 |
| ENSG00000067992 | 2676.834 | 0.217089 | 0.056008 | 3.876048 | 0.000106 | 0.004091 | 2.514347 |
| ENSG00000170871 | 2060.609 | 0.131071 | 0.033818 | 3.875783 | 0.000106 | 0.004091 | 2.514347 |
| ENSG00000084733 | 1379.422 | 0.14749  | 0.038117 | 3.86935  | 0.000109 | 0.004091 | 2.583187 |
| ENSG00000006715 | 1774.382 | 0.156428 | 0.040464 | 3.865846 | 0.000111 | 0.004112 | 2.583187 |
| ENSG00000067601 | 81.13136 | -0.31536 | 0.077846 | -4.0511  | 5.10E-05 | 0.004114 | 1.182918 |
| ENSG00000114744 | 325.1453 | 0.173901 | 0.044581 | 3.900815 | 9.59E-05 | 0.004114 | 2.225762 |

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| ENSG00000179082 | 24.78549 | -0.6784  | 0.166461 | -4.07539 | 4.59E-05 | 0.004114 | 1.053218 |
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| ENSG00000006071 | 1452.205 | -0.21385 | 0.054971 | -3.89024 | 0.0001   | 0.004114 | 2.293762 |
| ENSG00000152932 | 3987.162 | 0.365307 | 0.09438  | 3.870605 | 0.000109 | 0.004114 | 2.492774 |
| ENSG00000083099 | 475.2291 | 0.166297 | 0.043063 | 3.861687 | 0.000113 | 0.004114 | 2.583187 |
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| ENSG00000017260 | 1758.071 | 0.156734 | 0.040593 | 3.861091 | 0.000113 | 0.004171 | 2.514347 |
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| ENSG00000259067 | 5.147643 | -1.11673 | 0.24002  | -4.65268 | 3.28E-06 | 0.00419  | 0.071665 |
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| ENSG00000135636 | 726.819  | -0.28539 | 0.074001 | -3.85652 | 0.000115 | 0.00419  | 2.514347 |
| ENSG00000129084 | 125.3241 | 0.240377 | 0.061676 | 3.897415 | 9.72E-05 | 0.004207 | 2.108016 |
| ENSG00000143442 | 2083.397 | -0.14093 | 0.036576 | -3.85303 | 0.000117 | 0.004222 | 2.514347 |
| ENSG00000174684 | 1865.785 | 0.227703 | 0.059108 | 3.8523   | 0.000117 | 0.004261 | 2.492774 |
| ENSG00000141279 | 1491.591 | 0.13508  | 0.0349   | 3.870483 | 0.000109 | 0.004284 | 2.295759 |
| ENSG00000226419 | 304.0973 | -0.20648 | 0.053301 | -3.87392 | 0.000107 | 0.004344 | 2.225762 |
| ENSG00000196937 | 611.4421 | 0.259485 | 0.067627 | 3.836984 | 0.000125 | 0.004344 | 2.583187 |
| ENSG00000009307 | 4857.41  | 0.156677 | 0.040842 | 3.836162 | 0.000125 | 0.004348 | 2.583187 |
| ENSG00000142609 | 198.7433 | -0.32925 | 0.084576 | -3.89292 | 9.90E-05 | 0.004351 | 2.025126 |
| ENSG00000117598 | 224.3327 | 0.231841 | 0.059922 | 3.86908  | 0.000109 | 0.004351 | 2.225762 |
| ENSG00000083799 | 1748.068 | 0.139107 | 0.035954 | 3.869067 | 0.000109 | 0.004351 | 2.225762 |
| ENSG00000106993 | 402.1971 | 0.193467 | 0.050097 | 3.861857 | 0.000113 | 0.004351 | 2.295759 |
| ENSG00000125304 | 1164.129 | 0.210749 | 0.054582 | 3.861151 | 0.000113 | 0.004351 | 2.295759 |
| ENSG00000232406 | 158.416  | -0.26195 | 0.067921 | -3.85674 | 0.000115 | 0.004351 | 2.338927 |

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| ENSG00000125848 | 479.482  | 0.241055 | 0.062909 | 3.831839 | 0.000127 | 0.004351 | 2.583187 |
| ENSG00000215712 | 346.8737 | 0.175552 | 0.045404 | 3.866399 | 0.00011  | 0.004365 | 2.225762 |
| ENSG00000018510 | 784.04   | 0.16677  | 0.043213 | 3.859232 | 0.000114 | 0.004365 | 2.295759 |
| ENSG00000176871 | 2169.774 | 0.16159  | 0.042125 | 3.835967 | 0.000125 | 0.004365 | 2.514347 |
| ENSG00000136021 | 769.3457 | 0.143687 | 0.03718  | 3.864635 | 0.000111 | 0.004374 | 2.225762 |
| ENSG00000148925 | 1145.43  | 0.209454 | 0.054311 | 3.856605 | 0.000115 | 0.004374 | 2.295759 |
| ENSG00000150753 | 663.9041 | 0.220884 | 0.057292 | 3.855367 | 0.000116 | 0.004385 | 2.295759 |
| ENSG00000107798 | 700.2653 | 0.31676  | 0.082197 | 3.853653 | 0.000116 | 0.004389 | 2.295759 |
| ENSG00000182013 | 2596.296 | 0.204331 | 0.053304 | 3.833329 | 0.000126 | 0.004389 | 2.492774 |
| ENSG00000172667 | 2303.513 | 0.1723   | 0.044949 | 3.833263 | 0.000126 | 0.004389 | 2.492774 |
| ENSG00000161010 | 463.8658 | -0.18407 | 0.047419 | -3.88168 | 0.000104 | 0.004391 | 2.025126 |
| ENSG00000177879 | 467.3934 | 0.203554 | 0.052745 | 3.859191 | 0.000114 | 0.004391 | 2.225762 |
| ENSG00000095139 | 1275.743 | 0.140263 | 0.036688 | 3.823106 | 0.000132 | 0.004391 | 2.583187 |
| ENSG00000106537 | 705.7754 | 0.240853 | 0.063011 | 3.822404 | 0.000132 | 0.004391 | 2.583187 |
| ENSG00000101190 | 441.5333 | -0.27349 | 0.070901 | -3.85736 | 0.000115 | 0.004403 | 2.225762 |
| ENSG00000175582 | 2833.934 | 0.218442 | 0.057056 | 3.828568 | 0.000129 | 0.004411 | 2.492774 |
| ENSG00000108960 | 623.4419 | 0.308017 | 0.07995  | 3.852621 | 0.000117 | 0.004446 | 2.225762 |
| ENSG00000213199 | 163.867  | -0.29957 | 0.077771 | -3.85198 | 0.000117 | 0.004446 | 2.225762 |
| ENSG00000168036 | 3628.186 | 0.165259 | 0.042969 | 3.846025 | 0.00012  | 0.004446 | 2.295759 |
| ENSG00000136279 | 1669.716 | -0.12486 | 0.032469 | -3.84537 | 0.00012  | 0.004446 | 2.293762 |
| ENSG00000167595 | 137.9763 | -0.27964 | 0.072833 | -3.83948 | 0.000123 | 0.004446 | 2.338927 |
| ENSG00000196912 | 849.0807 | -0.29612 | 0.076955 | -3.84792 | 0.000119 | 0.004504 | 2.225762 |
| ENSG00000177302 | 578.8633 | -0.1381  | 0.03625  | -3.80954 | 0.000139 | 0.004525 | 2.583187 |
| ENSG00000178381 | 192.1313 | 0.219693 | 0.056524 | 3.886731 | 0.000102 | 0.004558 | 1.867169 |
| ENSG00000272578 | 59.81894 | -0.31339 | 0.07783  | -4.02656 | 5.66E-05 | 0.004622 | 1.020896 |
| ENSG00000187792 | 265.8979 | -0.23631 | 0.061183 | -3.86234 | 0.000112 | 0.004622 | 2.025126 |
| ENSG00000070961 | 7225.587 | 0.231258 | 0.060824 | 3.802068 | 0.000143 | 0.004622 | 2.583187 |
| ENSG00000132964 | 298.8897 | 0.1636   | 0.042413 | 3.857286 | 0.000115 | 0.004699 | 2.025126 |
| ENSG00000169567 | 1081.47  | 0.23824  | 0.062265 | 3.826204 | 0.00013  | 0.004699 | 2.293762 |
| ENSG00000246922 | 992.2473 | -0.22425 | 0.058539 | -3.83077 | 0.000128 | 0.004743 | 2.225762 |

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| ENSG00000025800 | 1709.22  | 0.128291 | 0.033767 | 3.799261 | 0.000145 | 0.004759 | 2.514347 |
| ENSG00000198843 | 1147.15  | 0.199559 | 0.052655 | 3.789965 | 0.000151 | 0.004799 | 2.583187 |
| ENSG00000114686 | 345.7839 | 0.282114 | 0.07323  | 3.852431 | 0.000117 | 0.004799 | 1.995423 |
| ENSG00000169490 | 289.9024 | 0.212921 | 0.055328 | 3.848351 | 0.000119 | 0.004799 | 2.025126 |
| ENSG00000116661 | 911.1405 | 0.272359 | 0.071891 | 3.788499 | 0.000152 | 0.004799 | 2.583187 |
| ENSG00000124299 | 407.3335 | 0.191166 | 0.049516 | 3.86072  | 0.000113 | 0.0048   | 1.918337 |
| ENSG00000178951 | 1570.711 | -0.21369 | 0.056327 | -3.7938  | 0.000148 | 0.0048   | 2.514347 |
| ENSG00000186106 | 850.4619 | 0.188316 | 0.049644 | 3.793323 | 0.000149 | 0.0048   | 2.514347 |
| ENSG00000135829 | 1618.433 | 0.147779 | 0.038751 | 3.81355  | 0.000137 | 0.004838 | 2.293762 |
| ENSG00000271717 | 20.4537  | -0.54898 | 0.132906 | -4.13059 | 3.62E-05 | 0.004975 | 0.583933 |
| ENSG00000137337 | 437.4951 | -0.19218 | 0.050068 | -3.8383  | 0.000124 | 0.004975 | 1.995423 |
| ENSG00000198380 | 894.9733 | 0.144045 | 0.037854 | 3.805275 | 0.000142 | 0.004975 | 2.293762 |
| ENSG00000166501 | 7413.639 | 0.226574 | 0.059878 | 3.783894 | 0.000154 | 0.004975 | 2.492774 |
| ENSG00000165280 | 2053.263 | 0.121464 | 0.032115 | 3.782147 | 0.000155 | 0.004975 | 2.514347 |
| ENSG00000259834 | 135.1272 | 0.343452 | 0.090193 | 3.807983 | 0.00014  | 0.005033 | 2.225762 |
| ENSG00000152495 | 1816.412 | 0.256786 | 0.067989 | 3.776887 | 0.000159 | 0.005039 | 2.514347 |
| ENSG00000277200 | 242.9088 | -0.25215 | 0.066396 | -3.79767 | 0.000146 | 0.005065 | 2.295759 |
| ENSG00000135018 | 2471.143 | 0.144052 | 0.038112 | 3.779729 | 0.000157 | 0.005077 | 2.456745 |
| ENSG00000153933 | 972.6615 | 0.14929  | 0.039401 | 3.788982 | 0.000151 | 0.005213 | 2.295759 |
| ENSG00000178502 | 828.4717 | 0.171141 | 0.045522 | 3.759513 | 0.00017  | 0.005213 | 2.583187 |
| ENSG00000197894 | 726.7844 | 0.202582 | 0.053532 | 3.784336 | 0.000154 | 0.005299 | 2.295759 |
| ENSG00000188312 | 113.1456 | -0.21593 | 0.057148 | -3.77841 | 0.000158 | 0.005315 | 2.338927 |
| ENSG00000198258 | 390.5741 | 0.240052 | 0.062989 | 3.811036 | 0.000138 | 0.005429 | 1.995423 |
| ENSG00000154511 | 525.9508 | 0.238421 | 0.063138 | 3.776189 | 0.000159 | 0.005429 | 2.295759 |
| ENSG00000077264 | 2661.34  | 0.221715 | 0.058975 | 3.759465 | 0.00017  | 0.005429 | 2.456745 |
| ENSG00000115520 | 315.9918 | 0.191437 | 0.050602 | 3.783174 | 0.000155 | 0.005433 | 2.225762 |
| ENSG00000156411 | 591.3382 | 0.261319 | 0.069229 | 3.774713 | 0.00016  | 0.005438 | 2.295759 |
| ENSG00000147123 | 365.023  | 0.196964 | 0.052198 | 3.773411 | 0.000161 | 0.005455 | 2.295759 |
| ENSG00000085433 | 2081.313 | 0.212284 | 0.056585 | 3.751587 | 0.000176 | 0.005471 | 2.492774 |
| ENSG00000081307 | 775.0317 | 0.139289 | 0.036932 | 3.771543 | 0.000162 | 0.005473 | 2.295759 |

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| ENSG00000077147 | 1652.034 | 0.163474 | 0.043698 | 3.740983 | 0.000183 | 0.005484 | 2.583187 |
| ENSG00000115947 | 725.9221 | 0.180813 | 0.047973 | 3.769038 | 0.000164 | 0.005501 | 2.293762 |
| ENSG00000205269 | 1497.904 | 0.169792 | 0.04541  | 3.739133 | 0.000185 | 0.005501 | 2.583187 |
| ENSG00000119772 | 1383.937 | -0.17032 | 0.045486 | -3.74451 | 0.000181 | 0.00551  | 2.514347 |
| ENSG00000181852 | 1123.372 | 0.162925 | 0.043511 | 3.744463 | 0.000181 | 0.00551  | 2.514347 |
| ENSG00000197713 | 632.5667 | 0.175142 | 0.046501 | 3.766386 | 0.000166 | 0.005515 | 2.29693  |
| ENSG00000273611 | 255.5211 | 0.172096 | 0.045618 | 3.772565 | 0.000162 | 0.005541 | 2.225762 |
| ENSG00000111237 | 330.6016 | 0.191007 | 0.050307 | 3.79681  | 0.000147 | 0.005541 | 1.995423 |
| ENSG00000145907 | 1333.379 | 0.126171 | 0.033526 | 3.763359 | 0.000168 | 0.005541 | 2.293762 |
| ENSG00000151806 | 570.8456 | 0.161631 | 0.042957 | 3.762657 | 0.000168 | 0.005541 | 2.295759 |
| ENSG00000133059 | 1392.136 | 0.136253 | 0.036218 | 3.761984 | 0.000169 | 0.005541 | 2.293762 |
| ENSG00000213585 | 1658.976 | 0.225017 | 0.059817 | 3.761746 | 0.000169 | 0.005541 | 2.295759 |
| ENSG00000189241 | 3797.953 | 0.169667 | 0.045346 | 3.741574 | 0.000183 | 0.005541 | 2.492774 |
| ENSG00000132694 | 2603.783 | -0.11492 | 0.030745 | -3.73771 | 0.000186 | 0.005557 | 2.514347 |
| ENSG00000152234 | 4261.024 | 0.247415 | 0.066249 | 3.734614 | 0.000188 | 0.005614 | 2.514347 |
| ENSG00000153814 | 409.6317 | 0.209513 | 0.055311 | 3.787931 | 0.000152 | 0.005621 | 2.025126 |
| ENSG00000114626 | 687.2168 | -0.22689 | 0.060298 | -3.76275 | 0.000168 | 0.005621 | 2.225762 |
| ENSG00000042753 | 442.7651 | 0.241659 | 0.064231 | 3.762358 | 0.000168 | 0.005621 | 2.225762 |
| ENSG00000057608 | 1340.623 | 0.199249 | 0.053057 | 3.755382 | 0.000173 | 0.005621 | 2.295759 |
| ENSG00000116161 | 1019.885 | 0.248057 | 0.066055 | 3.75531  | 0.000173 | 0.005621 | 2.295759 |
| ENSG00000284707 | 131.354  | -0.23607 | 0.062076 | -3.80284 | 0.000143 | 0.005627 | 1.867169 |
| ENSG00000162086 | 368.6047 | -0.16877 | 0.044968 | -3.75303 | 0.000175 | 0.005627 | 2.295759 |
| ENSG00000214176 | 604.2358 | -0.20539 | 0.054749 | -3.75151 | 0.000176 | 0.005627 | 2.29693  |
| ENSG00000198689 | 1817.621 | 0.228946 | 0.061309 | 3.734316 | 0.000188 | 0.005627 | 2.456745 |
| ENSG00000168016 | 1976.43  | -0.28063 | 0.07523  | -3.73033 | 0.000191 | 0.005627 | 2.514347 |
| ENSG00000174672 | 1551.782 | -0.20068 | 0.053916 | -3.72202 | 0.000198 | 0.005627 | 2.583187 |
| ENSG00000196498 | 3173.422 | -0.27789 | 0.074436 | -3.73326 | 0.000189 | 0.005639 | 2.456745 |
| ENSG00000171045 | 425.7856 | -0.23793 | 0.062864 | -3.7848  | 0.000154 | 0.005639 | 1.995423 |
| ENSG00000167608 | 59.92477 | -0.38231 | 0.096864 | -3.94692 | 7.92E-05 | 0.005649 | 1.023066 |
| ENSG00000144744 | 452.2007 | 0.187838 | 0.04952  | 3.793178 | 0.000149 | 0.005649 | 1.918337 |

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| ENSG00000134375 | 397.0334 | 0.259612 | 0.06875  | 3.776164 | 0.000159 | 0.005663 | 2.025126 |
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| ENSG00000066923 | 549.3864 | -0.20104 | 0.053566 | -3.75322 | 0.000175 | 0.005663 | 2.225762 |
| ENSG00000110274 | 836.2831 | -0.17607 | 0.046914 | -3.75297 | 0.000175 | 0.005663 | 2.225762 |
| ENSG00000084623 | 649.3114 | 0.152984 | 0.040851 | 3.744886 | 0.00018  | 0.005663 | 2.29693  |
| ENSG00000073921 | 2778.206 | 0.121623 | 0.032615 | 3.729093 | 0.000192 | 0.005663 | 2.456745 |
| ENSG00000134779 | 912.2432 | 0.136642 | 0.036425 | 3.751364 | 0.000176 | 0.005668 | 2.225762 |
| ENSG00000188419 | 867.2136 | 0.159326 | 0.04282  | 3.720838 | 0.000199 | 0.005668 | 2.514347 |
| ENSG00000161021 | 667.9111 | -0.20096 | 0.053727 | -3.74039 | 0.000184 | 0.00573  | 2.295759 |
| ENSG00000113552 | 385.5477 | 0.165726 | 0.043919 | 3.773428 | 0.000161 | 0.005744 | 1.995423 |
| ENSG00000112695 | 586.711  | 0.322265 | 0.086201 | 3.73854  | 0.000185 | 0.005744 | 2.29693  |
| ENSG00000090487 | 370.1046 | 0.155072 | 0.041482 | 3.738285 | 0.000185 | 0.005744 | 2.295759 |
| ENSG00000143158 | 507.3677 | 0.238455 | 0.063797 | 3.737735 | 0.000186 | 0.005751 | 2.293762 |
| ENSG00000127957 | 164.6539 | -0.20222 | 0.053663 | -3.76835 | 0.000164 | 0.005811 | 1.995423 |
| ENSG00000172663 | 149.4264 | -0.21652 | 0.057659 | -3.75508 | 0.000173 | 0.005811 | 2.108016 |
| ENSG00000164309 | 818.4288 | -0.28265 | 0.075556 | -3.74091 | 0.000183 | 0.005811 | 2.225762 |
| ENSG00000113407 | 507.7434 | 0.201196 | 0.053785 | 3.740769 | 0.000183 | 0.005811 | 2.225762 |
| ENSG00000135900 | 172.3078 | 0.18535  | 0.049203 | 3.76708  | 0.000165 | 0.005824 | 1.995423 |
| ENSG00000120438 | 1187.455 | 0.213147 | 0.057125 | 3.731206 | 0.000191 | 0.00583  | 2.295759 |
| ENSG00000092108 | 981.8342 | 0.149346 | 0.039959 | 3.737525 | 0.000186 | 0.005853 | 2.225762 |
| ENSG00000101843 | 345.7449 | 0.204466 | 0.054717 | 3.736757 | 0.000186 | 0.00586  | 2.225762 |
| ENSG00000160908 | 327.7955 | -0.14409 | 0.038269 | -3.76517 | 0.000166 | 0.005879 | 1.977088 |
| ENSG00000177054 | 220.5271 | 0.200188 | 0.053261 | 3.758636 | 0.000171 | 0.005935 | 1.995423 |
| ENSG00000163590 | 2568.476 | 0.161856 | 0.043471 | 3.723362 | 0.000197 | 0.005935 | 2.295759 |
| ENSG00000072803 | 1903.375 | 0.13831  | 0.037352 | 3.702898 | 0.000213 | 0.005935 | 2.492774 |
| ENSG00000158321 | 1286.215 | -0.15757 | 0.042658 | -3.69371 | 0.000221 | 0.005935 | 2.583187 |
| ENSG00000070718 | 1011.776 | 0.191625 | 0.051894 | 3.692645 | 0.000222 | 0.005943 | 2.583187 |
| ENSG00000140650 | 326.7273 | -0.20258 | 0.05432  | -3.72939 | 0.000192 | 0.005955 | 2.225762 |
| ENSG00000143727 | 558.119  | 0.193034 | 0.05177  | 3.728668 | 0.000192 | 0.005961 | 2.225762 |
| ENSG00000116406 | 978.9497 | 0.165495 | 0.044844 | 3.690431 | 0.000224 | 0.005962 | 2.583187 |



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| ENSG00000089289 | 298.3617 | 0.177254 | 0.047262 | 3.750456 | 0.000177 | 0.005985 | 2.025126 |
| ENSG00000055483 | 714.7057 | -0.1957  | 0.052529 | -3.72551 | 0.000195 | 0.006002 | 2.225762 |
| ENSG00000118094 | 132.7192 | -0.40125 | 0.107662 | -3.72692 | 0.000194 | 0.006021 | 2.189833 |
| ENSG00000174453 | 160.5065 | 0.317721 | 0.085271 | 3.726031 | 0.000195 | 0.006021 | 2.189833 |
| ENSG00000137575 | 1079.073 | 0.224476 | 0.060285 | 3.723567 | 0.000196 | 0.006021 | 2.225762 |
| ENSG00000151729 | 1802.709 | 0.217402 | 0.05879  | 3.697959 | 0.000217 | 0.006021 | 2.456745 |
| ENSG00000170017 | 1702.964 | 0.235611 | 0.063811 | 3.692323 | 0.000222 | 0.006021 | 2.514347 |
| ENSG00000039123 | 778.6604 | 0.132882 | 0.036067 | 3.684317 | 0.000229 | 0.006021 | 2.583187 |
| ENSG00000125863 | 479.8406 | 0.196493 | 0.052931 | 3.712278 | 0.000205 | 0.006059 | 2.293762 |
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| ENSG00000086061 | 2010.182 | 0.278286 | 0.075602 | 3.680926 | 0.000232 | 0.006208 | 2.514347 |
| ENSG00000104643 | 1049.038 | 0.182611 | 0.049319 | 3.702652 | 0.000213 | 0.006236 | 2.293762 |
| ENSG00000121989 | 372.2612 | 0.191558 | 0.051654 | 3.708495 | 0.000208 | 0.006254 | 2.225762 |
| ENSG00000104897 | 242.1599 | -0.23169 | 0.062481 | -3.70818 | 0.000209 | 0.006254 | 2.225762 |
| ENSG00000113384 | 545.9205 | 0.146302 | 0.03953  | 3.701082 | 0.000215 | 0.006254 | 2.293762 |
| ENSG00000152556 | 2360.97  | 0.185345 | 0.050395 | 3.677874 | 0.000235 | 0.00628  | 2.492774 |
| ENSG00000112186 | 1513.697 | 0.265457 | 0.07167  | 3.703898 | 0.000212 | 0.006326 | 2.225762 |
| ENSG00000186479 | 1527.757 | 0.193584 | 0.05237  | 3.696454 | 0.000219 | 0.006326 | 2.293762 |
| ENSG00000244932 | 40.60104 | -0.34075 | 0.08745  | -3.89657 | 9.76E-05 | 0.006327 | 1.020896 |
| ENSG00000108557 | 1276.443 | -0.24165 | 0.065406 | -3.69453 | 0.00022  | 0.006347 | 2.293762 |
| ENSG00000047932 | 708.0025 | 0.1673   | 0.045299 | 3.693261 | 0.000221 | 0.006367 | 2.293762 |
| ENSG00000136156 | 3484.643 | 0.151455 | 0.041289 | 3.6682   | 0.000244 | 0.006397 | 2.514347 |
| ENSG00000271646 | 32.15456 | -0.45412 | 0.116262 | -3.90603 | 9.38E-05 | 0.006398 | 0.963911 |
| ENSG00000226746 | 48.7737  | -0.39536 | 0.101854 | -3.8816  | 0.000104 | 0.006493 | 1.044965 |
| ENSG00000132313 | 749.4561 | 0.182971 | 0.049637 | 3.686201 | 0.000228 | 0.006493 | 2.293762 |
| ENSG00000111530 | 3060.297 | 0.171419 | 0.046727 | 3.668553 | 0.000244 | 0.006493 | 2.456745 |
| ENSG00000169446 | 427.9001 | 0.186246 | 0.05007  | 3.719721 | 0.000199 | 0.006496 | 1.995423 |
| ENSG00000213983 | 397.0033 | -0.32639 | 0.087748 | -3.7197  | 0.000199 | 0.006496 | 1.995423 |

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| ENSG00000075239 | 424.2648 | 0.158651 | 0.043066 | 3.683894 | 0.00023  | 0.006496 | 2.295759 |
| ENSG00000070831 | 1542.904 | 0.154147 | 0.042178 | 3.654708 | 0.000257 | 0.006496 | 2.583187 |
| ENSG00000181350 | 208.4565 | -0.21791 | 0.059171 | -3.6827  | 0.000231 | 0.006513 | 2.295759 |
| ENSG00000107779 | 508.3889 | 0.211098 | 0.057801 | 3.652134 | 0.00026  | 0.006513 | 2.583187 |
| ENSG00000243302 | 156.7309 | -0.24933 | 0.06681  | -3.73198 | 0.00019  | 0.006555 | 1.867169 |
| ENSG00000186660 | 866.2347 | 0.165691 | 0.044927 | 3.687995 | 0.000226 | 0.006555 | 2.225762 |
| ENSG00000172239 | 520.7785 | 0.156671 | 0.042583 | 3.679209 | 0.000234 | 0.006555 | 2.29693  |
| ENSG00000113387 | 1763.421 | 0.246543 | 0.067622 | 3.645901 | 0.000266 | 0.006627 | 2.583187 |
| ENSG00000288612 | 119.6936 | -0.32024 | 0.086728 | -3.69249 | 0.000222 | 0.006733 | 2.108016 |
| ENSG00000187699 | 296.7742 | 0.210023 | 0.057213 | 3.670896 | 0.000242 | 0.006733 | 2.295759 |
| ENSG00000184432 | 1805.015 | 0.109926 | 0.030084 | 3.654016 | 0.000258 | 0.006733 | 2.456745 |
| ENSG00000135678 | 302.1538 | 0.336939 | 0.090897 | 3.706828 | 0.00021  | 0.006749 | 1.977088 |
| ENSG00000166169 | 327.9966 | -0.15999 | 0.043226 | -3.70113 | 0.000215 | 0.006749 | 2.025126 |
| ENSG00000162704 | 618.9477 | 0.172688 | 0.047065 | 3.669127 | 0.000243 | 0.006749 | 2.295759 |
| ENSG00000163902 | 1017.237 | 0.172132 | 0.046926 | 3.66817  | 0.000244 | 0.006754 | 2.295759 |
| ENSG00000164024 | 378.3788 | 0.171052 | 0.046675 | 3.664757 | 0.000248 | 0.006833 | 2.295759 |
| ENSG00000117360 | 772.5294 | -0.16625 | 0.045668 | -3.64047 | 0.000272 | 0.006846 | 2.514347 |
| ENSG00000254656 | 147.547  | -0.30971 | 0.084393 | -3.66988 | 0.000243 | 0.006874 | 2.225762 |
| ENSG00000141750 | 818.8945 | -0.34989 | 0.095571 | -3.66103 | 0.000251 | 0.006874 | 2.295759 |
| ENSG00000124767 | 954.1221 | 0.217653 | 0.059828 | 3.638011 | 0.000275 | 0.006874 | 2.514347 |
| ENSG00000131149 | 933.338  | -0.22011 | 0.060508 | -3.63769 | 0.000275 | 0.006874 | 2.514347 |
| ENSG00000171497 | 207.6582 | 0.26162  | 0.071546 | 3.65665  | 0.000256 | 0.006981 | 2.295759 |
| ENSG00000196262 | 3167.242 | 0.207736 | 0.057199 | 3.631793 | 0.000281 | 0.007009 | 2.514347 |
| ENSG00000102172 | 608.5209 | 0.244137 | 0.067399 | 3.622271 | 0.000292 | 0.007066 | 2.583187 |
| ENSG00000135824 | 125.7385 | 0.386759 | 0.1057   | 3.659018 | 0.000253 | 0.007098 | 2.225762 |
| ENSG00000144959 | 1331.499 | 0.199404 | 0.05498  | 3.626859 | 0.000287 | 0.007108 | 2.514347 |
| ENSG00000187601 | 506.4631 | 0.23902  | 0.065527 | 3.647665 | 0.000265 | 0.007169 | 2.295759 |
| ENSG00000092199 | 3078.033 | 0.147402 | 0.040629 | 3.627992 | 0.000286 | 0.007218 | 2.456745 |
| ENSG00000047249 | 1550.704 | 0.217514 | 0.059679 | 3.644742 | 0.000268 | 0.007226 | 2.295759 |
| ENSG00000162241 | 105.389  | -0.31808 | 0.083493 | -3.8097  | 0.000139 | 0.007236 | 1.182918 |

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| ENSG00000279675 | 241.7603 | 0.255624 | 0.069474 | 3.679419 | 0.000234 | 0.007236 | 1.995423 |
| ENSG00000156110 | 337.4285 | 0.154781 | 0.042124 | 3.674405 | 0.000238 | 0.007236 | 2.025126 |
| ENSG00000168288 | 288.6983 | 0.249928 | 0.068449 | 3.651292 | 0.000261 | 0.007236 | 2.225762 |
| ENSG00000172292 | 992.3256 | 0.200148 | 0.054824 | 3.650766 | 0.000261 | 0.007236 | 2.225762 |
| ENSG00000154518 | 891.446  | 0.240121 | 0.065936 | 3.641746 | 0.000271 | 0.007238 | 2.295759 |
| ENSG00000168763 | 436.7435 | -0.17203 | 0.046806 | -3.67542 | 0.000237 | 0.00729  | 1.995423 |
| ENSG00000041982 | 318.4705 | 0.723429 | 0.19706  | 3.671116 | 0.000241 | 0.007293 | 2.025126 |
| ENSG00000196419 | 1377.432 | 0.190956 | 0.052514 | 3.636308 | 0.000277 | 0.007356 | 2.295759 |
| ENSG00000116209 | 1602.048 | 0.17827  | 0.049058 | 3.633854 | 0.000279 | 0.007414 | 2.295759 |
| ENSG00000262877 | 227.0145 | -0.47268 | 0.129838 | -3.64056 | 0.000272 | 0.007426 | 2.225762 |
| ENSG00000131100 | 2049.045 | 0.260985 | 0.072269 | 3.611283 | 0.000305 | 0.007426 | 2.492774 |
| ENSG00000228544 | 53.38018 | -0.32011 | 0.083575 | -3.83018 | 0.000128 | 0.007433 | 1.044965 |
| ENSG00000102032 | 107.6245 | 0.300306 | 0.08102  | 3.706549 | 0.00021  | 0.00744  | 1.695647 |
| ENSG00000114573 | 4333.828 | 0.257521 | 0.070942 | 3.630039 | 0.000283 | 0.00744  | 2.295759 |
| ENSG00000138459 | 559.8719 | 0.213096 | 0.058707 | 3.629819 | 0.000284 | 0.00744  | 2.295759 |
| ENSG00000113761 | 487.1015 | -0.12515 | 0.034484 | -3.62935 | 0.000284 | 0.00744  | 2.293762 |
| ENSG00000108406 | 390.9748 | 0.160884 | 0.044333 | 3.628962 | 0.000285 | 0.00744  | 2.295759 |
| ENSG00000139718 | 581.5335 | -0.25387 | 0.069963 | -3.62859 | 0.000285 | 0.00744  | 2.29693  |
| ENSG00000145016 | 859.4863 | -0.14597 | 0.040461 | -3.60768 | 0.000309 | 0.00744  | 2.514347 |
| ENSG00000102468 | 807.9407 | 0.246261 | 0.067892 | 3.627257 | 0.000286 | 0.00747  | 2.295759 |
| ENSG00000113845 | 384.8053 | 0.165123 | 0.045562 | 3.6241   | 0.00029  | 0.00755  | 2.295759 |
| ENSG0000019995  | 514.9471 | 0.152205 | 0.04195  | 3.628247 | 0.000285 | 0.007615 | 2.225762 |
| ENSG00000105699 | 206.1066 | -0.22547 | 0.062271 | -3.6208  | 0.000294 | 0.007615 | 2.295759 |
| ENSG00000118785 | 3367.533 | 0.667842 | 0.185587 | 3.598541 | 0.00032  | 0.007615 | 2.492774 |
| ENSG00000136193 | 5989.468 | 0.147213 | 0.040941 | 3.595764 | 0.000323 | 0.007615 | 2.514347 |
| ENSG00000172757 | 2843.361 | 0.169183 | 0.04713  | 3.589716 | 0.000331 | 0.007615 | 2.583187 |
| ENSG00000131943 | 626.745  | 0.131684 | 0.036692 | 3.588903 | 0.000332 | 0.007615 | 2.583187 |
| ENSG00000168118 | 592.4193 | 0.159861 | 0.044178 | 3.618607 | 0.000296 | 0.007622 | 2.29693  |
| ENSG00000261340 | 76.3569  | 0.342294 | 0.092668 | 3.693773 | 0.000221 | 0.007677 | 1.695647 |
| ENSG00000183775 | 2896.752 | 0.211404 | 0.058845 | 3.592567 | 0.000327 | 0.007677 | 2.514347 |

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| ENSG00000100058 | 292.1556 | -0.20773 | 0.056862 | -3.6532  | 0.000259 | 0.007691 | 1.977088 |
| ENSG00000148572 | 188.0877 | 0.203403 | 0.056149 | 3.622564 | 0.000292 | 0.007691 | 2.225762 |
| ENSG00000198160 | 664.7628 | 0.129222 | 0.035756 | 3.614035 | 0.000301 | 0.007691 | 2.29693  |
| ENSG00000080854 | 2137.073 | -0.27944 | 0.077782 | -3.59254 | 0.000327 | 0.007691 | 2.492774 |
| ENSG00000131238 | 1119.988 | 0.207252 | 0.057359 | 3.613267 | 0.000302 | 0.007705 | 2.293762 |
| ENSG00000154813 | 309.6463 | 0.201599 | 0.055811 | 3.612156 | 0.000304 | 0.007719 | 2.295759 |
| ENSG00000107984 | 18.87642 | 0.61009  | 0.154428 | 3.950646 | 7.79E-05 | 0.007728 | 0.583933 |
| ENSG00000282692 | 65.24793 | -0.36987 | 0.096926 | -3.81601 | 0.000136 | 0.007728 | 1.020896 |
| ENSG00000131591 | 248.4382 | -0.23549 | 0.064546 | -3.6484  | 0.000264 | 0.007728 | 1.977088 |
| ENSG00000198785 | 374.9296 | 0.28878  | 0.079282 | 3.642425 | 0.00027  | 0.007728 | 2.025126 |
| ENSG00000112033 | 559.4032 | -0.18787 | 0.052475 | -3.58021 | 0.000343 | 0.007728 | 2.583187 |
| ENSG00000088179 | 2329.103 | 0.164072 | 0.045861 | 3.577619 | 0.000347 | 0.00776  | 2.583187 |
| ENSG00000130508 | 282.6473 | -0.28233 | 0.077596 | -3.63841 | 0.000274 | 0.007807 | 2.025126 |
| ENSG00000165637 | 703.438  | 0.198559 | 0.055533 | 3.575501 | 0.00035  | 0.007807 | 2.583187 |
| ENSG00000243660 | 265.0111 | -0.19086 | 0.052479 | -3.63688 | 0.000276 | 0.007815 | 2.025126 |
| ENSG00000100150 | 386.3163 | -0.16355 | 0.044989 | -3.63531 | 0.000278 | 0.007815 | 2.025126 |
| ENSG00000054116 | 397.7045 | 0.14153  | 0.039208 | 3.609732 | 0.000307 | 0.007815 | 2.225762 |
| ENSG00000070047 | 970.2805 | -0.18259 | 0.050694 | -3.60189 | 0.000316 | 0.007815 | 2.293762 |
| ENSG00000064651 | 2190.06  | 0.219608 | 0.06137  | 3.578437 | 0.000346 | 0.007815 | 2.514347 |
| ENSG00000080823 | 519.7628 | -0.15422 | 0.043155 | -3.57363 | 0.000352 | 0.007815 | 2.583187 |
| ENSG00000083312 | 2092.44  | 0.129472 | 0.03624  | 3.57262  | 0.000353 | 0.007815 | 2.583187 |
| ENSG00000167193 | 817.6005 | 0.151682 | 0.042464 | 3.57198  | 0.000354 | 0.007815 | 2.583187 |
| ENSG00000177311 | 2429.947 | 0.136813 | 0.038304 | 3.57173  | 0.000355 | 0.007815 | 2.583187 |
| ENSG00000138018 | 1528.54  | 0.208505 | 0.058381 | 3.571428 | 0.000355 | 0.007815 | 2.583187 |
| ENSG00000215458 | 88.25942 | -0.3799  | 0.100581 | -3.77708 | 0.000159 | 0.007829 | 1.142898 |
| ENSG00000188827 | 423.8893 | -0.20387 | 0.056516 | -3.60723 | 0.000309 | 0.007829 | 2.225762 |
| ENSG00000100325 | 305.4803 | -0.16072 | 0.04464  | -3.60035 | 0.000318 | 0.007829 | 2.295759 |
| ENSG00000167468 | 1237.285 | 0.179407 | 0.049833 | 3.600164 | 0.000318 | 0.007829 | 2.293762 |
| ENSG00000185736 | 898.3131 | -0.28505 | 0.079201 | -3.59906 | 0.000319 | 0.007829 | 2.295759 |
| ENSG00000275023 | 3022.022 | -0.15716 | 0.044047 | -3.56802 | 0.00036  | 0.007829 | 2.583187 |

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| ENSG0000054983  | 606.2208 | 0.172961 | 0.048096 | 3.596183 | 0.000323 | 0.007881 | 2.29693  |
| ENSG00000112624 | 888.4626 | -0.13666 | 0.038327 | -3.5657  | 0.000363 | 0.007881 | 2.583187 |
| ENSG00000196591 | 525.9496 | 0.156402 | 0.043495 | 3.595888 | 0.000323 | 0.007889 | 2.293762 |
| ENSG00000162817 | 1392.926 | 0.226403 | 0.062997 | 3.593874 | 0.000326 | 0.007931 | 2.295759 |
| ENSG00000020181 | 307.4501 | -0.29876 | 0.082311 | -3.62965 | 0.000284 | 0.007937 | 1.995423 |
| ENSG00000176715 | 462.5806 | -0.14871 | 0.040882 | -3.63739 | 0.000275 | 0.007952 | 1.918337 |
| ENSG00000180998 | 412.226  | 0.286185 | 0.078888 | 3.627746 | 0.000286 | 0.007952 | 1.995423 |
| ENSG00000183049 | 3986.114 | -0.13212 | 0.037    | -3.57085 | 0.000356 | 0.007952 | 2.492774 |
| ENSG00000171862 | 2056.899 | 0.159469 | 0.0447   | 3.567528 | 0.00036  | 0.007952 | 2.514347 |
| ENSG00000001497 | 747.9653 | -0.20226 | 0.056812 | -3.56008 | 0.000371 | 0.007952 | 2.583187 |
| ENSG00000198431 | 834.5627 | 0.229252 | 0.063855 | 3.59018  | 0.00033  | 0.007955 | 2.293762 |
| ENSG00000174282 | 2911.322 | -0.12177 | 0.034211 | -3.55927 | 0.000372 | 0.007955 | 2.583187 |
| ENSG00000128656 | 8697.864 | 0.239295 | 0.067136 | 3.564327 | 0.000365 | 0.007999 | 2.514347 |
| ENSG00000228315 | 295.483  | -0.18952 | 0.05274  | -3.59357 | 0.000326 | 0.008062 | 2.225762 |
| ENSG00000162636 | 878.2016 | 0.228213 | 0.063512 | 3.593253 | 0.000327 | 0.008062 | 2.225762 |
| ENSG00000156671 | 1880.943 | 0.120052 | 0.033658 | 3.566788 | 0.000361 | 0.008062 | 2.456745 |
| ENSG00000006125 | 4527.305 | 0.1334   | 0.037438 | 3.563227 | 0.000366 | 0.008062 | 2.492774 |
| ENSG00000168743 | 92.14303 | 0.611    | 0.162832 | 3.752335 | 0.000175 | 0.008065 | 1.182918 |
| ENSG00000152484 | 784.5095 | 0.158446 | 0.044128 | 3.59059  | 0.00033  | 0.008065 | 2.225762 |
| ENSG00000160613 | 733.2833 | -0.15855 | 0.044242 | -3.58382 | 0.000339 | 0.008065 | 2.293762 |
| ENSG00000145687 | 1063.229 | 0.161101 | 0.045258 | 3.559654 | 0.000371 | 0.008065 | 2.514347 |
| ENSG00000265972 | 2004.698 | -0.46865 | 0.13193  | -3.55222 | 0.000382 | 0.008065 | 2.583187 |
| ENSG00000215717 | 512.2601 | 0.179542 | 0.050568 | 3.550505 | 0.000384 | 0.008086 | 2.583187 |
| ENSG00000162852 | 1111.348 | 0.208608 | 0.058262 | 3.580547 | 0.000343 | 0.008102 | 2.295759 |
| ENSG00000165973 | 476.6831 | 0.308276 | 0.086864 | 3.548953 | 0.000387 | 0.00811  | 2.583187 |
| ENSG00000137947 | 217.2617 | 0.222893 | 0.061741 | 3.610122 | 0.000306 | 0.008174 | 2.025126 |
| ENSG00000100216 | 314.3897 | 0.205722 | 0.057394 | 3.584385 | 0.000338 | 0.008186 | 2.225762 |
| ENSG00000119397 | 661.7427 | -0.18416 | 0.051495 | -3.57632 | 0.000348 | 0.008186 | 2.29693  |
| ENSG00000160094 | 436.4284 | -0.14446 | 0.039884 | -3.62209 | 0.000292 | 0.008192 | 1.918337 |
| ENSG00000011566 | 985.3582 | 0.122731 | 0.034331 | 3.574976 | 0.00035  | 0.008192 | 2.295759 |

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| ENSG00000154917 | 5275.775 | 0.160602 | 0.045316 | 3.544011 | 0.000394 | 0.008192 | 2.583187 |
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| ENSG00000164112 | 384.4795 | 0.282106 | 0.078143 | 3.610145 | 0.000306 | 0.008211 | 1.995423 |
| ENSG00000158014 | 13.12858 | -0.64406 | 0.165886 | -3.88253 | 0.000103 | 0.008242 | 0.670508 |
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| ENSG00000183155 | 193.7297 | 0.19817  | 0.055536 | 3.56834  | 0.000359 | 0.00833  | 2.295759 |
| ENSG00000136367 | 718.7331 | -0.26778 | 0.07558  | -3.54305 | 0.000396 | 0.008361 | 2.514347 |
| ENSG00000179361 | 88.50638 | -0.25175 | 0.067372 | -3.73668 | 0.000186 | 0.008367 | 1.182918 |
| ENSG00000155961 | 339.9046 | 0.225162 | 0.062543 | 3.600144 | 0.000318 | 0.008436 | 1.995423 |
| ENSG00000177337 | 189.1331 | -0.22648 | 0.062984 | -3.5959  | 0.000323 | 0.008436 | 2.025126 |
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| ENSG00000229569 | 21.80781 | -0.56289 | 0.144633 | -3.89185 | 9.95E-05 | 0.008451 | 0.616514 |
| ENSG00000234913 | 94.24932 | -0.3403  | 0.090967 | -3.74087 | 0.000183 | 0.008451 | 1.136415 |
| ENSG00000162627 | 113.4642 | 0.283437 | 0.078405 | 3.615027 | 0.0003   | 0.008451 | 1.867169 |
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| ENSG00000141424 | 630.4135 | 0.176621 | 0.049478 | 3.569676 | 0.000357 | 0.008451 | 2.225762 |
| ENSG00000136485 | 1184.588 | 0.113679 | 0.03191  | 3.562454 | 0.000367 | 0.008451 | 2.293762 |
| ENSG00000178741 | 496.7227 | 0.203703 | 0.0572   | 3.561255 | 0.000369 | 0.008451 | 2.295759 |
| ENSG00000136783 | 207.0332 | 0.239307 | 0.067227 | 3.559674 | 0.000371 | 0.008451 | 2.295759 |
| ENSG00000176641 | 621.4088 | 0.290392 | 0.082345 | 3.526544 | 0.000421 | 0.008504 | 2.583187 |
| ENSG00000173113 | 288.8412 | 0.199944 | 0.056085 | 3.565039 | 0.000364 | 0.008516 | 2.225762 |
| ENSG00000079385 | 74.07153 | -0.28534 | 0.076352 | -3.73712 | 0.000186 | 0.008522 | 1.136415 |
| ENSG00000165684 | 564.1998 | -0.20875 | 0.058571 | -3.564   | 0.000365 | 0.008526 | 2.225762 |
| ENSG00000285888 | 26.04961 | -0.44791 | 0.118631 | -3.77567 | 0.00016  | 0.008546 | 0.963911 |
| ENSG00000286989 | 91.65624 | -0.29597 | 0.079268 | -3.73372 | 0.000189 | 0.008546 | 1.142898 |
| ENSG00000128590 | 358.8732 | 0.216772 | 0.06019  | 3.601471 | 0.000316 | 0.008546 | 1.918337 |
| ENSG00000101247 | 390.853  | 0.191724 | 0.053452 | 3.586861 | 0.000335 | 0.008546 | 1.995423 |
| ENSG00000085449 | 431.959  | 0.175424 | 0.049282 | 3.559581 | 0.000371 | 0.008546 | 2.225762 |
| ENSG00000166946 | 528.3839 | 0.180699 | 0.050769 | 3.559252 | 0.000372 | 0.008546 | 2.225762 |

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| ENSG00000129933 | 1100.032 | -0.15199 | 0.042772 | -3.55356 | 0.00038  | 0.008546 | 2.295759 |
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| ENSG00000206527 | 686.3985 | 0.189744 | 0.053424 | 3.551641 | 0.000383 | 0.008546 | 2.295759 |
| ENSG00000106615 | 644.7548 | 0.203732 | 0.057381 | 3.550501 | 0.000384 | 0.008546 | 2.29693  |
| ENSG00000135535 | 986.7453 | 0.15718  | 0.044272 | 3.550355 | 0.000385 | 0.008546 | 2.295759 |
| ENSG00000152102 | 3003.506 | 0.118607 | 0.033562 | 3.533924 | 0.000409 | 0.008546 | 2.456745 |
| ENSG00000144635 | 643.6945 | 0.180806 | 0.051352 | 3.520917 | 0.00043  | 0.008546 | 2.583187 |
| ENSG00000180626 | 518.2192 | -0.17857 | 0.050729 | -3.52006 | 0.000431 | 0.008546 | 2.583187 |
| ENSG00000129993 | 103.6732 | -0.38758 | 0.106829 | -3.62804 | 0.000286 | 0.00857  | 1.695647 |
| ENSG00000104904 | 2346.825 | 0.158634 | 0.045009 | 3.524505 | 0.000424 | 0.008574 | 2.514347 |
| ENSG00000228594 | 200.9685 | -0.27988 | 0.078891 | -3.5477  | 0.000389 | 0.008589 | 2.295759 |
| ENSG00000168092 | 1986.395 | 0.154902 | 0.04368  | 3.54633  | 0.000391 | 0.008611 | 2.295759 |
| ENSG00000056586 | 1876.532 | 0.121225 | 0.034392 | 3.524832 | 0.000424 | 0.008611 | 2.492774 |
| ENSG00000086065 | 578.892  | 0.21839  | 0.06159  | 3.545899 | 0.000391 | 0.00862  | 2.293762 |
| ENSG00000180440 | 204.9135 | 0.377148 | 0.104831 | 3.597677 | 0.000321 | 0.008678 | 1.867169 |
| ENSG00000136522 | 208.8331 | 0.222179 | 0.062075 | 3.579223 | 0.000345 | 0.008704 | 1.995423 |
| ENSG00000150054 | 307.8862 | 0.228788 | 0.064443 | 3.550207 | 0.000385 | 0.008704 | 2.225762 |
| ENSG00000137876 | 574.7853 | 0.200295 | 0.056564 | 3.541011 | 0.000399 | 0.008726 | 2.295759 |
| ENSG00000277142 | 88.34691 | -0.25642 | 0.069181 | -3.70644 | 0.00021  | 0.008743 | 1.201846 |
| ENSG00000113966 | 336.804  | 0.229888 | 0.064352 | 3.57233  | 0.000354 | 0.008743 | 2.025126 |
| ENSG00000184428 | 190.7541 | -0.23381 | 0.065455 | -3.57211 | 0.000354 | 0.008743 | 2.025126 |
| ENSG00000158985 | 1336.211 | 0.185768 | 0.052472 | 3.540324 | 0.0004   | 0.008743 | 2.293762 |
| ENSG00000084693 | 400.6168 | -0.12526 | 0.035033 | -3.57537 | 0.00035  | 0.008747 | 1.995423 |
| ENSG00000162543 | 259.6017 | -0.23923 | 0.067613 | -3.53823 | 0.000403 | 0.008747 | 2.295759 |
| ENSG00000146066 | 155.1312 | 0.185242 | 0.052245 | 3.54562  | 0.000392 | 0.008761 | 2.225762 |
| ENSG00000175893 | 1751.042 | 0.138348 | 0.039468 | 3.505319 | 0.000456 | 0.008778 | 2.583187 |
| ENSG00000133624 | 476.1662 | -0.13945 | 0.039437 | -3.53605 | 0.000406 | 0.00878  | 2.29693  |
| ENSG00000137275 | 402.3297 | -0.16965 | 0.047545 | -3.5681  | 0.00036  | 0.008781 | 2.025126 |
| ENSG00000120137 | 2119.593 | 0.143559 | 0.040861 | 3.51337  | 0.000442 | 0.008781 | 2.492774 |
| ENSG00000234420 | 1324.519 | -0.1213  | 0.034618 | -3.50407 | 0.000458 | 0.008781 | 2.583187 |

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| ENSG00000081189 | 5883.445 | 0.205143 | 0.058429 | 3.510975 | 0.000446 | 0.008845 | 2.492774 |
| ENSG00000171388 | 228.6671 | 0.383506 | 0.108579 | 3.532041 | 0.000412 | 0.008855 | 2.295759 |
| ENSG00000104765 | 1995.053 | 0.182923 | 0.052058 | 3.513845 | 0.000442 | 0.008855 | 2.456745 |
| ENSG00000186566 | 1602.661 | -0.16027 | 0.045388 | -3.53106 | 0.000414 | 0.008868 | 2.295759 |
| ENSG00000135913 | 405.199  | -0.12854 | 0.036361 | -3.53518 | 0.000407 | 0.008994 | 2.225762 |
| ENSG00000168216 | 950.1146 | 0.174655 | 0.049986 | 3.494059 | 0.000476 | 0.009026 | 2.583187 |
| ENSG00000036257 | 1033.615 | 0.132351 | 0.03788  | 3.493973 | 0.000476 | 0.009026 | 2.583187 |
| ENSG00000109189 | 1564.687 | 0.157917 | 0.045202 | 3.493556 | 0.000477 | 0.009028 | 2.583187 |
| ENSG00000185947 | 164.5652 | 0.241476 | 0.068545 | 3.522879 | 0.000427 | 0.009086 | 2.295759 |
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| ENSG00000131966 | 560.6904 | 0.213708 | 0.060679 | 3.521946 | 0.000428 | 0.009105 | 2.295759 |
| ENSG00000166226 | 872.5437 | 0.18893  | 0.053558 | 3.527586 | 0.000419 | 0.00917  | 2.225762 |
| ENSG00000157680 | 2436.854 | 0.169156 | 0.048423 | 3.493309 | 0.000477 | 0.009223 | 2.514347 |
| ENSG00000082701 | 2441.925 | 0.100376 | 0.028718 | 3.495183 | 0.000474 | 0.009225 | 2.492774 |
| ENSG00000170919 | 699.2526 | -0.16983 | 0.048316 | -3.51497 | 0.00044  | 0.009295 | 2.293762 |
| ENSG00000130224 | 245.5992 | 0.186235 | 0.052455 | 3.550359 | 0.000385 | 0.009421 | 1.977088 |
| ENSG00000087448 | 1196.401 | 0.171654 | 0.048907 | 3.509767 | 0.000449 | 0.009454 | 2.293762 |
| ENSG00000146676 | 1629.461 | 0.135377 | 0.038598 | 3.507393 | 0.000453 | 0.009527 | 2.293762 |
| ENSG00000134121 | 5716.797 | 0.199159 | 0.056832 | 3.504369 | 0.000458 | 0.009614 | 2.295759 |
| ENSG00000111727 | 606.4033 | 0.139196 | 0.039734 | 3.503175 | 0.00046  | 0.009653 | 2.293762 |
| ENSG00000004779 | 392.1194 | 0.261377 | 0.073847 | 3.53942  | 0.000401 | 0.009654 | 1.995423 |
| ENSG00000186297 | 736.8736 | 0.342593 | 0.097601 | 3.510125 | 0.000448 | 0.009654 | 2.225762 |
| ENSG00000108582 | 1954.852 | 0.17511  | 0.050317 | 3.48014  | 0.000501 | 0.009654 | 2.492774 |
| ENSG00000134253 | 121.4327 | -0.2579  | 0.072523 | -3.55618 | 0.000376 | 0.009656 | 1.867169 |
| ENSG00000116906 | 440.4629 | 0.138726 | 0.039268 | 3.532821 | 0.000411 | 0.009715 | 2.025126 |
| ENSG00000129562 | 320.075  | 0.190314 | 0.054265 | 3.50712  | 0.000453 | 0.009726 | 2.225762 |
| ENSG00000279712 | 158.5772 | -0.36931 | 0.105205 | -3.5104  | 0.000447 | 0.009739 | 2.189833 |
| ENSG00000165175 | 884.26   | 0.245702 | 0.070884 | 3.466235 | 0.000528 | 0.009739 | 2.583187 |
| ENSG00000059758 | 1613.956 | 0.17012  | 0.048536 | 3.505012 | 0.000457 | 0.009765 | 2.225762 |
| ENSG00000265125 | 77.20965 | -0.32365 | 0.088206 | -3.66922 | 0.000243 | 0.009766 | 1.182918 |

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| ENSG00000173542 | 764.2846 | 0.20688  | 0.059589 | 3.471805 | 0.000517 | 0.009766 | 2.514347 |
| ENSG00000116459 | 1133.058 | 0.187098 | 0.053532 | 3.495059 | 0.000474 | 0.009786 | 2.293762 |
| ENSG00000071537 | 1836.858 | 0.13215  | 0.038009 | 3.476787 | 0.000507 | 0.009786 | 2.456745 |
| ENSG00000089094 | 589.4917 | -0.1574  | 0.045059 | -3.49319 | 0.000477 | 0.009816 | 2.29693  |
| ENSG00000164830 | 3743.205 | 0.201078 | 0.058086 | 3.461701 | 0.000537 | 0.009816 | 2.583187 |
| ENSG00000119013 | 262.8823 | 0.27052  | 0.077292 | 3.499982 | 0.000465 | 0.00985  | 2.225762 |
| ENSG00000167005 | 543.8582 | 0.184296 | 0.05278  | 3.491763 | 0.00048  | 0.00985  | 2.29693  |
| ENSG00000145675 | 5384.445 | 0.148897 | 0.042874 | 3.472908 | 0.000515 | 0.009862 | 2.456745 |
| ENSG00000183283 | 1203.717 | 0.163096 | 0.046612 | 3.498978 | 0.000467 | 0.009862 | 2.225762 |
| ENSG00000170632 | 325.8192 | 0.18029  | 0.051656 | 3.490228 | 0.000483 | 0.009867 | 2.295759 |
| ENSG00000114346 | 174.9631 | 0.266907 | 0.075672 | 3.527177 | 0.00042  | 0.009868 | 1.995423 |
| ENSG00000146151 | 353.4417 | 0.246516 | 0.069694 | 3.537134 | 0.000404 | 0.009872 | 1.918337 |
| ENSG00000049130 | 631.5022 | 0.232723 | 0.066701 | 3.489032 | 0.000485 | 0.009883 | 2.293762 |
| ENSG00000116199 | 1424.038 | 0.150564 | 0.043083 | 3.494763 | 0.000474 | 0.009956 | 2.225762 |
| ENSG00000143363 | 219.4695 | 0.163806 | 0.046899 | 3.492732 | 0.000478 | 0.010019 | 2.225762 |
| ENSG00000145715 | 1297.145 | 0.115299 | 0.033047 | 3.48897  | 0.000485 | 0.010068 | 2.225762 |
| ENSG00000130177 | 658.1677 | -0.13043 | 0.037457 | -3.48223 | 0.000497 | 0.010068 | 2.295759 |
| ENSG00000153989 | 282.7081 | 0.176377 | 0.05066  | 3.481609 | 0.000498 | 0.010068 | 2.295759 |
| ENSG00000103150 | 597.575  | -0.25207 | 0.07241  | -3.48116 | 0.000499 | 0.010068 | 2.293762 |
| ENSG00000196361 | 1626.587 | -0.17911 | 0.051457 | -3.4807  | 0.0005   | 0.010068 | 2.293762 |
| ENSG00000117533 | 619.2407 | 0.165787 | 0.047631 | 3.48065  | 0.0005   | 0.010068 | 2.295759 |
| ENSG00000079246 | 2875.856 | 0.162999 | 0.047235 | 3.450832 | 0.000559 | 0.010068 | 2.583187 |
| ENSG00000137845 | 1475.188 | 0.120725 | 0.034994 | 3.449827 | 0.000561 | 0.010068 | 2.583187 |
| ENSG00000119421 | 389.9196 | 0.206209 | 0.058654 | 3.515679 | 0.000439 | 0.010071 | 1.995423 |
| ENSG00000136877 | 283.5728 | -0.1941  | 0.055262 | -3.5123  | 0.000444 | 0.010071 | 2.025126 |
| ENSG00000280234 | 923.5117 | -0.32888 | 0.09431  | -3.48719 | 0.000488 | 0.010071 | 2.225762 |
| ENSG00000130962 | 478.3329 | 0.26657  | 0.07664  | 3.478222 | 0.000505 | 0.010071 | 2.29693  |
| ENSG00000109436 | 1170.794 | 0.169628 | 0.049115 | 3.45367  | 0.000553 | 0.010071 | 2.514347 |
| ENSG00000115561 | 791.102  | 0.154226 | 0.044746 | 3.446689 | 0.000568 | 0.010071 | 2.583187 |
| ENSG00000110321 | 5593.222 | 0.138535 | 0.040198 | 3.446292 | 0.000568 | 0.010071 | 2.583187 |

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| ENSG00000085231 | 91.45296 | 0.273107 | 0.0746   | 3.660947 | 0.000251 | 0.010084 | 1.136415 |
| ENSG00000132388 | 432.3143 | 0.133508 | 0.03803  | 3.510616 | 0.000447 | 0.010084 | 2.025126 |
| ENSG00000226696 | 109.2678 | -0.22437 | 0.064378 | -3.48516 | 0.000492 | 0.010084 | 2.225762 |
| ENSG00000104763 | 1296.531 | 0.211742 | 0.060768 | 3.484401 | 0.000493 | 0.010094 | 2.225762 |
| ENSG00000117758 | 1165.163 | 0.163594 | 0.047068 | 3.475675 | 0.00051  | 0.010098 | 2.295759 |
| ENSG00000107669 | 1041.024 | 0.150884 | 0.043418 | 3.475121 | 0.000511 | 0.010106 | 2.295759 |
| ENSG00000235316 | 81.16781 | -0.31485 | 0.086116 | -3.65612 | 0.000256 | 0.010181 | 1.136415 |
| ENSG00000183648 | 348.1487 | 0.202122 | 0.057589 | 3.50976  | 0.000449 | 0.010181 | 1.995423 |
| ENSG00000047621 | 447.6852 | 0.188242 | 0.053698 | 3.505558 | 0.000456 | 0.010181 | 2.025126 |
| ENSG00000138663 | 478.2243 | 0.231972 | 0.066669 | 3.479486 | 0.000502 | 0.010181 | 2.225762 |
| ENSG00000088812 | 2406.812 | 0.138567 | 0.040202 | 3.446722 | 0.000567 | 0.010181 | 2.514347 |
| ENSG00000100664 | 2867.449 | 0.168663 | 0.049022 | 3.440543 | 0.000581 | 0.010181 | 2.583187 |
| ENSG00000172466 | 1670.144 | 0.100226 | 0.029152 | 3.438034 | 0.000586 | 0.010219 | 2.583187 |
| ENSG0000011897  | 8742.944 | 0.177633 | 0.051212 | 3.46857  | 0.000523 | 0.010255 | 2.295759 |
| ENSG00000203761 | 79.92896 | -0.25759 | 0.072653 | -3.54542 | 0.000392 | 0.010339 | 1.695647 |
| ENSG00000109452 | 530.6018 | 0.178763 | 0.051468 | 3.473269 | 0.000514 | 0.010339 | 2.225762 |
| ENSG00000082996 | 857.302  | 0.197473 | 0.056981 | 3.465573 | 0.000529 | 0.010339 | 2.295759 |
| ENSG00000177728 | 1624.701 | -0.18458 | 0.053643 | -3.4409  | 0.00058  | 0.010339 | 2.514347 |
| ENSG00000110888 | 1400.629 | -0.15344 | 0.044599 | -3.44044 | 0.000581 | 0.010339 | 2.514347 |
| ENSG00000106153 | 1317.457 | 0.21764  | 0.062696 | 3.47138  | 0.000518 | 0.010391 | 2.225762 |
| ENSG00000041353 | 615.1517 | 0.403525 | 0.116262 | 3.470828 | 0.000519 | 0.0104   | 2.225762 |
| ENSG00000081087 | 364.2366 | 0.168053 | 0.048111 | 3.493002 | 0.000478 | 0.01051  | 2.025126 |
| ENSG00000244165 | 54.09844 | -0.29599 | 0.080768 | -3.66477 | 0.000248 | 0.010544 | 1.044965 |
| ENSG00000137814 | 229.4043 | 0.193076 | 0.055238 | 3.495369 | 0.000473 | 0.010546 | 1.995423 |
| ENSG00000074410 | 58.46098 | -0.57931 | 0.155914 | -3.71557 | 0.000203 | 0.010594 | 0.848718 |
| ENSG00000164209 | 1348.992 | 0.207515 | 0.060046 | 3.455952 | 0.000548 | 0.010594 | 2.295759 |
| ENSG00000118407 | 67.80753 | 0.377369 | 0.101639 | 3.712855 | 0.000205 | 0.01067  | 0.848718 |
| ENSG00000110675 | 1163.695 | 0.193677 | 0.056083 | 3.453404 | 0.000554 | 0.01067  | 2.293762 |
| ENSG00000104164 | 903.407  | 0.16549  | 0.048262 | 3.429007 | 0.000606 | 0.01067  | 2.514347 |
| ENSG00000168615 | 939.1147 | 0.170181 | 0.049312 | 3.451083 | 0.000558 | 0.010734 | 2.295759 |

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| ENSG00000178449 | 139.9454 | 0.244743 | 0.070464 | 3.473318 | 0.000514 | 0.01075  | 2.108016 |
| ENSG00000166128 | 615.0446 | 0.175751 | 0.050836 | 3.457192 | 0.000546 | 0.010759 | 2.225762 |
| ENSG00000131263 | 2415.391 | 0.170875 | 0.049802 | 3.431121 | 0.000601 | 0.010759 | 2.456745 |
| ENSG00000204116 | 1053.496 | 0.203676 | 0.059469 | 3.424917 | 0.000615 | 0.010759 | 2.514347 |
| ENSG00000145349 | 1452.047 | 0.241933 | 0.070647 | 3.424511 | 0.000616 | 0.010759 | 2.514347 |
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| ENSG00000242797 | 12.30617 | -0.60254 | 0.158932 | -3.79115 | 0.00015  | 0.010814 | 0.60691  |
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| ENSG00000230358 | 37.93617 | -0.37569 | 0.102684 | -3.65868 | 0.000254 | 0.010844 | 1.020896 |
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| ENSG00000114742 | 877.2981 | 0.112834 | 0.032782 | 3.441941 | 0.000578 | 0.010908 | 2.295759 |
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| ENSG00000128683 | 1655.068 | 0.325724 | 0.094647 | 3.441459 | 0.000579 | 0.010924 | 2.293762 |
| ENSG00000165194 | 716.9288 | 0.212159 | 0.061606 | 3.443812 | 0.000574 | 0.011136 | 2.225762 |
| ENSG00000113712 | 1291.355 | 0.114874 | 0.033436 | 3.435621 | 0.000591 | 0.011136 | 2.293762 |
| ENSG00000147416 | 3953.457 | 0.244196 | 0.071774 | 3.40228  | 0.000668 | 0.011164 | 2.583187 |
| ENSG00000153561 | 1687.662 | 0.15679  | 0.045669 | 3.433182 | 0.000597 | 0.011121 | 2.293762 |
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| ENSG00000164611 | 26.07652 | 0.514337 | 0.140484 | 3.661165 | 0.000251 | 0.011347 | 0.947688 |
| ENSG00000272927 | 32.11064 | -0.4661  | 0.127313 | -3.66103 | 0.000251 | 0.011347 | 0.947688 |
| ENSG00000112335 | 1065.443 | 0.187071 | 0.054589 | 3.426885 | 0.000611 | 0.011358 | 2.293762 |
| ENSG00000165629 | 904.2203 | 0.22678  | 0.066183 | 3.426567 | 0.000611 | 0.011358 | 2.295759 |
| ENSG00000119844 | 992.9476 | 0.144579 | 0.042501 | 3.40179  | 0.000669 | 0.011358 | 2.514347 |
| ENSG00000128191 | 463.494  | -0.14607 | 0.042637 | -3.42591 | 0.000613 | 0.011372 | 2.295759 |

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| ENSG00000137075 | 973.9808 | 0.111821 | 0.033008 | 3.387652 | 0.000705 | 0.011561 | 2.583187 |
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| ENSG00000128059 | 234.6509 | 0.196356 | 0.056868 | 3.452856 | 0.000555 | 0.011577 | 2.025126 |
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| ENSG00000204899 | 264.2663 | 0.207087 | 0.059924 | 3.455817 | 0.000549 | 0.011675 | 1.977088 |
| ENSG00000101134 | 157.7878 | 0.231176 | 0.067432 | 3.428293 | 0.000607 | 0.011675 | 2.189833 |
| ENSG00000163468 | 1272.152 | 0.172789 | 0.05058  | 3.416115 | 0.000635 | 0.011675 | 2.293762 |
| ENSG00000198590 | 167.193  | 0.266499 | 0.077276 | 3.44868  | 0.000563 | 0.011677 | 2.025126 |
| ENSG00000146267 | 1303.342 | 0.208703 | 0.061117 | 3.414793 | 0.000638 | 0.011677 | 2.295759 |
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| ENSG00000065989 | 864.6525 | -0.21774 | 0.064389 | -3.3816  | 0.000721 | 0.011685 | 2.583187 |
| ENSG00000047315 | 1073.552 | 0.196583 | 0.057453 | 3.421613 | 0.000623 | 0.011701 | 2.225762 |
| ENSG00000177000 | 713.2695 | -0.13563 | 0.039742 | -3.41269 | 0.000643 | 0.011719 | 2.293762 |
| ENSG00000080189 | 483.7199 | -0.14768 | 0.043286 | -3.41159 | 0.000646 | 0.011753 | 2.293762 |
| ENSG00000120053 | 1812.386 | 0.297787 | 0.087881 | 3.388523 | 0.000703 | 0.011753 | 2.492774 |
| ENSG00000169288 | 175.1708 | 0.211569 | 0.061352 | 3.448469 | 0.000564 | 0.011753 | 1.995423 |
| ENSG00000285796 | 157.1315 | -0.23041 | 0.06766  | -3.40545 | 0.000661 | 0.011753 | 2.338927 |
| ENSG00000124172 | 666.5428 | 0.23005  | 0.067515 | 3.407407 | 0.000656 | 0.011881 | 2.293762 |
| ENSG00000135324 | 250.9079 | 0.319137 | 0.092678 | 3.443501 | 0.000574 | 0.011937 | 1.995423 |
| ENSG00000278259 | 487.448  | -0.16552 | 0.048606 | -3.40528 | 0.000661 | 0.011937 | 2.295759 |
| ENSG00000132570 | 186.6837 | -0.213   | 0.062575 | -3.40388 | 0.000664 | 0.011984 | 2.295759 |
| ENSG00000145242 | 642.492  | 0.278789 | 0.081913 | 3.403457 | 0.000665 | 0.01199  | 2.295759 |
| ENSG00000121022 | 470.031  | 0.156509 | 0.045484 | 3.440955 | 0.00058  | 0.01199  | 1.995423 |
| ENSG00000011426 | 1660.776 | 0.44199  | 0.129567 | 3.411299 | 0.000647 | 0.01199  | 2.225762 |
| ENSG00000015475 | 521.7705 | 0.162976 | 0.047904 | 3.402138 | 0.000669 | 0.012002 | 2.293762 |
| ENSG00000014641 | 4049.209 | 0.286673 | 0.084271 | 3.401812 | 0.000669 | 0.012002 | 2.295759 |

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| ENSG00000111077 | 1375.026 | -0.2189  | 0.064357 | -3.40132 | 0.000671 | 0.012013 | 2.293762 |
| ENSG00000243696 | 68.13038 | -0.31224 | 0.086362 | -3.61549 | 0.0003   | 0.01204  | 1.020896 |
| ENSG00000236408 | 25.2561  | -0.42144 | 0.116817 | -3.60766 | 0.000309 | 0.01204  | 1.053218 |
| ENSG00000133422 | 505.2365 | -0.11682 | 0.034374 | -3.39851 | 0.000678 | 0.012081 | 2.29693  |
| ENSG00000082153 | 714.1219 | 0.199628 | 0.058624 | 3.405246 | 0.000661 | 0.01215  | 2.225762 |
| ENSG00000074696 | 1905.694 | 0.165109 | 0.048979 | 3.371008 | 0.000749 | 0.012172 | 2.514347 |
| ENSG00000166181 | 873.0876 | 0.150056 | 0.044202 | 3.394788 | 0.000687 | 0.012201 | 2.295759 |
| ENSG00000104231 | 443.5039 | 0.183047 | 0.053924 | 3.394518 | 0.000687 | 0.012201 | 2.295759 |
| ENSG00000169499 | 739.7354 | 0.161866 | 0.047686 | 3.394413 | 0.000688 | 0.012201 | 2.295759 |
| ENSG00000122335 | 366.6388 | 0.183902 | 0.054184 | 3.394063 | 0.000689 | 0.012204 | 2.295759 |
| ENSG00000086300 | 700.5163 | 0.293936 | 0.086629 | 3.393047 | 0.000691 | 0.012234 | 2.293762 |
| ENSG00000106299 | 1564.307 | 0.143714 | 0.042359 | 3.39279  | 0.000692 | 0.012234 | 2.295759 |
| ENSG00000182253 | 1616.449 | 0.189233 | 0.056199 | 3.367218 | 0.000759 | 0.012246 | 2.514347 |
| ENSG00000256443 | 187.8908 | -0.48415 | 0.141152 | -3.42995 | 0.000604 | 0.012254 | 1.995423 |
| ENSG00000236540 | 71.41893 | -0.3209  | 0.092402 | -3.47287 | 0.000515 | 0.012287 | 1.695647 |
| ENSG00000138798 | 58.87247 | 0.396589 | 0.110186 | 3.599275 | 0.000319 | 0.01233  | 1.044965 |
| ENSG00000136448 | 1957.292 | 0.106608 | 0.03176  | 3.356646 | 0.000789 | 0.01233  | 2.583187 |
| ENSG00000047578 | 634.3818 | -0.13368 | 0.039351 | -3.39703 | 0.000681 | 0.012332 | 2.225762 |
| ENSG00000074657 | 2288.064 | -0.12278 | 0.036479 | -3.36584 | 0.000763 | 0.012332 | 2.492774 |
| ENSG00000261971 | 54.93769 | -0.34612 | 0.096091 | -3.60207 | 0.000316 | 0.01239  | 1.023066 |
| ENSG00000140157 | 301.2509 | 0.173668 | 0.050708 | 3.424866 | 0.000615 | 0.01239  | 1.995423 |
| ENSG00000273079 | 7048.87  | 0.183297 | 0.054524 | 3.361775 | 0.000774 | 0.01239  | 2.514347 |
| ENSG00000188674 | 211.281  | 0.280827 | 0.082036 | 3.42323  | 0.000619 | 0.012439 | 1.995423 |
| ENSG00000279278 | 228.6504 | -0.22478 | 0.065358 | -3.43921 | 0.000583 | 0.012441 | 1.867169 |
| ENSG00000163904 | 956.3412 | 0.108542 | 0.032005 | 3.391428 | 0.000695 | 0.012441 | 2.225762 |
| ENSG00000229180 | 579.1741 | -0.20673 | 0.06108  | -3.38456 | 0.000713 | 0.012441 | 2.295759 |
| ENSG00000088986 | 1392.056 | 0.221245 | 0.065391 | 3.383429 | 0.000716 | 0.012441 | 2.293762 |
| ENSG00000119125 | 2210.334 | 0.292639 | 0.087092 | 3.360127 | 0.000779 | 0.012441 | 2.492774 |
| ENSG00000120896 | 491.9117 | -0.24579 | 0.073341 | -3.35139 | 0.000804 | 0.012441 | 2.583187 |

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| ENSG00000124535 | 596.8058 | 0.116426 | 0.034746 | 3.350777 | 0.000806 | 0.012441 | 2.583187 |
| ENSG00000136731 | 1278.092 | 0.09569  | 0.028293 | 3.382074 | 0.000719 | 0.012457 | 2.295759 |
| ENSG00000242265 | 2530.556 | 0.251424 | 0.0749   | 3.356787 | 0.000789 | 0.012457 | 2.514347 |
| ENSG00000117751 | 315.4274 | 0.148216 | 0.043837 | 3.381089 | 0.000722 | 0.012479 | 2.295759 |
| ENSG00000155275 | 471.5826 | -0.17899 | 0.052435 | -3.41355 | 0.000641 | 0.012537 | 2.025126 |
| ENSG00000163291 | 538.308  | 0.153472 | 0.045414 | 3.379371 | 0.000727 | 0.012537 | 2.295759 |
| ENSG00000183011 | 316.708  | 0.215239 | 0.063081 | 3.412088 | 0.000645 | 0.012564 | 2.025126 |
| ENSG00000185787 | 2103.533 | 0.126574 | 0.03747  | 3.378045 | 0.00073  | 0.012564 | 2.295759 |
| ENSG00000139278 | 192.4338 | 0.281032 | 0.0832   | 3.377792 | 0.000731 | 0.012564 | 2.295759 |
| ENSG00000164346 | 297.2553 | 0.254783 | 0.074599 | 3.415361 | 0.000637 | 0.012585 | 1.995423 |
| ENSG00000128524 | 363.2868 | 0.190935 | 0.056412 | 3.38466  | 0.000713 | 0.012607 | 2.225762 |
| ENSG00000173852 | 1098.299 | 0.243276 | 0.072602 | 3.350808 | 0.000806 | 0.012607 | 2.514347 |
| ENSG00000154174 | 1345.755 | 0.195589 | 0.057995 | 3.372499 | 0.000745 | 0.012751 | 2.295759 |
| ENSG00000136935 | 515.7854 | -0.13186 | 0.039022 | -3.37902 | 0.000727 | 0.012806 | 2.225762 |
| ENSG00000145730 | 1688.942 | 0.219063 | 0.064991 | 3.370681 | 0.00075  | 0.012806 | 2.293762 |
| ENSG00000122545 | 5596.046 | 0.145832 | 0.043593 | 3.345322 | 0.000822 | 0.012806 | 2.514347 |
| ENSG00000123395 | 106.3934 | 0.23812  | 0.067185 | 3.544253 | 0.000394 | 0.01282  | 1.201846 |
| ENSG00000184517 | 388.977  | 0.171913 | 0.05046  | 3.406907 | 0.000657 | 0.012858 | 1.995423 |
| ENSG00000106723 | 2562.473 | 0.136744 | 0.040821 | 3.349854 | 0.000809 | 0.012858 | 2.456745 |
| ENSG00000062725 | 1402.85  | 0.152688 | 0.045346 | 3.367151 | 0.000759 | 0.012916 | 2.293762 |
| ENSG00000066583 | 100.1494 | 0.278013 | 0.078439 | 3.544316 | 0.000394 | 0.01294  | 1.182918 |
| ENSG00000102003 | 5719.8   | 0.256748 | 0.076802 | 3.342979 | 0.000829 | 0.01294  | 2.492774 |
| ENSG00000198740 | 1334.244 | 0.185766 | 0.055733 | 3.33316  | 0.000859 | 0.01294  | 2.583187 |
| ENSG00000118242 | 141.9036 | 0.240168 | 0.07119  | 3.373609 | 0.000742 | 0.012948 | 2.225762 |
| ENSG00000108561 | 426.6094 | 0.189246 | 0.056247 | 3.364561 | 0.000767 | 0.012958 | 2.295759 |
| ENSG00000092140 | 405.4104 | 0.141619 | 0.041628 | 3.401962 | 0.000669 | 0.012983 | 1.995423 |
| ENSG00000119574 | 150.8532 | -0.20563 | 0.060898 | -3.37659 | 0.000734 | 0.012983 | 2.189833 |
| ENSG00000215397 | 37.62081 | -0.64802 | 0.181031 | -3.57963 | 0.000344 | 0.013037 | 1.020896 |
| ENSG00000087053 | 996.5976 | 0.179387 | 0.053893 | 3.328599 | 0.000873 | 0.013057 | 2.583187 |
| ENSG00000140015 | 966.4966 | 0.239464 | 0.071268 | 3.360068 | 0.000779 | 0.013113 | 2.293762 |

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| ENSG00000073969 | 3152.774 | 0.264727 | 0.079395 | 3.334304 | 0.000855 | 0.013114 | 2.514347 |
| ENSG00000100425 | 689.1819 | -0.14082 | 0.041921 | -3.35915 | 0.000782 | 0.013118 | 2.295759 |
| ENSG00000086102 | 913.651  | -0.12865 | 0.038694 | -3.32481 | 0.000885 | 0.01318  | 2.583187 |
| ENSG00000142864 | 1322.589 | 0.118826 | 0.035744 | 3.324367 | 0.000886 | 0.013187 | 2.583187 |
| ENSG00000163818 | 437.3077 | 0.178331 | 0.052589 | 3.391007 | 0.000696 | 0.013191 | 2.025126 |
| ENSG00000120705 | 795.3251 | 0.146477 | 0.044068 | 3.323861 | 0.000888 | 0.013191 | 2.583187 |
| ENSG00000156030 | 1031.347 | -0.14704 | 0.043813 | -3.35599 | 0.000791 | 0.0132   | 2.295759 |
| ENSG00000198818 | 211.5074 | 0.171219 | 0.050177 | 3.41229  | 0.000644 | 0.013207 | 1.867169 |
| ENSG00000178568 | 2320.941 | 0.194739 | 0.058438 | 3.332418 | 0.000861 | 0.013208 | 2.492774 |
| ENSG00000121858 | 67.06577 | -0.707   | 0.197452 | -3.58064 | 0.000343 | 0.013211 | 0.989117 |
| ENSG00000127415 | 250.909  | -0.24764 | 0.073003 | -3.3922  | 0.000693 | 0.013211 | 1.995423 |
| ENSG00000173818 | 308.2285 | -0.15906 | 0.046892 | -3.39211 | 0.000694 | 0.013211 | 1.995423 |
| ENSG00000050030 | 828.2668 | 0.169512 | 0.050421 | 3.361913 | 0.000774 | 0.013211 | 2.225762 |
| ENSG00000188732 | 185.7903 | 0.227763 | 0.067751 | 3.361762 | 0.000774 | 0.013211 | 2.225762 |
| ENSG00000233321 | 207.6555 | -0.25344 | 0.075555 | -3.35442 | 0.000795 | 0.013211 | 2.295759 |
| ENSG00000138032 | 574.3534 | 0.160716 | 0.048386 | 3.321546 | 0.000895 | 0.013211 | 2.583187 |
| ENSG00000255247 | 11.42048 | -0.66112 | 0.164304 | -4.02374 | 5.73E-05 | 0.01324  | 0.163912 |
| ENSG00000183495 | 1859.696 | -0.15403 | 0.046208 | -3.33332 | 0.000858 | 0.01324  | 2.456745 |
| ENSG00000250722 | 233.8071 | 0.361904 | 0.106759 | 3.389913 | 0.000699 | 0.013262 | 1.995423 |
| ENSG00000170092 | 86.58892 | -0.29037 | 0.084568 | -3.4336  | 0.000596 | 0.013271 | 1.695647 |
| ENSG00000155876 | 632.9064 | 0.172408 | 0.051457 | 3.350512 | 0.000807 | 0.013271 | 2.295759 |
| ENSG00000165264 | 279.3237 | 0.205102 | 0.061225 | 3.349983 | 0.000808 | 0.013283 | 2.295759 |
| ENSG00000137825 | 443.5249 | 0.273449 | 0.080461 | 3.398536 | 0.000677 | 0.013301 | 1.918337 |
| ENSG00000036054 | 485.8977 | 0.13348  | 0.039858 | 3.348909 | 0.000811 | 0.013301 | 2.29693  |
| ENSG00000169032 | 1247.47  | 0.198532 | 0.05929  | 3.348494 | 0.000813 | 0.013314 | 2.295759 |
| ENSG00000198961 | 7986.767 | 0.192683 | 0.057888 | 3.328562 | 0.000873 | 0.013353 | 2.456745 |
| ENSG00000159720 | 1350.991 | 0.148581 | 0.044282 | 3.355292 | 0.000793 | 0.013359 | 2.225762 |
| ENSG00000069329 | 1897.914 | 0.190122 | 0.057126 | 3.328097 | 0.000874 | 0.013359 | 2.456745 |
| ENSG00000111229 | 458.9719 | 0.180391 | 0.053367 | 3.380197 | 0.000724 | 0.013392 | 2.025126 |
| ENSG00000104131 | 517.017  | 0.131888 | 0.03942  | 3.345708 | 0.000821 | 0.013392 | 2.293762 |

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| ENSG00000139163 | 1717.817 | 0.166114 | 0.050168 | 3.311165 | 0.000929 | 0.013448 | 2.583187 |
| ENSG00000127337 | 96.84985 | 0.289504 | 0.084505 | 3.425888 | 0.000613 | 0.013495 | 1.695647 |
| ENSG00000180901 | 1481.28  | 0.124569 | 0.037268 | 3.342495 | 0.00083  | 0.013495 | 2.295759 |
| ENSG00000185053 | 108.9886 | 0.257703 | 0.075823 | 3.398744 | 0.000677 | 0.013515 | 1.867169 |
| ENSG00000102890 | 100.5049 | -0.28093 | 0.079798 | -3.5205  | 0.000431 | 0.013559 | 1.182918 |
| ENSG00000182264 | 27.50924 | -0.43584 | 0.120851 | -3.60646 | 0.00031  | 0.013596 | 0.848718 |
| ENSG00000145782 | 688.7609 | 0.128419 | 0.038457 | 3.339301 | 0.00084  | 0.013596 | 2.295759 |
| ENSG00000156804 | 965.7151 | 0.208164 | 0.062188 | 3.347324 | 0.000816 | 0.013599 | 2.225762 |
| ENSG00000175606 | 198.0828 | 0.227277 | 0.067899 | 3.347281 | 0.000816 | 0.013599 | 2.225762 |
| ENSG00000147421 | 1186.162 | 0.143988 | 0.043128 | 3.338614 | 0.000842 | 0.013601 | 2.293762 |
| ENSG00000250571 | 156.7098 | -0.23288 | 0.0686   | -3.39476 | 0.000687 | 0.013603 | 1.867169 |
| ENSG00000116030 | 609.6683 | 0.168821 | 0.050577 | 3.337877 | 0.000844 | 0.013603 | 2.29693  |
| ENSG00000141577 | 196.2169 | -0.24469 | 0.072481 | -3.37588 | 0.000736 | 0.013622 | 1.995423 |
| ENSG00000141994 | 140.4252 | -0.24448 | 0.072761 | -3.36002 | 0.000779 | 0.013644 | 2.108016 |
| ENSG00000142230 | 780.7856 | 0.12923  | 0.038735 | 3.336225 | 0.000849 | 0.01365  | 2.293762 |
| ENSG00000278845 | 143.2345 | 0.185651 | 0.055456 | 3.347751 | 0.000815 | 0.013689 | 2.189833 |
| ENSG00000105819 | 703.3906 | 0.135881 | 0.041155 | 3.301713 | 0.000961 | 0.013689 | 2.583187 |
| ENSG00000254561 | 61.38345 | -0.57506 | 0.161509 | -3.56053 | 0.00037  | 0.013716 | 0.989117 |
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| ENSG00000152944 | 464.836  | 0.161054 | 0.048317 | 3.333284 | 0.000858 | 0.013716 | 2.295759 |
| ENSG00000133606 | 881.9217 | 0.114929 | 0.03448  | 3.333208 | 0.000859 | 0.013716 | 2.293762 |
| ENSG00000139287 | 18.99639 | 0.603762 | 0.163282 | 3.697675 | 0.000218 | 0.013752 | 0.578677 |
| ENSG00000019505 | 2054.996 | 0.181835 | 0.054576 | 3.331748 | 0.000863 | 0.013752 | 2.295759 |
| ENSG00000124496 | 462.1991 | -0.2016  | 0.05963  | -3.38085 | 0.000723 | 0.013762 | 1.918337 |
| ENSG00000177613 | 546.6935 | 0.154797 | 0.046937 | 3.297973 | 0.000974 | 0.013762 | 2.583187 |
| ENSG00000183317 | 527.9433 | -0.19775 | 0.059379 | -3.33024 | 0.000868 | 0.01379  | 2.293762 |
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| ENSG00000198556 | 217.3639 | -0.17824 | 0.053428 | -3.33612 | 0.00085  | 0.013892 | 2.225762 |
| ENSG00000125520 | 167.8238 | -0.26626 | 0.079213 | -3.36136 | 0.000776 | 0.013925 | 2.025126 |
| ENSG00000127824 | 1424.425 | 0.260607 | 0.078349 | 3.32622  | 0.00088  | 0.013941 | 2.293762 |



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| ENSG00000243156 | 2540.903 | -0.17847 | 0.05408  | -3.30011 | 0.000966 | 0.013948 | 2.514347 |
| ENSG00000122584 | 270.1691 | 0.278282 | 0.082825 | 3.3599   | 0.00078  | 0.013953 | 2.025126 |
| ENSG00000196914 | 6835.426 | 0.127693 | 0.038676 | 3.30163  | 0.000961 | 0.013953 | 2.492774 |
| ENSG00000105662 | 1754.137 | -0.24779 | 0.075281 | -3.2916  | 0.000996 | 0.013953 | 2.583187 |
| ENSG00000126214 | 1066.517 | 0.113429 | 0.034468 | 3.290829 | 0.000999 | 0.013978 | 2.583187 |
| ENSG00000160949 | 134.6208 | -0.24752 | 0.073956 | -3.34689 | 0.000817 | 0.013989 | 2.108016 |
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| ENSG00000134108 | 1717.562 | 0.172854 | 0.051888 | 3.331275 | 0.000864 | 0.013998 | 2.225762 |
| ENSG00000149313 | 991.3393 | 0.19572  | 0.059375 | 3.296318 | 0.00098  | 0.014028 | 2.514347 |
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| ENSG00000141837 | 3262.342 | -0.20844 | 0.063445 | -3.28536 | 0.001019 | 0.014141 | 2.583187 |
| ENSG00000143977 | 85.04806 | 0.261854 | 0.074654 | 3.507563 | 0.000452 | 0.014178 | 1.142898 |
| ENSG00000145495 | 5247.899 | 0.141212 | 0.042584 | 3.316075 | 0.000913 | 0.014234 | 2.295759 |
| ENSG00000112110 | 287.3382 | 0.187171 | 0.056309 | 3.323974 | 0.000887 | 0.014252 | 2.225762 |
| ENSG00000075089 | 265.3189 | 0.203693 | 0.061443 | 3.315177 | 0.000916 | 0.014252 | 2.295759 |
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| ENSG00000179846 | 50.45896 | -0.34009 | 0.096238 | -3.53382 | 0.00041  | 0.014292 | 1.020896 |
| ENSG00000205302 | 506.677  | 0.148504 | 0.044819 | 3.313444 | 0.000922 | 0.014292 | 2.29693  |
| ENSG00000091164 | 1231.572 | 0.146076 | 0.043979 | 3.321535 | 0.000895 | 0.014314 | 2.225762 |
| ENSG00000138660 | 360.9156 | 0.182872 | 0.054568 | 3.351282 | 0.000804 | 0.014319 | 1.995423 |
| ENSG00000131171 | 1004.726 | 0.18747  | 0.056596 | 3.312451 | 0.000925 | 0.014319 | 2.295759 |
| ENSG00000100811 | 1365.256 | 0.106218 | 0.032406 | 3.277752 | 0.001046 | 0.014366 | 2.583187 |
| ENSG00000187391 | 3959.64  | -0.10393 | 0.03171  | -3.27764 | 0.001047 | 0.014366 | 2.583187 |
| ENSG00000104490 | 2293.817 | 0.301    | 0.091669 | 3.283553 | 0.001025 | 0.01444  | 2.514347 |
| ENSG00000104388 | 1609.449 | 0.183918 | 0.056148 | 3.275576 | 0.001054 | 0.014444 | 2.583187 |
| ENSG00000259666 | 44.90322 | -0.42579 | 0.120892 | -3.52205 | 0.000428 | 0.014473 | 1.044965 |
| ENSG00000135932 | 1965.106 | 0.158672 | 0.048249 | 3.288621 | 0.001007 | 0.014473 | 2.456745 |
| ENSG00000126821 | 388.7051 | 0.154355 | 0.046144 | 3.345064 | 0.000823 | 0.014546 | 1.995423 |

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| ENSG00000124380 | 285.5455 | 0.140994 | 0.042231 | 3.338612 | 0.000842 | 0.014655 | 2.025126 |
| ENSG00000196376 | 1222.633 | 0.198033 | 0.060461 | 3.275376 | 0.001055 | 0.014779 | 2.514347 |
| ENSG00000144290 | 3126.407 | 0.19125  | 0.058535 | 3.267248 | 0.001086 | 0.014791 | 2.583187 |
| ENSG00000279792 | 74.29747 | -0.25058 | 0.071966 | -3.48194 | 0.000498 | 0.014791 | 1.182918 |
| ENSG00000280222 | 171.4279 | -0.3229  | 0.096706 | -3.33902 | 0.000841 | 0.014795 | 1.995423 |
| ENSG00000068654 | 1261.468 | -0.12523 | 0.038266 | -3.27276 | 0.001065 | 0.01486  | 2.514347 |
| ENSG00000110955 | 3936.117 | 0.231121 | 0.070591 | 3.274081 | 0.00106  | 0.014904 | 2.492774 |
| ENSG00000145794 | 1251.546 | 0.214996 | 0.065734 | 3.27067  | 0.001073 | 0.014942 | 2.514347 |
| ENSG00000147526 | 5341.144 | 0.141385 | 0.043257 | 3.268503 | 0.001081 | 0.015042 | 2.514347 |
| ENSG00000176444 | 402.4087 | -0.14831 | 0.044912 | -3.30218 | 0.000959 | 0.015064 | 2.225762 |
| ENSG00000144366 | 266.8848 | 0.235013 | 0.070624 | 3.327686 | 0.000876 | 0.015098 | 2.025126 |
| ENSG00000113558 | 2330.465 | 0.156055 | 0.0479   | 3.257924 | 0.001122 | 0.015155 | 2.583187 |
| ENSG00000022267 | 1612.371 | 0.155006 | 0.047117 | 3.289768 | 0.001003 | 0.015221 | 2.295759 |
| ENSG00000227398 | 194.0466 | -0.16633 | 0.049971 | -3.32856 | 0.000873 | 0.015226 | 1.995423 |
| ENSG00000076984 | 331.1749 | -0.16488 | 0.049552 | -3.32735 | 0.000877 | 0.015226 | 1.995423 |
| ENSG00000184232 | 313.4588 | -0.30563 | 0.091961 | -3.32345 | 0.000889 | 0.015226 | 2.025126 |
| ENSG00000072818 | 136.0819 | -0.24933 | 0.075508 | -3.30208 | 0.00096  | 0.015226 | 2.189833 |
| ENSG00000142507 | 387.2648 | 0.184595 | 0.055992 | 3.296831 | 0.000978 | 0.015226 | 2.225762 |
| ENSG00000076108 | 1346.86  | -0.14663 | 0.044941 | -3.26272 | 0.001103 | 0.015226 | 2.514347 |
| ENSG00000140280 | 248.013  | 0.187531 | 0.05704  | 3.287719 | 0.00101  | 0.015228 | 2.295759 |
| ENSG00000155846 | 650.8276 | -0.1376  | 0.041855 | -3.28752 | 0.001011 | 0.015228 | 2.295759 |
| ENSG00000070761 | 231.773  | 0.223041 | 0.067151 | 3.321487 | 0.000895 | 0.015279 | 2.025126 |
| ENSG00000106367 | 578.3222 | 0.195076 | 0.059211 | 3.294581 | 0.000986 | 0.015289 | 2.225762 |
| ENSG00000269858 | 221.5118 | -0.18117 | 0.054208 | -3.34208 | 0.000832 | 0.015361 | 1.867169 |
| ENSG00000128563 | 358.9753 | -0.15459 | 0.046526 | -3.32276 | 0.000891 | 0.015393 | 1.995423 |
| ENSG00000134248 | 180.7908 | 0.215524 | 0.065483 | 3.291296 | 0.000997 | 0.015426 | 2.225762 |
| ENSG00000172575 | 646.7184 | 0.224678 | 0.069164 | 3.248493 | 0.00116  | 0.015448 | 2.583187 |
| ENSG00000114480 | 212.5575 | 0.217482 | 0.066128 | 3.288823 | 0.001006 | 0.015533 | 2.225762 |
| ENSG00000041357 | 422.9224 | 0.164591 | 0.050189 | 3.279431 | 0.00104  | 0.015541 | 2.295759 |
| ENSG00000163682 | 1731.883 | 0.214859 | 0.066192 | 3.245988 | 0.00117  | 0.015541 | 2.583187 |

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| ENSG00000134153 | 216.3511 | 0.187706 | 0.056606 | 3.316013 | 0.000913 | 0.015681 | 1.995423 |
| ENSG00000126261 | 992.229  | 0.133936 | 0.040771 | 3.285108 | 0.001019 | 0.015681 | 2.225762 |
| ENSG00000111269 | 1005.1   | 0.173525 | 0.053396 | 3.249785 | 0.001155 | 0.015711 | 2.514347 |
| ENSG00000153936 | 590.3995 | 0.191107 | 0.058957 | 3.241449 | 0.001189 | 0.015732 | 2.583187 |
| ENSG00000038532 | 1381.441 | -0.12444 | 0.038401 | -3.24042 | 0.001194 | 0.015775 | 2.583187 |
| ENSG00000164764 | 50.6307  | 0.376641 | 0.107474 | 3.504493 | 0.000457 | 0.015776 | 0.989117 |
| ENSG00000076003 | 211.9249 | 0.215366 | 0.065027 | 3.311969 | 0.000926 | 0.015822 | 1.995423 |
| ENSG00000196378 | 197.5189 | -0.21974 | 0.066976 | -3.28091 | 0.001035 | 0.015828 | 2.225762 |
| ENSG00000240024 | 130.4223 | 0.205296 | 0.062512 | 3.284097 | 0.001023 | 0.015892 | 2.189833 |
| ENSG00000174405 | 469.836  | 0.182401 | 0.055631 | 3.27875  | 0.001043 | 0.01592  | 2.225762 |
| ENSG00000197043 | 3481.224 | 0.198964 | 0.060864 | 3.269018 | 0.001079 | 0.015947 | 2.295759 |
| ENSG00000204469 | 4660.031 | -0.14869 | 0.045755 | -3.24978 | 0.001155 | 0.015947 | 2.456745 |
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| ENSG00000112902 | 953.8934 | 0.223119 | 0.068276 | 3.26788  | 0.001084 | 0.015995 | 2.293762 |
| ENSG00000155189 | 614.122  | 0.140971 | 0.043042 | 3.275195 | 0.001056 | 0.016019 | 2.225762 |
| ENSG00000231312 | 471.2905 | -0.1619  | 0.049564 | -3.26646 | 0.001089 | 0.016019 | 2.295759 |
| ENSG00000178980 | 2776.971 | 0.137719 | 0.042598 | 3.233016 | 0.001225 | 0.016019 | 2.583187 |
| ENSG00000103342 | 1469.933 | 0.107278 | 0.033187 | 3.232522 | 0.001227 | 0.016025 | 2.583187 |
| ENSG00000153339 | 970.5001 | 0.127067 | 0.038808 | 3.274238 | 0.001059 | 0.016029 | 2.225762 |
| ENSG00000125826 | 526.5271 | -0.16285 | 0.049865 | -3.26592 | 0.001091 | 0.016029 | 2.293762 |
| ENSG00000184678 | 338.9535 | -0.23963 | 0.072611 | -3.30026 | 0.000966 | 0.016048 | 2.025126 |
| ENSG00000184863 | 1743.325 | -0.14352 | 0.043972 | -3.26393 | 0.001099 | 0.016077 | 2.295759 |
| ENSG00000014824 | 1526.777 | 0.17722  | 0.054298 | 3.263858 | 0.001099 | 0.016077 | 2.295759 |
| ENSG00000033867 | 1338.581 | 0.18308  | 0.055956 | 3.27184  | 0.001069 | 0.016107 | 2.225762 |
| ENSG00000133169 | 1431.051 | 0.278352 | 0.086215 | 3.228562 | 0.001244 | 0.016145 | 2.583187 |
| ENSG00000272335 | 286.7363 | 0.180464 | 0.055189 | 3.269963 | 0.001076 | 0.016185 | 2.225762 |
| ENSG00000100519 | 713.2807 | 0.169258 | 0.052487 | 3.22477  | 0.001261 | 0.016331 | 2.583187 |
| ENSG00000135597 | 1395.194 | -0.13298 | 0.040815 | -3.25821 | 0.001121 | 0.016341 | 2.293762 |
| ENSG00000240583 | 726.7186 | 0.626509 | 0.19185  | 3.265621 | 0.001092 | 0.016391 | 2.225762 |
| ENSG00000269044 | 130.1414 | -0.19841 | 0.060787 | -3.26407 | 0.001098 | 0.016436 | 2.225762 |

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| ENSG00000166848 | 1717.127 | 0.173551 | 0.053309 | 3.25554  | 0.001132 | 0.016436 | 2.295759 |
| ENSG00000118564 | 1600.434 | 0.117021 | 0.036233 | 3.22967  | 0.001239 | 0.016436 | 2.514347 |
| ENSG00000103042 | 321.1915 | -0.16084 | 0.049333 | -3.2604  | 0.001113 | 0.016635 | 2.225762 |
| ENSG00000260022 | 12.03889 | -0.63084 | 0.174741 | -3.61018 | 0.000306 | 0.016682 | 0.60691  |
| ENSG00000152207 | 89.76717 | -0.42668 | 0.127916 | -3.3356  | 0.000851 | 0.016682 | 1.695647 |
| ENSG00000075303 | 422.3135 | 0.187082 | 0.056682 | 3.300539 | 0.000965 | 0.016682 | 1.918337 |
| ENSG00000141429 | 472.6681 | 0.187172 | 0.056915 | 3.288645 | 0.001007 | 0.016682 | 1.995423 |
| ENSG00000269069 | 160.4956 | -0.22382 | 0.068608 | -3.26238 | 0.001105 | 0.016682 | 2.189833 |
| ENSG00000143207 | 610.2037 | 0.125956 | 0.038765 | 3.24919  | 0.001157 | 0.016682 | 2.293762 |
| ENSG00000138138 | 1007.128 | 0.185178 | 0.056995 | 3.249006 | 0.001158 | 0.016682 | 2.293762 |
| ENSG00000044115 | 2182.874 | 0.118891 | 0.036878 | 3.223936 | 0.001264 | 0.016682 | 2.514347 |
| ENSG00000174327 | 19.49917 | -0.49493 | 0.136828 | -3.61721 | 0.000298 | 0.016821 | 0.583933 |
| ENSG00000227500 | 446.4399 | -0.16513 | 0.050257 | -3.28568 | 0.001017 | 0.016821 | 1.995423 |
| ENSG00000133107 | 165.7535 | 0.267433 | 0.082409 | 3.245204 | 0.001174 | 0.016847 | 2.295759 |
| ENSG00000240891 | 662.4005 | 0.274171 | 0.084509 | 3.244302 | 0.001177 | 0.016877 | 2.29693  |
| ENSG00000277449 | 69.047   | -0.27132 | 0.078078 | -3.47498 | 0.000511 | 0.016947 | 0.989117 |
| ENSG00000164081 | 282.6209 | 0.139129 | 0.042445 | 3.27786  | 0.001046 | 0.016947 | 2.025126 |
| ENSG00000127995 | 1030.243 | 0.179811 | 0.055459 | 3.242254 | 0.001186 | 0.016947 | 2.293762 |
| ENSG00000162989 | 1299.006 | 0.181081 | 0.055854 | 3.242034 | 0.001187 | 0.016947 | 2.293762 |
| ENSG00000166971 | 640.241  | 0.121031 | 0.037336 | 3.24165  | 0.001188 | 0.016947 | 2.29693  |
| ENSG00000178234 | 967.5419 | 0.138879 | 0.043292 | 3.207967 | 0.001337 | 0.016947 | 2.583187 |
| ENSG00000184076 | 238.9393 | 0.251018 | 0.076633 | 3.275593 | 0.001054 | 0.017036 | 2.025126 |
| ENSG00000166557 | 268.3767 | 0.164479 | 0.050783 | 3.238837 | 0.0012   | 0.017076 | 2.295759 |
| ENSG00000159082 | 2887.401 | 0.187386 | 0.05828  | 3.215266 | 0.001303 | 0.017076 | 2.492774 |
| ENSG00000151366 | 312.6644 | 0.192993 | 0.058981 | 3.272117 | 0.001067 | 0.017192 | 2.025126 |
| ENSG00000121905 | 955.0631 | 0.211567 | 0.065366 | 3.236642 | 0.001209 | 0.017192 | 2.293762 |
| ENSG00000185730 | 264.2551 | -0.17126 | 0.052258 | -3.27728 | 0.001048 | 0.017245 | 1.977088 |
| ENSG00000154822 | 710.1947 | 0.167171 | 0.051533 | 3.243945 | 0.001179 | 0.017245 | 2.225762 |
| ENSG00000126698 | 679.0386 | 0.158998 | 0.049153 | 3.234758 | 0.001217 | 0.017245 | 2.295759 |
| ENSG00000176903 | 1638.301 | 0.133105 | 0.041083 | 3.239941 | 0.001196 | 0.017452 | 2.225762 |

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| ENSG00000177679 | 1101.339 | -0.21025 | 0.064938 | -3.23771 | 0.001205 | 0.017557 | 2.225762 |
| ENSG00000272505 | 404.3334 | -0.19875 | 0.06091  | -3.26303 | 0.001102 | 0.017612 | 2.025126 |
| ENSG00000071553 | 1445.419 | 0.159112 | 0.049704 | 3.20118  | 0.001369 | 0.017612 | 2.514347 |
| ENSG00000144711 | 5866.227 | -0.14887 | 0.046621 | -3.19329 | 0.001407 | 0.017612 | 2.583187 |
| ENSG00000115568 | 663.1171 | -0.14602 | 0.045731 | -3.19308 | 0.001408 | 0.017612 | 2.583187 |
| ENSG00000259495 | 182.9182 | -0.18995 | 0.05782  | -3.28522 | 0.001019 | 0.017623 | 1.867169 |
| ENSG00000163444 | 586.0264 | 0.186072 | 0.05771  | 3.224249 | 0.001263 | 0.017734 | 2.295759 |
| ENSG00000127022 | 5324.195 | 0.141844 | 0.044258 | 3.204953 | 0.001351 | 0.017734 | 2.456745 |
| ENSG00000059145 | 316.8309 | -0.19486 | 0.059791 | -3.25899 | 0.001118 | 0.017774 | 2.025126 |
| ENSG00000166747 | 1667.038 | 0.106151 | 0.032932 | 3.223359 | 0.001267 | 0.017774 | 2.293762 |
| ENSG00000110218 | 333.3292 | 0.235623 | 0.073146 | 3.22129  | 0.001276 | 0.017872 | 2.295759 |
| ENSG00000225756 | 35.74854 | -0.39309 | 0.11408  | -3.44576 | 0.000569 | 0.017918 | 1.020896 |
| ENSG00000009950 | 379.038  | -0.24987 | 0.076421 | -3.26961 | 0.001077 | 0.01794  | 1.918337 |
| ENSG00000180287 | 185.0822 | 0.236681 | 0.072713 | 3.255012 | 0.001134 | 0.01794  | 2.025126 |
| ENSG00000103091 | 701.9846 | -0.13058 | 0.040451 | -3.22799 | 0.001247 | 0.01794  | 2.225762 |
| ENSG00000073050 | 203.0472 | -0.15222 | 0.047166 | -3.22735 | 0.001249 | 0.01794  | 2.225762 |
| ENSG00000108424 | 1958.759 | 0.097359 | 0.030424 | 3.200106 | 0.001374 | 0.01794  | 2.456745 |
| ENSG00000169504 | 1506.129 | 0.259041 | 0.081136 | 3.192685 | 0.00141  | 0.01794  | 2.514347 |
| ENSG00000102271 | 303.6811 | 0.249368 | 0.076554 | 3.257396 | 0.001124 | 0.017988 | 1.995423 |
| ENSG00000136450 | 668.8132 | 0.116343 | 0.036164 | 3.21705  | 0.001295 | 0.017988 | 2.29693  |
| ENSG00000028310 | 588.0431 | -0.1326  | 0.04168  | -3.18129 | 0.001466 | 0.018091 | 2.583187 |
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| ENSG00000197860 | 1837.076 | 0.176532 | 0.055522 | 3.179505 | 0.001475 | 0.018172 | 2.583187 |
| ENSG00000279759 | 245.5191 | -0.23664 | 0.072898 | -3.2462  | 0.00117  | 0.018328 | 2.025126 |
| ENSG00000162415 | 270.6757 | -0.1261  | 0.039169 | -3.21932 | 0.001285 | 0.018328 | 2.225762 |
| ENSG00000171314 | 713.4036 | 0.210498 | 0.066267 | 3.176499 | 0.001491 | 0.018328 | 2.583187 |
| ENSG00000169139 | 999.8571 | 0.174449 | 0.054363 | 3.208941 | 0.001332 | 0.018401 | 2.293762 |
| ENSG00000124795 | 722.7205 | 0.146987 | 0.0463   | 3.174641 | 0.0015   | 0.018401 | 2.583187 |
| ENSG00000120992 | 223.8563 | 0.2068   | 0.063664 | 3.248328 | 0.001161 | 0.018407 | 1.995423 |

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| ENSG00000213923  | 967.2384 | -0.12217 | 0.037979 | -3.21676 | 0.001296 | 0.018407 | 2.225762 |
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| ENSG00000163625  | 5514.974 | 0.07811  | 0.024351 | 3.207608 | 0.001338 | 0.018408 | 2.295759 |
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| ENSG00000168291  | 471.9417 | 0.203039 | 0.063365 | 3.204272 | 0.001354 | 0.018543 | 2.295759 |
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| ENSG00000215440  | 123.9863 | -0.25856 | 0.079358 | -3.25817 | 0.001121 | 0.01879  | 1.867169 |
| ENSG00000176209  | 167.9247 | 0.21213  | 0.066127 | 3.20792  | 0.001337 | 0.01879  | 2.225762 |
| ENSG00000165023  | 4248.079 | 0.24541  | 0.07729  | 3.175185 | 0.001497 | 0.01879  | 2.492774 |
| ENSG00000168374  | 559.2347 | 0.152205 | 0.047606 | 3.197187 | 0.001388 | 0.018892 | 2.295759 |
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| ENSG00000177051  | 142.6654 | -0.19383 | 0.059586 | -3.253   | 0.001142 | 0.019003 | 1.867169 |
| ENSG00000158286  | 312.6318 | -0.21996 | 0.067965 | -3.23639 | 0.001211 | 0.019003 | 1.977088 |
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| ENSG00000113361  | 548.5886 | 0.233949 | 0.073239 | 3.194329 | 0.001402 | 0.019003 | 2.295759 |
| ENSG00000119396  | 1361.62  | 0.129876 | 0.040669 | 3.193462 | 0.001406 | 0.019003 | 2.293762 |
| ENSG00000154473  | 616.459  | 0.130306 | 0.040806 | 3.193316 | 0.001406 | 0.019003 | 2.293762 |
| ENSG00000158458  | 158.2323 | -0.17558 | 0.055059 | -3.18894 | 0.001428 | 0.019003 | 2.338927 |
| ENSG00000198198  | 1778.416 | -0.15808 | 0.049535 | -3.19134 | 0.001416 | 0.019101 | 2.295759 |
| ENSG00000113262  | 77.79762 | -0.2986  | 0.088514 | -3.37344 | 0.000742 | 0.01911  | 1.201846 |
| ENSG00000161203  | 3358.532 | 0.163783 | 0.051649 | 3.171054 | 0.001519 | 0.019112 | 2.456745 |
| ENSG00000163644  | 2691.605 | 0.129792 | 0.041136 | 3.155237 | 0.001604 | 0.019175 | 2.583187 |
| ENSG00000169783  | 1132.373 | -0.22712 | 0.07122  | -3.18896 | 0.001428 | 0.019194 | 2.295759 |

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| ENSG00000145864 | 5213.204 | 0.216094 | 0.068346 | 3.161765 | 0.001568 | 0.01922  | 2.514347 |
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| ENSG00000136738 | 535.7108 | 0.168382 | 0.052863 | 3.185224 | 0.001446 | 0.019289 | 2.29693  |
| ENSG00000224383 | 36.79595 | 0.492965 | 0.144873 | 3.402745 | 0.000667 | 0.019386 | 1.053218 |
| ENSG00000004139 | 259.9529 | -0.16548 | 0.051425 | -3.21792 | 0.001291 | 0.019386 | 2.025126 |
| ENSG00000131508 | 702.5267 | 0.134734 | 0.04232  | 3.183693 | 0.001454 | 0.019386 | 2.293762 |
| ENSG00000149218 | 1762.284 | 0.185605 | 0.058322 | 3.182441 | 0.00146  | 0.019386 | 2.295759 |
| ENSG00000153902 | 875.0778 | -0.21002 | 0.066003 | -3.182   | 0.001463 | 0.019386 | 2.295759 |
| ENSG00000275342 | 347.883  | -0.2483  | 0.078033 | -3.18195 | 0.001463 | 0.019386 | 2.295759 |
| ENSG00000164924 | 5719.454 | 0.176005 | 0.055734 | 3.157952 | 0.001589 | 0.019386 | 2.492774 |
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| ENSG00000089737 | 3723.111 | 0.166859 | 0.053006 | 3.147942 | 0.001644 | 0.019386 | 2.583187 |
| ENSG00000136463 | 149.9546 | 0.190918 | 0.059553 | 3.205876 | 0.001347 | 0.019405 | 2.108016 |
| ENSG00000119401 | 438.5523 | 0.133678 | 0.042024 | 3.18101  | 0.001468 | 0.019405 | 2.295759 |
| ENSG00000233436 | 102.0111 | -0.25022 | 0.074316 | -3.36691 | 0.00076  | 0.019442 | 1.182918 |
| ENSG00000160961 | 472.4979 | -0.16616 | 0.051417 | -3.23156 | 0.001231 | 0.019442 | 1.918337 |
| ENSG00000116791 | 156.1246 | 0.325723 | 0.101644 | 3.204551 | 0.001353 | 0.019442 | 2.108016 |
| ENSG00000187109 | 3459.255 | 0.126041 | 0.039974 | 3.153076 | 0.001616 | 0.019442 | 2.514347 |
| ENSG00000229020 | 21.65936 | -0.55411 | 0.144144 | -3.84414 | 0.000121 | 0.019529 | 0.187229 |
| ENSG00000110492 | 67.45768 | -0.42846 | 0.123984 | -3.45576 | 0.000549 | 0.019529 | 0.848718 |
| ENSG00000197362 | 246.5822 | -0.17312 | 0.053781 | -3.21907 | 0.001286 | 0.019632 | 1.977088 |
| ENSG00000087095 | 1895.035 | 0.136077 | 0.042852 | 3.175517 | 0.001496 | 0.019647 | 2.295759 |
| ENSG00000267169 | 113.1552 | -0.26442 | 0.08292  | -3.18889 | 0.001428 | 0.019651 | 2.189833 |
| ENSG00000172465 | 273.3595 | 0.184384 | 0.057304 | 3.217635 | 0.001293 | 0.019672 | 1.977088 |

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| ENSG00000145348 | 917.1766 | 0.117138 | 0.036897 | 3.174687 | 0.0015   | 0.019672 | 2.293762 |
| ENSG00000226237 | 34.20145 | -0.3724  | 0.10958  | -3.39847 | 0.000678 | 0.019673 | 1.035363 |
| ENSG00000052795 | 1463.991 | 0.136923 | 0.043503 | 3.147445 | 0.001647 | 0.019674 | 2.514347 |
| ENSG00000280434 | 88.29491 | -0.34512 | 0.102404 | -3.37018 | 0.000751 | 0.019702 | 1.142898 |
| ENSG00000185728 | 992.8187 | 0.119011 | 0.037826 | 3.146314 | 0.001653 | 0.019702 | 2.514347 |
| ENSG00000139364 | 3640.909 | 0.101504 | 0.03234  | 3.138611 | 0.001698 | 0.019702 | 2.583187 |
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| ENSG00000105605 | 593.9509 | -0.16153 | 0.050917 | -3.17252 | 0.001511 | 0.019707 | 2.293762 |
| ENSG00000168096 | 476.6292 | -0.15496 | 0.049391 | -3.13736 | 0.001705 | 0.019724 | 2.583187 |
| ENSG00000178163 | 637.1407 | 0.14837  | 0.046782 | 3.171537 | 0.001516 | 0.019725 | 2.295759 |
| ENSG00000231824 | 18.03484 | 0.637618 | 0.179637 | 3.549473 | 0.000386 | 0.019725 | 0.583933 |
| ENSG00000175727 | 1009.405 | -0.17293 | 0.054998 | -3.14424 | 0.001665 | 0.019746 | 2.514347 |
| ENSG00000129460 | 201.5149 | 0.162235 | 0.051026 | 3.179442 | 0.001476 | 0.01975  | 2.225762 |
| ENSG00000205482 | 48.25809 | -0.32835 | 0.095223 | -3.44828 | 0.000564 | 0.019787 | 0.848718 |
| ENSG00000148154 | 580.8793 | 0.203302 | 0.06485  | 3.134964 | 0.001719 | 0.01979  | 2.583187 |
| ENSG00000105298 | 287.3495 | -0.16735 | 0.05281  | -3.16887 | 0.00153  | 0.019797 | 2.295759 |
| ENSG00000188612 | 591.4605 | 0.152109 | 0.048004 | 3.168658 | 0.001531 | 0.019797 | 2.295759 |
| ENSG00000101266 | 1449.952 | 0.083847 | 0.026685 | 3.142073 | 0.001678 | 0.019797 | 2.514347 |
| ENSG00000267904 | 65.26206 | -0.27232 | 0.080357 | -3.38881 | 0.000702 | 0.019917 | 1.044965 |
| ENSG00000125356 | 466.6388 | 0.224203 | 0.069688 | 3.217256 | 0.001294 | 0.019986 | 1.918337 |
| ENSG00000124333 | 380.3151 | 0.176424 | 0.055039 | 3.205447 | 0.001349 | 0.020004 | 1.995423 |
| ENSG00000145293 | 730.9114 | 0.187587 | 0.059275 | 3.164686 | 0.001553 | 0.020018 | 2.293762 |
| ENSG00000106052 | 1821.76  | 0.118272 | 0.037703 | 3.136904 | 0.001707 | 0.020068 | 2.514347 |
| ENSG00000287558 | 67.52559 | -0.53241 | 0.157285 | -3.38501 | 0.000712 | 0.020078 | 1.044965 |
| ENSG00000114735 | 326.5542 | -0.15102 | 0.04711  | -3.20572 | 0.001347 | 0.020078 | 1.977088 |
| ENSG00000204348 | 167.5176 | -0.15018 | 0.046941 | -3.19924 | 0.001378 | 0.020078 | 2.025126 |
| ENSG00000107679 | 2204.594 | 0.150924 | 0.04809  | 3.13836  | 0.001699 | 0.020078 | 2.492774 |
| ENSG00000261678 | 1087.725 | -0.34411 | 0.10977  | -3.13487 | 0.001719 | 0.020127 | 2.514347 |
| ENSG00000141084 | 387.478  | -0.14899 | 0.046369 | -3.21307 | 0.001313 | 0.020134 | 1.918337 |
| ENSG00000181191 | 695.9917 | 0.185921 | 0.058828 | 3.160447 | 0.001575 | 0.020149 | 2.295759 |

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| ENSG00000099341 | 813.9379 | 0.167749 | 0.053664 | 3.12594  | 0.001772 | 0.020149 | 2.583187 |
| ENSG00000170381 | 304.6037 | 0.451751 | 0.141167 | 3.200113 | 0.001374 | 0.0202   | 1.995423 |
| ENSG00000068912 | 761.1392 | 0.175195 | 0.05547  | 3.158343 | 0.001587 | 0.020263 | 2.295759 |
| ENSG00000027847 | 250.6515 | -0.13785 | 0.043165 | -3.19341 | 0.001406 | 0.020275 | 2.025126 |
| ENSG00000116141 | 996.8468 | 0.115553 | 0.036488 | 3.166852 | 0.001541 | 0.020275 | 2.225762 |
| ENSG00000171467 | 1002.286 | -0.13134 | 0.041478 | -3.1665  | 0.001543 | 0.020275 | 2.225762 |
| ENSG00000130770 | 546.3529 | 0.1553   | 0.049187 | 3.157309 | 0.001592 | 0.020275 | 2.29693  |
| ENSG00000163947 | 1061.133 | 0.164125 | 0.051983 | 3.157305 | 0.001592 | 0.020275 | 2.293762 |
| ENSG00000135930 | 484.9359 | 0.115947 | 0.03673  | 3.156729 | 0.001595 | 0.020279 | 2.295759 |
| ENSG00000241553 | 399.1282 | 0.144264 | 0.045704 | 3.15649  | 0.001597 | 0.020279 | 2.295759 |
| ENSG00000142039 | 224.0259 | -0.18004 | 0.056884 | -3.16515 | 0.00155  | 0.020289 | 2.225762 |
| ENSG00000234500 | 58.97846 | -0.36668 | 0.106805 | -3.43318 | 0.000597 | 0.020461 | 0.848718 |
| ENSG00000144848 | 332.7627 | 0.174136 | 0.054543 | 3.19263  | 0.00141  | 0.020519 | 1.995423 |
| ENSG00000166159 | 383.6066 | -0.18677 | 0.058572 | -3.18868 | 0.001429 | 0.020519 | 2.025126 |
| ENSG00000169714 | 1848.17  | 0.126805 | 0.04054  | 3.127901 | 0.001761 | 0.020519 | 2.492774 |
| ENSG00000286379 | 14.85021 | -0.51135 | 0.145097 | -3.5242  | 0.000425 | 0.020528 | 0.600464 |
| ENSG00000171617 | 10915.51 | 0.224983 | 0.072202 | 3.116045 | 0.001833 | 0.020559 | 2.583187 |
| ENSG00000143753 | 489.0084 | 0.139056 | 0.044626 | 3.116037 | 0.001833 | 0.020559 | 2.583187 |
| ENSG00000272595 | 45.51798 | -0.47436 | 0.140898 | -3.36669 | 0.000761 | 0.020889 | 1.053218 |
| ENSG00000170340 | 207.2078 | 0.210317 | 0.066099 | 3.181823 | 0.001464 | 0.020889 | 2.025126 |
| ENSG00000022355 | 3698.892 | 0.263735 | 0.084774 | 3.111044 | 0.001864 | 0.020889 | 2.583187 |
| ENSG00000123545 | 451.6214 | 0.246022 | 0.078228 | 3.144942 | 0.001661 | 0.020899 | 2.295759 |
| ENSG00000004897 | 1328.205 | 0.144719 | 0.046422 | 3.117489 | 0.001824 | 0.020936 | 2.514347 |
| ENSG00000105953 | 1898.863 | 0.121967 | 0.039041 | 3.124048 | 0.001784 | 0.020939 | 2.456745 |
| ENSG00000109445 | 201.3945 | 0.169683 | 0.053997 | 3.142442 | 0.001675 | 0.021029 | 2.295759 |
| ENSG00000116191 | 286.2493 | 0.1998   | 0.062775 | 3.182791 | 0.001459 | 0.021031 | 1.995423 |
| ENSG00000145391 | 1630.293 | 0.119449 | 0.038342 | 3.115347 | 0.001837 | 0.021031 | 2.514347 |
| ENSG00000122042 | 1745.583 | 0.128062 | 0.040764 | 3.141534 | 0.001681 | 0.021045 | 2.295759 |
| ENSG00000164751 | 317.5321 | 0.136754 | 0.043537 | 3.141116 | 0.001683 | 0.021053 | 2.295759 |
| ENSG00000160551 | 5108.8   | 0.107199 | 0.03413  | 3.140885 | 0.001684 | 0.021053 | 2.295759 |

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| ENSG00000114209 | 337.984  | 0.153993 | 0.049034 | 3.140555 | 0.001686 | 0.021053 | 2.295759 |
| ENSG00000110880 | 1264.531 | 0.097209 | 0.031299 | 3.105801 | 0.001898 | 0.021053 | 2.583187 |
| ENSG00000229894 | 40.15349 | -0.2887  | 0.085826 | -3.36383 | 0.000769 | 0.021065 | 1.044965 |
| ENSG00000112210 | 210.8097 | 0.20213  | 0.063657 | 3.175284 | 0.001497 | 0.021134 | 2.025126 |
| ENSG00000033178 | 999.5952 | 0.124588 | 0.039689 | 3.139117 | 0.001695 | 0.021134 | 2.293762 |
| ENSG00000168014 | 974.4576 | -0.09131 | 0.029095 | -3.1382  | 0.0017   | 0.021154 | 2.295759 |
| ENSG00000172824 | 877.8133 | -0.28625 | 0.09097  | -3.14667 | 0.001651 | 0.021181 | 2.225762 |
| ENSG00000134186 | 391.963  | 0.116976 | 0.037178 | 3.146329 | 0.001653 | 0.02119  | 2.225762 |
| ENSG00000164163 | 544.1711 | 0.159919 | 0.050979 | 3.136987 | 0.001707 | 0.021195 | 2.293762 |
| ENSG00000116667 | 2411.863 | 0.122044 | 0.03921  | 3.112582 | 0.001855 | 0.021195 | 2.492774 |
| ENSG00000136986 | 336.6797 | 0.144148 | 0.045442 | 3.172157 | 0.001513 | 0.021248 | 2.025126 |
| ENSG00000261879 | 149.8018 | -0.24073 | 0.07655  | -3.14471 | 0.001662 | 0.021248 | 2.225762 |
| ENSG00000172403 | 1278.835 | 0.28935  | 0.092033 | 3.143995 | 0.001667 | 0.021277 | 2.225762 |
| ENSG00000236908 | 42.96966 | -0.42018 | 0.12305  | -3.41468 | 0.000639 | 0.021364 | 0.848718 |
| ENSG00000163807 | 464.9913 | 0.151916 | 0.048373 | 3.140517 | 0.001687 | 0.021465 | 2.225762 |
| ENSG00000011677 | 496.6304 | 0.24156  | 0.07713  | 3.131854 | 0.001737 | 0.021465 | 2.295759 |
| ENSG00000139977 | 731.6775 | 0.129826 | 0.041454 | 3.131795 | 0.001737 | 0.021465 | 2.293762 |
| ENSG00000163125 | 1221.248 | -0.09353 | 0.029787 | -3.14008 | 0.001689 | 0.021481 | 2.225762 |
| ENSG00000172458 | 393.6317 | -0.23556 | 0.07504  | -3.13919 | 0.001694 | 0.021511 | 2.225762 |
| ENSG00000114405 | 336.1743 | 0.192491 | 0.061324 | 3.138909 | 0.001696 | 0.021511 | 2.225762 |
| ENSG00000132950 | 352.0238 | -0.13793 | 0.043943 | -3.13878 | 0.001697 | 0.021511 | 2.225762 |
| ENSG00000175497 | 1527.632 | 0.179943 | 0.05798  | 3.103544 | 0.001912 | 0.021511 | 2.514347 |
| ENSG00000156076 | 345.2835 | -0.55325 | 0.174517 | -3.17017 | 0.001523 | 0.02153  | 1.995423 |
| ENSG00000161057 | 633.7869 | 0.166242 | 0.052995 | 3.136963 | 0.001707 | 0.021611 | 2.225762 |
| ENSG00000169760 | 877.9898 | 0.137123 | 0.044222 | 3.100767 | 0.00193  | 0.021615 | 2.514347 |
| ENSG00000253649 | 431.5328 | -0.18024 | 0.057639 | -3.12707 | 0.001766 | 0.021637 | 2.295759 |
| ENSG00000205559 | 134.4269 | -0.20122 | 0.064465 | -3.12131 | 0.0018   | 0.021641 | 2.338927 |
| ENSG00000121067 | 670.8765 | 0.1142   | 0.036528 | 3.126395 | 0.00177  | 0.021654 | 2.295759 |
| ENSG00000105705 | 456.79   | -0.12817 | 0.04089  | -3.13445 | 0.001722 | 0.021715 | 2.225762 |
| ENSG00000145743 | 1126.667 | 0.122282 | 0.039134 | 3.124682 | 0.00178  | 0.021748 | 2.295759 |

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| ENSG00000147231 | 105.0878 | 0.306715 | 0.092555 | 3.313885 | 0.00092  | 0.021781 | 1.182918 |
| ENSG00000178662 | 3752.508 | 0.189105 | 0.061067 | 3.096693 | 0.001957 | 0.021781 | 2.514347 |
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| ENSG00000166603 | 24.76075 | 0.631761 | 0.187251 | 3.373864 | 0.000741 | 0.021855 | 0.947688 |
| ENSG00000164405 | 371.5494 | 0.201254 | 0.063648 | 3.161976 | 0.001567 | 0.021895 | 1.995423 |
| ENSG00000134970 | 666.2072 | 0.164419 | 0.052523 | 3.130416 | 0.001746 | 0.021895 | 2.225762 |
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| ENSG00000184575 | 1336.716 | 0.137301 | 0.044001 | 3.120384 | 0.001806 | 0.021937 | 2.293762 |
| ENSG00000205085 | 218.9479 | -0.23276 | 0.07374  | -3.15647 | 0.001597 | 0.021952 | 2.025126 |
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| ENSG00000127870 | 741.6794 | 0.15707  | 0.050218 | 3.127792 | 0.001761 | 0.021995 | 2.225762 |
| ENSG00000160883 | 70.08736 | -0.53648 | 0.15974  | -3.35843 | 0.000784 | 0.022011 | 0.989117 |
| ENSG00000160570 | 285.5638 | 0.199788 | 0.063246 | 3.158899 | 0.001584 | 0.022027 | 1.995423 |
| ENSG00000101752 | 2211.514 | 0.131019 | 0.042027 | 3.117485 | 0.001824 | 0.022035 | 2.295759 |
| ENSG00000136810 | 339.218  | 0.2222   | 0.070457 | 3.153722 | 0.001612 | 0.02206  | 2.025126 |
| ENSG00000120334 | 51.39193 | 0.264425 | 0.078775 | 3.356726 | 0.000789 | 0.022081 | 0.989117 |
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| ENSG00000169442 | 5.073635 | 1.059364 | 0.264492 | 4.005278 | 6.19E-05 | 0.022121 | 0.077262 |
| ENSG00000137727 | 628.1987 | 0.156862 | 0.050204 | 3.124518 | 0.001781 | 0.022121 | 2.225762 |
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| ENSG00000138801 | 852.483  | 0.180934 | 0.058596 | 3.087853 | 0.002016 | 0.022121 | 2.514347 |
| ENSG00000245025 | 95.48854 | -0.26229 | 0.081896 | -3.20267 | 0.001362 | 0.022137 | 1.695647 |
| ENSG00000186462 | 1154.772 | 0.220175 | 0.070706 | 3.11393  | 0.001846 | 0.022171 | 2.293762 |
| ENSG00000166847 | 2283.196 | 0.092519 | 0.029727 | 3.112291 | 0.001856 | 0.022259 | 2.295759 |
| ENSG00000138443 | 3896.136 | 0.108966 | 0.03532  | 3.085122 | 0.002035 | 0.022259 | 2.514347 |
| ENSG00000179832 | 2083.291 | -0.18196 | 0.058853 | -3.09172 | 0.00199  | 0.022264 | 2.456745 |
| ENSG00000249626 | 26.98589 | -0.43813 | 0.130441 | -3.35882 | 0.000783 | 0.022304 | 0.963911 |
| ENSG00000167447 | 193.1066 | 0.164744 | 0.051959 | 3.170658 | 0.001521 | 0.022318 | 1.867169 |
| ENSG00000108064 | 356.6175 | 0.137459 | 0.043622 | 3.151153 | 0.001626 | 0.022318 | 1.995423 |

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| ENSG00000119705 | 223.2336 | 0.219695 | 0.07043  | 3.11933  | 0.001813 | 0.022318 | 2.225762 |
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| ENSG00000151743 | 225.6037 | 0.18461  | 0.058255 | 3.168996 | 0.00153  | 0.022339 | 1.867169 |
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| ENSG00000234608 | 146.105  | 0.196709 | 0.063397 | 3.102814 | 0.001917 | 0.022339 | 2.338927 |
| ENSG00000034713 | 1089.231 | 0.123651 | 0.039795 | 3.107204 | 0.001889 | 0.022395 | 2.295759 |
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| ENSG00000125249 | 2684.861 | 0.147037 | 0.047337 | 3.106189 | 0.001895 | 0.022439 | 2.295759 |
| ENSG00000179841 | 791.8065 | 0.184944 | 0.060067 | 3.078936 | 0.002077 | 0.022442 | 2.514347 |
| ENSG00000115540 | 327.6444 | 0.17858  | 0.057346 | 3.114071 | 0.001845 | 0.022502 | 2.225762 |
| ENSG00000108654 | 5464.512 | 0.082654 | 0.026858 | 3.07746  | 0.002088 | 0.022521 | 2.514347 |
| ENSG00000158864 | 1053.77  | 0.169289 | 0.05453  | 3.104492 | 0.001906 | 0.022522 | 2.293762 |
| ENSG00000213341 | 358.5296 | 0.141438 | 0.045435 | 3.112992 | 0.001852 | 0.022525 | 2.225762 |
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| ENSG00000139112 | 3175.902 | 0.190489 | 0.062077 | 3.068603 | 0.002151 | 0.022525 | 2.583187 |
| ENSG00000137312 | 1633.727 | 0.133074 | 0.042762 | 3.111971 | 0.001858 | 0.022564 | 2.225762 |
| ENSG00000100744 | 258.5723 | 0.204225 | 0.06563  | 3.111745 | 0.00186  | 0.022564 | 2.225762 |
| ENSG00000099284 | 265.9958 | -0.12078 | 0.038953 | -3.10077 | 0.00193  | 0.022687 | 2.295759 |
| ENSG00000109846 | 2724.485 | 0.301621 | 0.09728  | 3.100552 | 0.001932 | 0.022687 | 2.295759 |
| ENSG00000080822 | 2386.855 | 0.285605 | 0.092934 | 3.073195 | 0.002118 | 0.022695 | 2.514347 |
| ENSG00000089248 | 356.347  | 0.169882 | 0.054814 | 3.099234 | 0.00194  | 0.022739 | 2.295759 |
| ENSG00000144895 | 628.1993 | 0.162819 | 0.052537 | 3.09914  | 0.001941 | 0.022739 | 2.29693  |
| ENSG00000117983 | 76.58001 | -0.55178 | 0.167706 | -3.29018 | 0.001001 | 0.022745 | 1.182918 |
| ENSG00000196072 | 411.5943 | 0.185455 | 0.059062 | 3.140019 | 0.001689 | 0.022745 | 1.995423 |
| ENSG00000197782 | 435.7609 | 0.124505 | 0.039682 | 3.137533 | 0.001704 | 0.022906 | 1.995423 |
| ENSG00000114867 | 2900.103 | 0.101317 | 0.033098 | 3.061101 | 0.002205 | 0.022906 | 2.583187 |

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| ENSG00000287655 | 17.054   | -0.55521 | 0.160293 | -3.46372 | 0.000533 | 0.022923 | 0.622589 |
| ENSG00000197045 | 2122.512 | 0.169352 | 0.054708 | 3.095543 | 0.001965 | 0.022923 | 2.295759 |
| ENSG00000242259 | 476.5597 | 0.119992 | 0.038793 | 3.093149 | 0.00198  | 0.02308  | 2.29693  |
| ENSG00000171208 | 473.7807 | 0.203567 | 0.065833 | 3.092165 | 0.001987 | 0.023152 | 2.295759 |
| ENSG00000265443 | 67.81285 | -0.32838 | 0.098811 | -3.32331 | 0.00089  | 0.023208 | 1.023066 |
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| ENSG00000011201 | 408.4104 | 0.317194 | 0.100893 | 3.143856 | 0.001667 | 0.023208 | 1.918337 |
| ENSG00000114450 | 496.0081 | 0.246394 | 0.079492 | 3.099602 | 0.001938 | 0.023222 | 2.225762 |
| ENSG00000165410 | 826.2693 | 0.19291  | 0.06298  | 3.063048 | 0.002191 | 0.023225 | 2.514347 |
| ENSG00000180964 | 408.1709 | 0.172189 | 0.054791 | 3.14267  | 0.001674 | 0.023234 | 1.918337 |
| ENSG00000170540 | 2420.288 | 0.187796 | 0.061321 | 3.062503 | 0.002195 | 0.023234 | 2.514347 |
| ENSG00000168785 | 1379.11  | 0.133404 | 0.043186 | 3.08906  | 0.002008 | 0.023261 | 2.295759 |
| ENSG00000176422 | 200.8693 | -0.1494  | 0.047795 | -3.12586 | 0.001773 | 0.023266 | 2.025126 |
| ENSG00000205710 | 42.72683 | -0.28462 | 0.085704 | -3.32102 | 0.000897 | 0.023315 | 1.020896 |
| ENSG00000126860 | 265.7412 | 0.373621 | 0.12064  | 3.096998 | 0.001955 | 0.023315 | 2.225762 |
| ENSG00000187105 | 152.5488 | -0.17437 | 0.056581 | -3.08172 | 0.002058 | 0.023335 | 2.338927 |
| ENSG00000146476 | 245.3105 | 0.192706 | 0.06155  | 3.130912 | 0.001743 | 0.023358 | 1.977088 |
| ENSG00000164187 | 1999.574 | 0.164893 | 0.05378  | 3.066075 | 0.002169 | 0.023378 | 2.456745 |
| ENSG00000183023 | 7099.792 | 0.216423 | 0.070754 | 3.058823 | 0.002222 | 0.023386 | 2.514347 |
| ENSG00000133134 | 770.2414 | 0.267924 | 0.086827 | 3.085732 | 0.002031 | 0.023408 | 2.293762 |
| ENSG00000249436 | 59.68932 | 0.427464 | 0.126853 | 3.369764 | 0.000752 | 0.023423 | 0.848718 |
| ENSG00000182841 | 228.1748 | -0.21878 | 0.070717 | -3.09377 | 0.001976 | 0.023446 | 2.225762 |
| ENSG00000267321 | 63.24987 | 0.237895 | 0.071534 | 3.325636 | 0.000882 | 0.023494 | 0.989117 |
| ENSG00000164258 | 302.74   | 0.200177 | 0.064155 | 3.120186 | 0.001807 | 0.023494 | 2.025126 |
| ENSG00000142784 | 1173.776 | -0.12292 | 0.039745 | -3.09271 | 0.001983 | 0.023494 | 2.225762 |
| ENSG00000108829 | 422.287  | 0.130068 | 0.042183 | 3.083444 | 0.002046 | 0.023494 | 2.295759 |
| ENSG00000163320 | 906.7381 | 0.15288  | 0.049585 | 3.083163 | 0.002048 | 0.023494 | 2.293762 |
| ENSG00000226049 | 143.8166 | -0.27786 | 0.089406 | -3.10782 | 0.001885 | 0.023508 | 2.108016 |
| ENSG00000167863 | 500.1701 | 0.185982 | 0.060339 | 3.082288 | 0.002054 | 0.023509 | 2.295759 |
| ENSG00000122515 | 1482.075 | -0.17714 | 0.057474 | -3.08204 | 0.002056 | 0.02351  | 2.295759 |

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| ENSG00000103363 | 667.6225 | 0.14806  | 0.048045 | 3.0817   | 0.002058 | 0.02351  | 2.29693  |
| ENSG00000006327 | 26.89991 | 0.694484 | 0.207523 | 3.34654  | 0.000818 | 0.023539 | 0.911386 |
| ENSG00000182831 | 1448.52  | 0.087642 | 0.028777 | 3.045551 | 0.002323 | 0.023556 | 2.583187 |
| ENSG00000134243 | 7840.968 | 0.15663  | 0.051297 | 3.053428 | 0.002262 | 0.023558 | 2.514347 |
| ENSG00000166862 | 319.5079 | -0.17992 | 0.057583 | -3.12455 | 0.001781 | 0.023558 | 1.977088 |
| ENSG00000124214 | 1280.728 | 0.092976 | 0.030095 | 3.089398 | 0.002006 | 0.023558 | 2.225762 |
| ENSG00000187189 | 2634.601 | 0.144942 | 0.047606 | 3.044591 | 0.00233  | 0.023564 | 2.583187 |
| ENSG00000180694 | 247.2963 | 0.169593 | 0.054342 | 3.120856 | 0.001803 | 0.023593 | 1.995423 |
| ENSG00000128609 | 1405.984 | 0.2082   | 0.067612 | 3.079309 | 0.002075 | 0.023598 | 2.293762 |
| ENSG00000196689 | 197.1224 | -0.22107 | 0.07181  | -3.07849 | 0.002081 | 0.023626 | 2.295759 |
| ENSG00000090263 | 213.7441 | 0.167344 | 0.054212 | 3.086871 | 0.002023 | 0.023675 | 2.225762 |
| ENSG00000143793 | 162.7219 | -0.18578 | 0.060202 | -3.08594 | 0.002029 | 0.023733 | 2.225762 |
| ENSG00000242173 | 641.1575 | 0.165172 | 0.054313 | 3.041085 | 0.002357 | 0.02374  | 2.583187 |
| ENSG00000228623 | 234.6479 | -0.19385 | 0.062849 | -3.08444 | 0.002039 | 0.023778 | 2.225762 |
| ENSG00000182287 | 526.329  | 0.189651 | 0.061493 | 3.084126 | 0.002042 | 0.023778 | 2.225762 |
| ENSG00000257093 | 1880.26  | 0.110917 | 0.036066 | 3.075393 | 0.002102 | 0.023778 | 2.295759 |
| ENSG00000109270 | 558.8994 | 0.162984 | 0.053004 | 3.07494  | 0.002105 | 0.023778 | 2.29693  |
| ENSG00000171490 | 868.5067 | 0.110461 | 0.036333 | 3.040224 | 0.002364 | 0.023778 | 2.583187 |
| ENSG00000116288 | 895.1173 | 0.164472 | 0.053493 | 3.074632 | 0.002108 | 0.023803 | 2.293762 |
| ENSG00000119335 | 1779.735 | 0.140083 | 0.046101 | 3.038617 | 0.002377 | 0.023818 | 2.583187 |
| ENSG00000185684 | 368.8124 | -0.18646 | 0.059652 | -3.12572 | 0.001774 | 0.023885 | 1.918337 |
| ENSG00000265354 | 345.4202 | 0.16762  | 0.053627 | 3.125666 | 0.001774 | 0.023885 | 1.918337 |
| ENSG00000146776 | 349.6586 | -0.13719 | 0.044522 | -3.08132 | 0.002061 | 0.023885 | 2.225762 |
| ENSG00000129625 | 2848.661 | 0.162401 | 0.053212 | 3.051965 | 0.002273 | 0.023885 | 2.456745 |
| ENSG00000072042 | 738.6986 | 0.166183 | 0.054715 | 3.03725  | 0.002387 | 0.023885 | 2.583187 |
| ENSG00000281961 | 32.18739 | -0.40438 | 0.122695 | -3.29583 | 0.000981 | 0.024002 | 1.053218 |
| ENSG00000196323 | 1552.723 | 0.125859 | 0.041469 | 3.035029 | 0.002405 | 0.024002 | 2.583187 |
| ENSG00000166200 | 910.1478 | 0.144386 | 0.04704  | 3.069448 | 0.002145 | 0.024068 | 2.293762 |
| ENSG00000196990 | 1349.112 | -0.178   | 0.057829 | -3.078   | 0.002084 | 0.024086 | 2.225762 |
| ENSG00000132952 | 377.1838 | 0.142493 | 0.04565  | 3.121386 | 0.0018   | 0.024105 | 1.918337 |

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| ENSG00000122406 | 1676.265 | 0.172806 | 0.056827 | 3.040933 | 0.002358 | 0.024105 | 2.514347 |
| ENSG00000204685 | 94.7779  | -0.20069 | 0.063584 | -3.15627 | 0.001598 | 0.02416  | 1.695647 |
| ENSG00000106688 | 617.14   | 0.19779  | 0.064494 | 3.066766 | 0.002164 | 0.02416  | 2.29693  |
| ENSG00000085365 | 1855.126 | 0.147789 | 0.048507 | 3.046757 | 0.002313 | 0.02416  | 2.456745 |
| ENSG00000150394 | 630.1467 | 0.233272 | 0.076089 | 3.065771 | 0.002171 | 0.024248 | 2.293762 |
| ENSG00000120686 | 600.8021 | 0.16856  | 0.054828 | 3.074317 | 0.00211  | 0.024267 | 2.225762 |
| ENSG00000182173 | 224.8446 | -0.17271 | 0.05637  | -3.06391 | 0.002185 | 0.024335 | 2.295759 |
| ENSG00000023228 | 3994.637 | 0.128416 | 0.042405 | 3.028346 | 0.002459 | 0.024335 | 2.583187 |
| ENSG00000127184 | 1008.129 | 0.197888 | 0.064404 | 3.072614 | 0.002122 | 0.024338 | 2.225762 |
| ENSG00000115966 | 1250.992 | 0.108504 | 0.035418 | 3.063568 | 0.002187 | 0.024338 | 2.295759 |
| ENSG00000131044 | 89.03149 | -0.26142 | 0.080397 | -3.25165 | 0.001147 | 0.024355 | 1.201846 |
| ENSG00000137414 | 911.0458 | 0.126319 | 0.041128 | 3.071341 | 0.002131 | 0.024392 | 2.225762 |
| ENSG00000126432 | 1328.52  | 0.183707 | 0.059993 | 3.062114 | 0.002198 | 0.024392 | 2.295759 |
| ENSG00000132872 | 1971.566 | 0.269559 | 0.088107 | 3.059454 | 0.002217 | 0.02459  | 2.295759 |
| ENSG00000229325 | 71.78253 | 0.252958 | 0.077521 | 3.26309  | 0.001102 | 0.024672 | 1.136415 |
| ENSG00000175311 | 20.12821 | -0.46509 | 0.135613 | -3.42953 | 0.000605 | 0.024686 | 0.622231 |
| ENSG00000173141 | 279.5646 | 0.160284 | 0.05179  | 3.094864 | 0.001969 | 0.024686 | 2.025126 |
| ENSG00000061273 | 633.4927 | -0.17789 | 0.058178 | -3.05765 | 0.002231 | 0.024686 | 2.29693  |
| ENSG00000174292 | 61.93424 | -0.30129 | 0.091522 | -3.29203 | 0.000995 | 0.02472  | 1.020896 |
| ENSG00000225907 | 17.99097 | -0.52662 | 0.140736 | -3.7419  | 0.000183 | 0.024732 | 0.187229 |
| ENSG00000100461 | 687.9048 | 0.114325 | 0.037854 | 3.02014  | 0.002527 | 0.024782 | 2.583187 |
| ENSG00000231738 | 15.73184 | 0.598108 | 0.175588 | 3.406309 | 0.000658 | 0.024865 | 0.670508 |
| ENSG00000186184 | 396.8909 | 0.128252 | 0.041275 | 3.107239 | 0.001888 | 0.024891 | 1.918337 |
| ENSG00000163635 | 868.4037 | -0.09072 | 0.029708 | -3.05392 | 0.002259 | 0.024891 | 2.295759 |
| ENSG00000172301 | 438.5311 | 0.195157 | 0.063747 | 3.061446 | 0.002203 | 0.025006 | 2.225762 |
| ENSG00000232233 | 37.66362 | -0.33048 | 0.100657 | -3.28322 | 0.001026 | 0.025017 | 1.035363 |
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| ENSG00000249478 | 98.17735 | -0.30018 | 0.092183 | -3.25638 | 0.001128 | 0.025021 | 1.136415 |
| ENSG00000116679 | 985.5516 | 0.160527 | 0.052449 | 3.060644 | 0.002209 | 0.025021 | 2.225762 |
| ENSG00000168438 | 661.3005 | 0.159485 | 0.052281 | 3.050512 | 0.002285 | 0.025028 | 2.29693  |

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| ENSG00000165156 | 1202.965 | 0.127581 | 0.0422   | 3.023272 | 0.002501 | 0.025028 | 2.514347 |
| ENSG00000165152 | 1161.306 | 0.18812  | 0.061698 | 3.049056 | 0.002296 | 0.025167 | 2.293762 |
| ENSG00000153214 | 278.3584 | 0.205214 | 0.066418 | 3.089735 | 0.002003 | 0.025214 | 1.995423 |
| ENSG00000163743 | 369.6455 | 0.15015  | 0.048597 | 3.089721 | 0.002003 | 0.025214 | 1.995423 |
| ENSG00000164442 | 355.7303 | 0.202785 | 0.0654   | 3.100703 | 0.001931 | 0.025256 | 1.918337 |
| ENSG00000170153 | 821.5615 | 0.154076 | 0.050582 | 3.04605  | 0.002319 | 0.025351 | 2.293762 |
| ENSG00000224271 | 851.1917 | -0.27518 | 0.090106 | -3.05394 | 0.002259 | 0.025431 | 2.225762 |
| ENSG00000011260 | 369.5901 | 0.153777 | 0.050361 | 3.053493 | 0.002262 | 0.025442 | 2.225762 |
| ENSG00000010256 | 1374.748 | 0.18535  | 0.061443 | 3.016634 | 0.002556 | 0.025442 | 2.514347 |
| ENSG00000164284 | 262.9679 | 0.172719 | 0.056058 | 3.081103 | 0.002062 | 0.025471 | 2.025126 |
| ENSG00000233840 | 115.3876 | 0.26258  | 0.084567 | 3.104989 | 0.001903 | 0.025472 | 1.867169 |
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| ENSG00000169255 | 530.962  | 0.185477 | 0.06077  | 3.052098 | 0.002272 | 0.025484 | 2.225762 |
| ENSG00000139211 | 66.06187 | 0.49834  | 0.152007 | 3.278395 | 0.001044 | 0.025496 | 1.020896 |
| ENSG00000179010 | 2155.388 | 0.155553 | 0.051131 | 3.042239 | 0.002348 | 0.025496 | 2.295759 |
| ENSG00000134910 | 500.8594 | 0.132776 | 0.043673 | 3.040238 | 0.002364 | 0.025636 | 2.29693  |
| ENSG00000158683 | 146.2337 | -0.22496 | 0.073668 | -3.05372 | 0.00226  | 0.025676 | 2.189833 |
| ENSG00000038274 | 604.9366 | 0.160887 | 0.052932 | 3.039519 | 0.00237  | 0.025676 | 2.295759 |
| ENSG00000143198 | 1061.867 | 0.140646 | 0.04685  | 3.002054 | 0.002682 | 0.025807 | 2.583187 |
| ENSG00000261647 | 132.6858 | -0.23593 | 0.077031 | -3.06273 | 0.002193 | 0.02583  | 2.108016 |
| ENSG00000173744 | 1617.023 | 0.097061 | 0.031954 | 3.037491 | 0.002386 | 0.02583  | 2.293762 |
| ENSG00000173660 | 862.3465 | 0.213714 | 0.070397 | 3.035838 | 0.002399 | 0.025922 | 2.295759 |
| ENSG00000188517 | 155.3413 | 0.263185 | 0.08686  | 3.02999  | 0.002446 | 0.025924 | 2.338927 |
| ENSG00000197223 | 136.7022 | 0.204332 | 0.065979 | 3.096917 | 0.001955 | 0.025941 | 1.867169 |
| ENSG00000108799 | 1711.98  | -0.10189 | 0.033573 | -3.03501 | 0.002405 | 0.025941 | 2.295759 |
| ENSG00000139505 | 846.9049 | 0.175331 | 0.057618 | 3.042983 | 0.002342 | 0.02604  | 2.225762 |
| ENSG00000149577 | 863.0275 | -0.17403 | 0.05737  | -3.03349 | 0.002417 | 0.026059 | 2.293762 |
| ENSG00000172432 | 425.5356 | -0.1188  | 0.039053 | -3.04214 | 0.002349 | 0.026061 | 2.225762 |
| ENSG00000279207 | 207.509  | 0.267084 | 0.088061 | 3.032926 | 0.002422 | 0.026061 | 2.295759 |
| ENSG00000259924 | 103.1548 | -0.24331 | 0.077917 | -3.12265 | 0.001792 | 0.026083 | 1.695647 |



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| ENSG00000287990 | 73.58792 | -0.22687 | 0.070313 | -3.2266  | 0.001253 | 0.026115 | 1.182918 |
| ENSG00000144619 | 602.3657 | 0.183168 | 0.061144 | 2.995703 | 0.002738 | 0.026122 | 2.583187 |
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| ENSG00000120696 | 260.1436 | 0.149671 | 0.049257 | 3.038593 | 0.002377 | 0.026245 | 2.225762 |
| ENSG00000132849 | 595.8786 | -0.14704 | 0.048397 | -3.03821 | 0.00238  | 0.026245 | 2.225762 |
| ENSG00000035687 | 533.0236 | 0.204949 | 0.067648 | 3.029658 | 0.002448 | 0.026245 | 2.295759 |
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| ENSG00000255302 | 2149.519 | 0.183883 | 0.061213 | 3.003979 | 0.002665 | 0.026245 | 2.492774 |
| ENSG00000126524 | 759.9406 | 0.158482 | 0.052959 | 2.992548 | 0.002767 | 0.026271 | 2.583187 |
| ENSG00000182359 | 305.4076 | 0.19134  | 0.063005 | 3.03689  | 0.00239  | 0.026325 | 2.225762 |
| ENSG00000138074 | 424.3259 | -0.29346 | 0.095304 | -3.07918 | 0.002076 | 0.026487 | 1.918337 |
| ENSG00000140259 | 224.6607 | 0.152762 | 0.049804 | 3.067241 | 0.00216  | 0.026487 | 1.995423 |
| ENSG00000177103 | 871.0981 | -0.22984 | 0.076878 | -2.98961 | 0.002793 | 0.026487 | 2.583187 |
| ENSG00000175445 | 352.4809 | 0.341071 | 0.110795 | 3.078394 | 0.002081 | 0.026524 | 1.918337 |
| ENSG00000280375 | 25.35797 | -0.50244 | 0.151721 | -3.31161 | 0.000928 | 0.026528 | 0.848718 |
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| ENSG00000171365 | 229.198  | 0.202621 | 0.066822 | 3.032271 | 0.002427 | 0.026528 | 2.225762 |
| ENSG00000159461 | 1604.64  | 0.104148 | 0.034351 | 3.031878 | 0.00243  | 0.026528 | 2.225762 |
| ENSG00000154582 | 325.5221 | 0.167166 | 0.055141 | 3.031623 | 0.002432 | 0.026528 | 2.225762 |
| ENSG00000135940 | 1355.329 | 0.179585 | 0.059391 | 3.023764 | 0.002497 | 0.026528 | 2.293762 |
| ENSG00000058804 | 229.8097 | 0.161683 | 0.053486 | 3.022898 | 0.002504 | 0.026528 | 2.295759 |
| ENSG00000149547 | 507.3229 | 0.125119 | 0.041395 | 3.02256  | 0.002506 | 0.026528 | 2.29693  |
| ENSG00000170500 | 5912.484 | 0.127878 | 0.042592 | 3.002426 | 0.002678 | 0.026528 | 2.456745 |
| ENSG00000169213 | 764.5487 | 0.397698 | 0.132787 | 2.995002 | 0.002744 | 0.026528 | 2.514347 |
| ENSG00000078124 | 1046.231 | 0.165099 | 0.055147 | 2.993803 | 0.002755 | 0.026562 | 2.514347 |
| ENSG00000154864 | 583.0886 | 0.381816 | 0.126472 | 3.018987 | 0.002536 | 0.026747 | 2.29693  |
| ENSG00000122965 | 748.093  | -0.16546 | 0.054638 | -3.02829 | 0.002459 | 0.026749 | 2.225762 |
| ENSG00000198356 | 333.7394 | 0.175171 | 0.057208 | 3.062028 | 0.002198 | 0.026847 | 1.977088 |

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| ENSG00000174989 | 272.4308 | -0.13959 | 0.045627 | -3.0594  | 0.002218 | 0.026847 | 1.995423 |
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| ENSG00000144320 | 1093.85  | 0.131738 | 0.043681 | 3.015899 | 0.002562 | 0.026918 | 2.293762 |
| ENSG00000196405 | 2177.263 | -0.13237 | 0.044423 | -2.97967 | 0.002886 | 0.026918 | 2.583187 |
| ENSG00000108433 | 646.6904 | -0.11036 | 0.036599 | -3.0153  | 0.002567 | 0.02693  | 2.295759 |
| ENSG00000184164 | 255.5228 | -0.15757 | 0.051632 | -3.05187 | 0.002274 | 0.027025 | 2.025126 |
| ENSG00000189266 | 466.8881 | 0.191313 | 0.063507 | 3.012483 | 0.002591 | 0.027127 | 2.295759 |
| ENSG00000081154 | 1190.873 | 0.12577  | 0.042252 | 2.976659 | 0.002914 | 0.027127 | 2.583187 |
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| ENSG00000103197 | 2083.412 | -0.14234 | 0.047591 | -2.99084 | 0.002782 | 0.027182 | 2.456745 |
| ENSG00000181396 | 393.1876 | -0.14601 | 0.047665 | -3.0633  | 0.002189 | 0.027355 | 1.918337 |
| ENSG00000112406 | 698.4975 | 0.161073 | 0.054022 | 2.981596 | 0.002868 | 0.027355 | 2.514347 |
| ENSG00000109738 | 989.1611 | 0.215841 | 0.071771 | 3.00736  | 0.002635 | 0.027506 | 2.293762 |
| ENSG00000108469 | 499.234  | -0.13805 | 0.045907 | -3.00725 | 0.002636 | 0.027506 | 2.295759 |
| ENSG00000181652 | 40.1445  | -0.27641 | 0.085473 | -3.23387 | 0.001221 | 0.027742 | 1.053218 |
| ENSG00000068796 | 1501.021 | 0.11625  | 0.038702 | 3.003705 | 0.002667 | 0.027742 | 2.295759 |
| ENSG00000159433 | 1738.539 | -0.17831 | 0.060085 | -2.96769 | 0.003    | 0.027742 | 2.583187 |
| ENSG00000174501 | 1790.197 | -0.15074 | 0.050793 | -2.96768 | 0.003001 | 0.027742 | 2.583187 |
| ENSG00000071127 | 1091.662 | 0.165435 | 0.055112 | 3.001794 | 0.002684 | 0.027899 | 2.295759 |
| ENSG00000182117 | 128.3638 | 0.248481 | 0.082093 | 3.026837 | 0.002471 | 0.027958 | 2.108016 |
| ENSG00000198920 | 487.9898 | -0.1158  | 0.038472 | -3.00997 | 0.002613 | 0.027977 | 2.225762 |
| ENSG00000275389 | 30.66481 | -0.38035 | 0.11556  | -3.29139 | 0.000997 | 0.027977 | 0.848718 |
| ENSG00000119986 | 226.7139 | 0.210291 | 0.069117 | 3.042543 | 0.002346 | 0.027983 | 1.995423 |
| ENSG00000164347 | 410.0795 | 0.156552 | 0.052208 | 2.99864  | 0.002712 | 0.028086 | 2.295759 |
| ENSG00000126945 | 645.8023 | 0.155441 | 0.051841 | 2.998424 | 0.002714 | 0.028086 | 2.29693  |
| ENSG00000200488 | 16.22895 | 0.43233  | 0.128098 | 3.374988 | 0.000738 | 0.028164 | 0.622589 |
| ENSG00000197951 | 366.3536 | -0.13201 | 0.043494 | -3.03517 | 0.002404 | 0.028164 | 2.025126 |
| ENSG00000089693 | 1353.156 | 0.144683 | 0.048862 | 2.961052 | 0.003066 | 0.028164 | 2.583187 |

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| ENSG0000019102  | 70.26376 | -0.43948 | 0.135474 | -3.24402 | 0.001179 | 0.02822  | 0.989117 |
| ENSG00000143106 | 458.3097 | 0.211802 | 0.069801 | 3.034344 | 0.002411 | 0.02822  | 2.025126 |
| ENSG00000187555 | 1692.376 | 0.09886  | 0.032897 | 3.00519  | 0.002654 | 0.02822  | 2.225762 |
| ENSG00000117152 | 4533.03  | 0.27899  | 0.093125 | 2.995856 | 0.002737 | 0.02822  | 2.295759 |
| ENSG00000124702 | 1969.969 | 0.15008  | 0.050529 | 2.970202 | 0.002976 | 0.028235 | 2.492774 |
| ENSG00000079974 | 307.0809 | -0.13742 | 0.04527  | -3.03555 | 0.002401 | 0.02841  | 1.995423 |
| ENSG00000204396 | 217.4159 | -0.2369  | 0.078059 | -3.03486 | 0.002407 | 0.02841  | 1.995423 |
| ENSG00000123728 | 218.5139 | 0.147309 | 0.048612 | 3.030303 | 0.002443 | 0.02841  | 2.025126 |
| ENSG00000166432 | 609.5009 | -0.21963 | 0.073383 | -2.99292 | 0.002763 | 0.02841  | 2.293762 |
| ENSG00000181163 | 1357.527 | 0.150203 | 0.050194 | 2.992459 | 0.002767 | 0.02841  | 2.293762 |
| ENSG00000096401 | 774.7675 | 0.12155  | 0.041005 | 2.964272 | 0.003034 | 0.02841  | 2.514347 |
| ENSG00000147454 | 818.4663 | -0.16833 | 0.05693  | -2.95685 | 0.003108 | 0.02841  | 2.583187 |
| ENSG00000158863 | 739.0757 | -0.13463 | 0.045003 | -2.99152 | 0.002776 | 0.02845  | 2.295759 |
| ENSG00000264538 | 638.6661 | -0.08905 | 0.029768 | -2.99159 | 0.002775 | 0.02845  | 2.293762 |
| ENSG00000142453 | 455.4977 | -0.12602 | 0.04155  | -3.03303 | 0.002421 | 0.028512 | 1.995423 |
| ENSG00000126883 | 891.3035 | -0.10842 | 0.036151 | -2.99893 | 0.002709 | 0.028586 | 2.225762 |
| ENSG00000133794 | 692.0097 | 0.128824 | 0.043101 | 2.988908 | 0.0028   | 0.028604 | 2.295759 |
| ENSG00000140983 | 810.9186 | -0.17072 | 0.057653 | -2.9611  | 0.003065 | 0.028604 | 2.514347 |
| ENSG00000126464 | 996.5611 | -0.24272 | 0.080969 | -2.99764 | 0.002721 | 0.028635 | 2.225762 |
| ENSG00000125166 | 1212.591 | 0.193225 | 0.064656 | 2.988511 | 0.002803 | 0.028635 | 2.293762 |
| ENSG00000174607 | 1103.741 | 0.429205 | 0.14367  | 2.987448 | 0.002813 | 0.028686 | 2.295759 |
| ENSG00000175161 | 5747.081 | 0.147574 | 0.049415 | 2.98641  | 0.002823 | 0.028765 | 2.295759 |
| ENSG00000100600 | 474.7917 | 0.185997 | 0.062108 | 2.994745 | 0.002747 | 0.028847 | 2.225762 |
| ENSG00000272333 | 835.1068 | -0.18991 | 0.064401 | -2.94889 | 0.003189 | 0.028847 | 2.583187 |
| ENSG00000007545 | 253.489  | -0.1222  | 0.040333 | -3.02971 | 0.002448 | 0.028893 | 1.977088 |
| ENSG00000121864 | 361.0132 | 0.131186 | 0.043401 | 3.022638 | 0.002506 | 0.028893 | 2.025126 |
| ENSG00000140307 | 182.8616 | 0.174493 | 0.057274 | 3.046608 | 0.002314 | 0.028907 | 1.867169 |
| ENSG00000111144 | 399.1577 | 0.132979 | 0.044447 | 2.99185  | 0.002773 | 0.028981 | 2.225762 |
| ENSG00000262001 | 241.5764 | -0.15527 | 0.052055 | -2.9828  | 0.002856 | 0.028981 | 2.295759 |
| ENSG00000111911 | 842.381  | 0.112415 | 0.037689 | 2.98271  | 0.002857 | 0.028981 | 2.293762 |

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| ENSG00000186166 | 573.4546 | -0.16957 | 0.056857 | -2.98248 | 0.002859 | 0.028981 | 2.295759 |
| ENSG00000165816 | 114.298  | -0.26298 | 0.086388 | -3.04416 | 0.002333 | 0.029052 | 1.867169 |
| ENSG00000089818 | 1205.566 | 0.187198 | 0.063583 | 2.944145 | 0.003238 | 0.029127 | 2.583187 |
| ENSG00000248994 | 371.8081 | -0.22456 | 0.075123 | -2.98922 | 0.002797 | 0.029177 | 2.225762 |
| ENSG00000106105 | 1198.629 | 0.146858 | 0.049163 | 2.987185 | 0.002816 | 0.029353 | 2.225762 |
| ENSG00000166006 | 1214.117 | 0.158488 | 0.053068 | 2.986508 | 0.002822 | 0.0294   | 2.225762 |
| ENSG00000198169 | 390.4655 | -0.16636 | 0.054881 | -3.03122 | 0.002436 | 0.029425 | 1.918337 |
| ENSG00000168959 | 1260.98  | 0.150187 | 0.051087 | 2.939819 | 0.003284 | 0.029444 | 2.583187 |
| ENSG00000164919 | 782.0786 | 0.206336 | 0.069335 | 2.975919 | 0.002921 | 0.029451 | 2.295759 |
| ENSG00000163686 | 527.1825 | 0.181726 | 0.061083 | 2.975046 | 0.002929 | 0.029478 | 2.29693  |
| ENSG00000067064 | 807.5447 | 0.227997 | 0.077362 | 2.947142 | 0.003207 | 0.029478 | 2.514347 |
| ENSG00000077380 | 1298.979 | 0.146659 | 0.049765 | 2.947046 | 0.003208 | 0.029478 | 2.514347 |
| ENSG00000111790 | 1185.925 | 0.127315 | 0.042801 | 2.97459  | 0.002934 | 0.029531 | 2.293762 |
| ENSG00000228510 | 33.79399 | -0.5083  | 0.158204 | -3.21294 | 0.001314 | 0.029676 | 1.020896 |
| ENSG00000146376 | 142.0843 | 0.251147 | 0.08465  | 2.966897 | 0.003008 | 0.029676 | 2.338927 |
| ENSG00000096092 | 341.8792 | 0.208547 | 0.069946 | 2.98155  | 0.002868 | 0.029694 | 2.225762 |
| ENSG00000105983 | 1232.656 | 0.117803 | 0.039528 | 2.980224 | 0.00288  | 0.029783 | 2.225762 |
| ENSG00000104714 | 282.3563 | -0.18867 | 0.063311 | -2.98006 | 0.002882 | 0.029783 | 2.225762 |
| ENSG00000105993 | 973.5149 | 0.184505 | 0.062879 | 2.934304 | 0.003343 | 0.029783 | 2.583187 |
| ENSG00000175416 | 983.9266 | 0.138125 | 0.046959 | 2.94142  | 0.003267 | 0.02987  | 2.514347 |
| ENSG00000276255 | 45.46355 | -0.34504 | 0.107796 | -3.20088 | 0.00137  | 0.029885 | 1.053218 |
| ENSG00000164031 | 1747.787 | 0.150772 | 0.051416 | 2.932383 | 0.003364 | 0.029896 | 2.583187 |
| ENSG00000196230 | 1617.555 | 0.180201 | 0.061311 | 2.939151 | 0.003291 | 0.029996 | 2.514347 |
| ENSG00000134030 | 2521.081 | -0.11694 | 0.039898 | -2.93085 | 0.00338  | 0.029996 | 2.583187 |
| ENSG00000137955 | 485.0552 | 0.119985 | 0.040939 | 2.930822 | 0.003381 | 0.029996 | 2.583187 |
| ENSG00000082146 | 319.4286 | 0.15156  | 0.050929 | 2.975922 | 0.002921 | 0.030025 | 2.225762 |
| ENSG00000102144 | 3834.227 | 0.168443 | 0.05678  | 2.966595 | 0.003011 | 0.030025 | 2.295759 |
| ENSG00000173821 | 3497.469 | -0.12999 | 0.044134 | -2.94545 | 0.003225 | 0.030025 | 2.456745 |
| ENSG00000070366 | 754.9293 | -0.11271 | 0.037877 | -2.97562 | 0.002924 | 0.03003  | 2.225762 |
| ENSG00000143420 | 2380.53  | 0.124807 | 0.042081 | 2.965919 | 0.003018 | 0.030031 | 2.295759 |

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| ENSG00000248837 | 47.46264 | -0.48747 | 0.152052 | -3.20595 | 0.001346 | 0.030042 | 1.023066 |
| ENSG00000183337 | 429.9418 | -0.16925 | 0.056894 | -2.9748  | 0.002932 | 0.030047 | 2.225762 |
| ENSG00000064763 | 483.6883 | 0.160051 | 0.053977 | 2.96518  | 0.003025 | 0.030047 | 2.295759 |
| ENSG00000113555 | 180.1134 | -0.17754 | 0.059124 | -3.00283 | 0.002675 | 0.030072 | 2.025126 |
| ENSG00000271447 | 158.6656 | -0.33449 | 0.113065 | -2.95843 | 0.003092 | 0.030072 | 2.338927 |
| ENSG00000182149 | 1228.735 | 0.073548 | 0.025047 | 2.936405 | 0.00332  | 0.030072 | 2.514347 |
| ENSG00000166922 | 1438.302 | 0.250957 | 0.085716 | 2.927769 | 0.003414 | 0.030072 | 2.583187 |
| ENSG00000142303 | 685.2858 | -0.20749 | 0.070879 | -2.92739 | 0.003418 | 0.030081 | 2.583187 |
| ENSG00000131797 | 299.9711 | -0.14077 | 0.046779 | -3.00932 | 0.002618 | 0.030088 | 1.977088 |
| ENSG00000100612 | 290.9394 | 0.181376 | 0.061226 | 2.962395 | 0.003053 | 0.030171 | 2.295759 |
| ENSG00000148337 | 1133.608 | -0.1348  | 0.04594  | -2.93438 | 0.003342 | 0.030171 | 2.514347 |
| ENSG00000182827 | 390.677  | 0.136094 | 0.045813 | 2.970645 | 0.002972 | 0.030222 | 2.225762 |
| ENSG00000196715 | 644.1548 | 0.122729 | 0.041442 | 2.961464 | 0.003062 | 0.030222 | 2.293762 |
| ENSG00000178074 | 392.8562 | 0.136351 | 0.046044 | 2.961287 | 0.003064 | 0.030222 | 2.295759 |
| ENSG00000145476 | 693.6833 | -0.19787 | 0.067649 | -2.92501 | 0.003444 | 0.030222 | 2.583187 |
| ENSG00000138769 | 459.4498 | 0.183013 | 0.060697 | 3.015199 | 0.002568 | 0.030228 | 1.918337 |
| ENSG00000170946 | 308.9539 | 0.12649  | 0.04218  | 2.998797 | 0.00271  | 0.030228 | 2.025126 |
| ENSG00000179933 | 143.6654 | 0.19511  | 0.066035 | 2.954627 | 0.00313  | 0.030228 | 2.338927 |
| ENSG00000094916 | 4609.282 | 0.089726 | 0.030572 | 2.934913 | 0.003336 | 0.030228 | 2.492774 |
| ENSG00000100596 | 1503.535 | 0.180142 | 0.06086  | 2.959935 | 0.003077 | 0.030272 | 2.293762 |
| ENSG00000164176 | 2742.95  | 0.300632 | 0.10235  | 2.937309 | 0.003311 | 0.030392 | 2.456745 |
| ENSG00000115421 | 472.3984 | 0.118793 | 0.040041 | 2.966765 | 0.00301  | 0.030475 | 2.225762 |
| ENSG00000073146 | 92.69057 | -0.24273 | 0.07961  | -3.04893 | 0.002297 | 0.030508 | 1.695647 |
| ENSG00000278156 | 87.31068 | -0.19292 | 0.063293 | -3.0481  | 0.002303 | 0.030555 | 1.695647 |
| ENSG00000185630 | 2512.008 | 0.085148 | 0.029012 | 2.934953 | 0.003336 | 0.030555 | 2.456745 |
| ENSG00000240053 | 31.9249  | -0.38392 | 0.119295 | -3.21827 | 0.00129  | 0.030598 | 0.947688 |
| ENSG00000062096 | 23.66396 | 0.590321 | 0.161435 | 3.65671  | 0.000255 | 0.030644 | 0.187229 |
| ENSG00000105926 | 1689.731 | 0.168695 | 0.057095 | 2.954669 | 0.00313  | 0.030644 | 2.293762 |
| ENSG00000147457 | 529.7226 | 0.095364 | 0.032286 | 2.953743 | 0.003139 | 0.030691 | 2.295759 |
| ENSG00000008083 | 730.0775 | -0.12359 | 0.041845 | -2.95339 | 0.003143 | 0.030707 | 2.295759 |

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| ENSG00000171303 | 186.397  | 0.168326 | 0.057023 | 2.951869 | 0.003159 | 0.030829 | 2.295759 |
| ENSG00000007168 | 5516.297 | 0.137853 | 0.047152 | 2.923593 | 0.00346  | 0.030829 | 2.514347 |
| ENSG00000282978 | 15.57073 | -0.47078 | 0.1408   | -3.34359 | 0.000827 | 0.030836 | 0.600464 |
| ENSG00000160602 | 39.49811 | -0.34906 | 0.109487 | -3.18811 | 0.001432 | 0.030925 | 1.035363 |
| ENSG00000077279 | 339.7343 | 0.163738 | 0.054703 | 2.993245 | 0.00276  | 0.030925 | 1.995423 |
| ENSG00000167904 | 177.8101 | 0.139893 | 0.04742  | 2.950082 | 0.003177 | 0.030925 | 2.295759 |
| ENSG00000179388 | 424.4981 | -0.18251 | 0.060982 | -2.99289 | 0.002763 | 0.030931 | 1.995423 |
| ENSG00000259657 | 12.8714  | -0.43898 | 0.132581 | -3.31101 | 0.00093  | 0.030944 | 0.670508 |
| ENSG00000081148 | 66.94775 | 0.282495 | 0.088541 | 3.190567 | 0.00142  | 0.030944 | 1.023066 |
| ENSG00000132912 | 1266.959 | 0.121658 | 0.041651 | 2.920926 | 0.00349  | 0.030944 | 2.514347 |
| ENSG00000162630 | 691.3571 | 0.242758 | 0.082337 | 2.948356 | 0.003195 | 0.031005 | 2.295759 |
| ENSG00000239521 | 865.4734 | -0.13714 | 0.046386 | -2.9566  | 0.003111 | 0.0311   | 2.225762 |
| ENSG00000173611 | 1624.002 | 0.13562  | 0.046598 | 2.910447 | 0.003609 | 0.0311   | 2.583187 |
| ENSG00000081181 | 112.6083 | 0.217319 | 0.07339  | 2.961145 | 0.003065 | 0.03111  | 2.189833 |
| ENSG00000102466 | 799.1661 | 0.152695 | 0.05232  | 2.918503 | 0.003517 | 0.03111  | 2.514347 |
| ENSG00000221914 | 902.8915 | 0.128671 | 0.043677 | 2.945959 | 0.00322  | 0.031152 | 2.295759 |
| ENSG00000086598 | 826.7291 | 0.141406 | 0.047848 | 2.955299 | 0.003124 | 0.031154 | 2.225762 |
| ENSG00000104497 | 169.7551 | 0.207297 | 0.070148 | 2.955131 | 0.003125 | 0.031154 | 2.225762 |
| ENSG00000151090 | 1923.043 | 0.137267 | 0.046605 | 2.945357 | 0.003226 | 0.031156 | 2.295759 |
| ENSG00000230102 | 18.21792 | -0.56489 | 0.169617 | -3.33037 | 0.000867 | 0.03117  | 0.616514 |
| ENSG00000078401 | 213.0729 | 0.532019 | 0.180075 | 2.954421 | 0.003133 | 0.03117  | 2.225762 |
| ENSG00000147592 | 49.47062 | 0.290621 | 0.090949 | 3.195448 | 0.001396 | 0.031223 | 0.989117 |
| ENSG00000119787 | 783.4446 | 0.131962 | 0.044823 | 2.944076 | 0.003239 | 0.031223 | 2.295759 |
| ENSG00000058091 | 2435.665 | 0.177762 | 0.060995 | 2.914387 | 0.003564 | 0.031335 | 2.514347 |
| ENSG00000233705 | 603.6421 | 0.220709 | 0.075011 | 2.94237  | 0.003257 | 0.031346 | 2.295759 |
| ENSG00000007923 | 461.3529 | -0.11651 | 0.039601 | -2.94204 | 0.003261 | 0.031361 | 2.295759 |
| ENSG00000122585 | 138.7645 | 0.452415 | 0.150551 | 3.005061 | 0.002655 | 0.031382 | 1.867169 |
| ENSG00000013561 | 774.7526 | 0.127092 | 0.043753 | 2.904729 | 0.003676 | 0.031382 | 2.583187 |
| ENSG00000156687 | 882.652  | 0.164743 | 0.056578 | 2.911802 | 0.003594 | 0.031501 | 2.514347 |
| ENSG00000287855 | 53.33726 | -0.38507 | 0.121032 | -3.18156 | 0.001465 | 0.031511 | 1.023066 |

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| ENSG00000163938 | 423.4965 | 0.147329 | 0.049471 | 2.978101 | 0.0029   | 0.031511 | 2.025126 |
| ENSG00000103257 | 1246.06  | -0.25532 | 0.087699 | -2.91135 | 0.003599 | 0.031511 | 2.514347 |
| ENSG00000184601 | 58.79807 | -0.40642 | 0.127405 | -3.18997 | 0.001423 | 0.031632 | 0.989117 |
| ENSG00000218793 | 5.62421  | 0.964938 | 0.254305 | 3.794407 | 0.000148 | 0.031664 | 0.102715 |
| ENSG00000053770 | 1465.716 | 0.134335 | 0.046317 | 2.900326 | 0.003728 | 0.031694 | 2.583187 |
| ENSG00000110013 | 386.8311 | 0.159018 | 0.053451 | 2.975012 | 0.00293  | 0.031755 | 2.025126 |
| ENSG00000155970 | 1178.313 | 0.164716 | 0.056126 | 2.934739 | 0.003338 | 0.031926 | 2.293762 |
| ENSG00000165443 | 1365.069 | 0.151554 | 0.05165  | 2.934265 | 0.003343 | 0.031928 | 2.295759 |
| ENSG00000215475 | 130.3721 | 0.200433 | 0.068093 | 2.94351  | 0.003245 | 0.031945 | 2.225762 |
| ENSG00000067048 | 562.1811 | 0.479127 | 0.163355 | 2.933046 | 0.003357 | 0.031999 | 2.29693  |
| ENSG00000114656 | 174.2146 | -0.15891 | 0.053492 | -2.97065 | 0.002972 | 0.032077 | 2.025126 |
| ENSG00000135341 | 964.3654 | 0.105471 | 0.035974 | 2.931898 | 0.003369 | 0.032077 | 2.295759 |
| ENSG00000119865 | 796.5217 | 0.123089 | 0.042513 | 2.895361 | 0.003787 | 0.032077 | 2.583187 |
| ENSG00000100441 | 385.253  | -0.13843 | 0.047084 | -2.93999 | 0.003282 | 0.03219  | 2.225762 |
| ENSG00000099246 | 1508.479 | 0.119133 | 0.040656 | 2.930259 | 0.003387 | 0.03219  | 2.295759 |
| ENSG00000080371 | 1075.209 | 0.102369 | 0.035276 | 2.901972 | 0.003708 | 0.03219  | 2.514347 |
| ENSG00000187398 | 308.4261 | 0.244459 | 0.082362 | 2.968118 | 0.002996 | 0.0322   | 2.025126 |
| ENSG00000130540 | 1894.692 | 0.212842 | 0.072648 | 2.929786 | 0.003392 | 0.0322   | 2.295759 |
| ENSG00000105204 | 273.9821 | -0.16789 | 0.057315 | -2.92924 | 0.003398 | 0.0322   | 2.295759 |
| ENSG00000143157 | 1266.034 | 0.111644 | 0.038479 | 2.901442 | 0.003714 | 0.0322   | 2.514347 |
| ENSG00000122068 | 794.0779 | 0.111179 | 0.038435 | 2.892683 | 0.00382  | 0.0322   | 2.583187 |
| ENSG00000180773 | 505.4628 | 0.16718  | 0.057806 | 2.892108 | 0.003827 | 0.032209 | 2.583187 |
| ENSG00000113615 | 389.9876 | 0.116213 | 0.039111 | 2.971378 | 0.002965 | 0.032282 | 1.995423 |
| ENSG00000102878 | 493.1386 | -0.18031 | 0.061578 | -2.92818 | 0.00341  | 0.032282 | 2.293762 |
| ENSG00000118402 | 462.5995 | 0.210886 | 0.071805 | 2.93694  | 0.003315 | 0.032323 | 2.225762 |
| ENSG00000180592 | 106.5687 | -0.18828 | 0.062372 | -3.01872 | 0.002538 | 0.032455 | 1.695647 |
| ENSG00000067704 | 763.3733 | 0.127486 | 0.043568 | 2.92612  | 0.003432 | 0.032455 | 2.293762 |
| ENSG00000111711 | 463.2529 | 0.182858 | 0.06161  | 2.968002 | 0.002997 | 0.032546 | 1.995423 |
| ENSG00000167619 | 371.2952 | -0.19179 | 0.06559  | -2.92403 | 0.003455 | 0.03259  | 2.295759 |
| ENSG00000008441 | 3065.674 | -0.17525 | 0.060481 | -2.89762 | 0.00376  | 0.032642 | 2.492774 |

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| ENSG00000100023 | 687.5606 | -0.12487 | 0.042613 | -2.93029 | 0.003386 | 0.032907 | 2.225762 |
| ENSG00000067715 | 13164.55 | 0.223027 | 0.077131 | 2.891528 | 0.003834 | 0.032958 | 2.514347 |
| ENSG00000152749 | 572.3642 | 0.145504 | 0.049671 | 2.929334 | 0.003397 | 0.03297  | 2.225762 |
| ENSG00000260855 | 130.2786 | -0.24093 | 0.082266 | -2.92861 | 0.003405 | 0.033027 | 2.225762 |
| ENSG00000075223 | 376.4417 | 0.356843 | 0.12065  | 2.957674 | 0.0031   | 0.033027 | 2.025126 |
| ENSG00000167548 | 3575.695 | -0.18086 | 0.062771 | -2.88124 | 0.003961 | 0.033068 | 2.583187 |
| ENSG00000114279 | 2480.317 | 0.192597 | 0.066654 | 2.889503 | 0.003859 | 0.033074 | 2.514347 |
| ENSG00000136531 | 6181.91  | 0.177756 | 0.061491 | 2.890777 | 0.003843 | 0.033206 | 2.492774 |
| ENSG00000072609 | 739.2371 | -0.14685 | 0.050356 | -2.91622 | 0.003543 | 0.033241 | 2.293762 |
| ENSG00000170185 | 501.2872 | 0.110588 | 0.037926 | 2.915863 | 0.003547 | 0.033241 | 2.295759 |
| ENSG00000234409 | 65.396   | -0.43808 | 0.138652 | -3.15953 | 0.00158  | 0.033284 | 1.020896 |
| ENSG00000235609 | 66.68717 | 0.335821 | 0.106653 | 3.148723 | 0.00164  | 0.033724 | 1.044965 |
| ENSG00000253208 | 21.92678 | -0.40589 | 0.123114 | -3.29687 | 0.000978 | 0.033746 | 0.622231 |
| ENSG00000052802 | 657.8856 | 0.297953 | 0.102052 | 2.919631 | 0.003504 | 0.033759 | 2.225762 |
| ENSG00000226328 | 214.1898 | 0.160459 | 0.055141 | 2.909947 | 0.003615 | 0.033759 | 2.295759 |
| ENSG00000100614 | 2841.908 | 0.116845 | 0.040548 | 2.881614 | 0.003956 | 0.033759 | 2.514347 |
| ENSG00000119899 | 310.0715 | 0.12512  | 0.043    | 2.909746 | 0.003617 | 0.033761 | 2.295759 |
| ENSG00000173221 | 260.1344 | 0.225413 | 0.076475 | 2.947548 | 0.003203 | 0.033871 | 2.025126 |
| ENSG00000151292 | 630.6039 | 0.140593 | 0.048359 | 2.90731  | 0.003646 | 0.033949 | 2.29693  |
| ENSG00000110090 | 736.4023 | -0.23427 | 0.081613 | -2.87045 | 0.004099 | 0.033949 | 2.583187 |
| ENSG00000238113 | 211.153  | -0.20825 | 0.070611 | -2.94927 | 0.003185 | 0.033974 | 1.995423 |
| ENSG00000170677 | 467.6224 | 0.206636 | 0.070167 | 2.944905 | 0.003231 | 0.033974 | 2.025126 |
| ENSG00000106113 | 120.0896 | -0.28507 | 0.09759  | -2.92107 | 0.003488 | 0.033974 | 2.189833 |
| ENSG00000124574 | 468.5118 | -0.15668 | 0.053748 | -2.91511 | 0.003556 | 0.033974 | 2.225762 |
| ENSG00000132485 | 929.2536 | 0.129171 | 0.044429 | 2.907323 | 0.003645 | 0.033974 | 2.293762 |
| ENSG00000146701 | 1180.069 | 0.140774 | 0.048435 | 2.906487 | 0.003655 | 0.033974 | 2.293762 |
| ENSG00000163946 | 1786.525 | 0.085761 | 0.029511 | 2.906053 | 0.00366  | 0.033974 | 2.295759 |
| ENSG00000198780 | 1205.303 | 0.134297 | 0.046214 | 2.905975 | 0.003661 | 0.033974 | 2.295759 |
| ENSG00000140740 | 1670.185 | 0.154645 | 0.05322  | 2.905748 | 0.003664 | 0.033974 | 2.293762 |
| ENSG00000146007 | 576.6562 | 0.183047 | 0.063001 | 2.905459 | 0.003667 | 0.033974 | 2.295759 |

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| ENSG00000278090 | 29.03583 | -0.4149  | 0.131034 | -3.16631 | 0.001544 | 0.034015 | 0.963911 |
| ENSG00000239763 | 42.52796 | -0.32245 | 0.102679 | -3.14035 | 0.001687 | 0.034015 | 1.053218 |
| ENSG00000198089 | 631.0956 | -0.1536  | 0.053567 | -2.86747 | 0.004138 | 0.034015 | 2.583187 |
| ENSG00000224255 | 11.85866 | -0.61347 | 0.162167 | -3.78293 | 0.000155 | 0.034073 | 0.0964   |
| ENSG00000255710 | 31.94841 | -0.37201 | 0.118512 | -3.13901 | 0.001695 | 0.034073 | 1.053218 |
| ENSG00000170624 | 346.1648 | 0.172008 | 0.058454 | 2.942611 | 0.003255 | 0.034073 | 2.025126 |
| ENSG00000106479 | 460.9522 | -0.10098 | 0.034776 | -2.9037  | 0.003688 | 0.034073 | 2.295759 |
| ENSG00000198612 | 863.6663 | 0.15924  | 0.055563 | 2.865958 | 0.004157 | 0.034073 | 2.583187 |
| ENSG00000008294 | 4954.461 | 0.089018 | 0.031067 | 2.865325 | 0.004166 | 0.03412  | 2.583187 |
| ENSG00000157219 | 180.2578 | 0.213961 | 0.072642 | 2.945405 | 0.003225 | 0.034179 | 1.995423 |
| ENSG00000103591 | 568.0467 | 0.144316 | 0.049576 | 2.911033 | 0.003602 | 0.034204 | 2.225762 |
| ENSG00000286653 | 23.22767 | 0.569336 | 0.157624 | 3.611989 | 0.000304 | 0.034235 | 0.187229 |
| ENSG00000153093 | 31.37086 | -0.34714 | 0.110663 | -3.13688 | 0.001708 | 0.034235 | 1.053218 |
| ENSG00000165389 | 140.9282 | 0.16938  | 0.058105 | 2.91508  | 0.003556 | 0.034235 | 2.189833 |
| ENSG00000105738 | 942.7606 | -0.18354 | 0.063913 | -2.87178 | 0.004082 | 0.034235 | 2.514347 |
| ENSG00000144357 | 3158.099 | 0.116195 | 0.040464 | 2.87154  | 0.004085 | 0.034235 | 2.514347 |
| ENSG00000132017 | 143.0085 | -0.18319 | 0.063299 | -2.89404 | 0.003803 | 0.034246 | 2.338927 |
| ENSG00000187902 | 942.381  | -0.20853 | 0.072632 | -2.87106 | 0.004091 | 0.034248 | 2.514347 |
| ENSG00000162188 | 105.9103 | 0.30339  | 0.097834 | 3.101082 | 0.001928 | 0.03429  | 1.182918 |
| ENSG00000129559 | 297.7426 | 0.1806   | 0.062306 | 2.89858  | 0.003749 | 0.03433  | 2.295759 |
| ENSG00000134077 | 317.4966 | 0.124419 | 0.042788 | 2.907795 | 0.00364  | 0.034363 | 2.225762 |
| ENSG00000172209 | 531.1836 | 0.217783 | 0.074919 | 2.906911 | 0.00365  | 0.034411 | 2.225762 |
| ENSG00000107295 | 2409.116 | 0.229392 | 0.07976  | 2.876039 | 0.004027 | 0.034411 | 2.456745 |
| ENSG00000101367 | 695.0794 | 0.117601 | 0.04112  | 2.859926 | 0.004237 | 0.034411 | 2.583187 |
| ENSG00000279568 | 28.38006 | -0.38463 | 0.121153 | -3.17478 | 0.001499 | 0.034475 | 0.911386 |
| ENSG00000116489 | 751.0989 | 0.133332 | 0.046496 | 2.86762  | 0.004136 | 0.034475 | 2.514347 |
| ENSG00000107854 | 1347.553 | 0.093904 | 0.032855 | 2.858103 | 0.004262 | 0.03455  | 2.583187 |
| ENSG00000233822 | 83.66245 | 0.268992 | 0.090016 | 2.988278 | 0.002806 | 0.034629 | 1.695647 |
| ENSG00000104936 | 475.0516 | -0.17809 | 0.061542 | -2.89383 | 0.003806 | 0.034707 | 2.293762 |
| ENSG00000157388 | 1420.47  | -0.13767 | 0.047434 | -2.90233 | 0.003704 | 0.03479  | 2.225762 |

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| ENSG00000176383 | 92.00725 | -0.21269 | 0.068475 | -3.10611 | 0.001896 | 0.034794 | 1.136415 |
| ENSG00000287677 | 84.77997 | -0.44789 | 0.144264 | -3.10464 | 0.001905 | 0.034794 | 1.142898 |
| ENSG00000188599 | 88.47083 | -0.23494 | 0.075924 | -3.09436 | 0.001972 | 0.034794 | 1.182918 |
| ENSG00000113441 | 2860.981 | 0.109087 | 0.038063 | 2.865927 | 0.004158 | 0.034794 | 2.492774 |
| ENSG00000273108 | 62.59144 | -0.29529 | 0.092538 | -3.191   | 0.001418 | 0.034819 | 0.848718 |
| ENSG00000095319 | 672.5697 | -0.10334 | 0.035745 | -2.89095 | 0.003841 | 0.034819 | 2.293762 |
| ENSG00000241685 | 136.3505 | 0.156655 | 0.054303 | 2.884832 | 0.003916 | 0.034819 | 2.338927 |
| ENSG00000122218 | 2705.049 | 0.115244 | 0.040166 | 2.86922  | 0.004115 | 0.034819 | 2.456745 |
| ENSG00000113161 | 1209.451 | 0.210037 | 0.073375 | 2.862534 | 0.004203 | 0.034819 | 2.514347 |
| ENSG00000050748 | 2112.013 | 0.141323 | 0.04938  | 2.861971 | 0.00421  | 0.034819 | 2.514347 |
| ENSG00000168913 | 587.7424 | -0.32542 | 0.11409  | -2.85235 | 0.00434  | 0.034905 | 2.583187 |
| ENSG00000246223 | 26.76047 | -0.4613  | 0.145647 | -3.16727 | 0.001539 | 0.034993 | 0.911386 |
| ENSG00000130176 | 93.02917 | 0.833615 | 0.279545 | 2.982044 | 0.002863 | 0.034993 | 1.695647 |
| ENSG00000105514 | 234.7363 | -0.1759  | 0.060901 | -2.88833 | 0.003873 | 0.034993 | 2.295759 |
| ENSG00000198743 | 1510.054 | 0.35575  | 0.124398 | 2.859772 | 0.004239 | 0.034993 | 2.514347 |
| ENSG00000130638 | 1342.047 | 0.119934 | 0.041946 | 2.859234 | 0.004247 | 0.034993 | 2.514347 |
| ENSG00000141198 | 244.3453 | 0.178271 | 0.060817 | 2.931289 | 0.003376 | 0.035029 | 1.995423 |
| ENSG00000224086 | 275.6984 | -0.17727 | 0.061194 | -2.89684 | 0.003769 | 0.035048 | 2.225762 |
| ENSG00000272645 | 96.49982 | -0.24226 | 0.078115 | -3.10136 | 0.001926 | 0.035061 | 1.136415 |
| ENSG00000126756 | 87.96699 | 0.199696 | 0.067004 | 2.980355 | 0.002879 | 0.0351   | 1.695647 |
| ENSG00000152147 | 125.3558 | 0.17971  | 0.06094  | 2.948949 | 0.003189 | 0.035263 | 1.867169 |
| ENSG00000174871 | 360.8623 | 0.210796 | 0.071694 | 2.940209 | 0.00328  | 0.035263 | 1.918337 |
| ENSG00000126733 | 269.8466 | 0.264353 | 0.091663 | 2.883974 | 0.003927 | 0.035263 | 2.295759 |
| ENSG00000164506 | 2722.371 | 0.131697 | 0.046007 | 2.862543 | 0.004203 | 0.035263 | 2.456745 |
| ENSG00000099917 | 860.2244 | -0.12955 | 0.045505 | -2.84693 | 0.004414 | 0.035263 | 2.583187 |
| ENSG00000118985 | 1462.273 | 0.156314 | 0.054931 | 2.845651 | 0.004432 | 0.035349 | 2.583187 |
| ENSG00000234509 | 17.26794 | -0.43769 | 0.129527 | -3.37919 | 0.000727 | 0.035383 | 0.42288  |
| ENSG00000259494 | 68.61685 | 0.19917  | 0.063673 | 3.12801  | 0.00176  | 0.035383 | 1.023066 |
| ENSG00000164638 | 320.7372 | 0.286995 | 0.099238 | 2.891985 | 0.003828 | 0.035383 | 2.225762 |
| ENSG00000135436 | 47.03979 | -0.2806  | 0.089731 | -3.12709 | 0.001765 | 0.035384 | 1.020896 |

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| ENSG00000203397 | 58.90623 | -0.25228 | 0.080838 | -3.12082 | 0.001803 | 0.035384 | 1.044965 |
| ENSG00000221826 | 25.51575 | -0.42399 | 0.135966 | -3.11834 | 0.001819 | 0.035384 | 1.053218 |
| ENSG00000024862 | 235.102  | 0.166219 | 0.056833 | 2.924703 | 0.003448 | 0.035384 | 1.995423 |
| ENSG00000228810 | 126.5184 | 0.22398  | 0.077356 | 2.895462 | 0.003786 | 0.035384 | 2.189833 |
| ENSG00000103248 | 190.921  | -0.13932 | 0.048178 | -2.89172 | 0.003831 | 0.035384 | 2.225762 |
| ENSG00000167978 | 9009.592 | -0.21876 | 0.076619 | -2.85523 | 0.004301 | 0.035384 | 2.492774 |
| ENSG00000099822 | 1298.064 | -0.22371 | 0.078429 | -2.85241 | 0.004339 | 0.035384 | 2.514347 |
| ENSG00000143164 | 1597.875 | 0.162488 | 0.056981 | 2.851632 | 0.00435  | 0.035384 | 2.514347 |
| ENSG00000104133 | 1729.486 | -0.0707  | 0.024855 | -2.84437 | 0.00445  | 0.035384 | 2.583187 |
| ENSG00000162813 | 177.1329 | 0.13695  | 0.0474   | 2.889256 | 0.003862 | 0.035468 | 2.225762 |
| ENSG00000240356 | 51.86481 | 0.317053 | 0.099706 | 3.179868 | 0.001473 | 0.035471 | 0.848718 |
| ENSG00000144668 | 516.8671 | 0.1293   | 0.044916 | 2.878704 | 0.003993 | 0.035501 | 2.29693  |
| ENSG00000145332 | 508.0131 | 0.140104 | 0.048668 | 2.878791 | 0.003992 | 0.03552  | 2.293762 |
| ENSG00000105355 | 196.1681 | 0.232647 | 0.079613 | 2.92221  | 0.003476 | 0.035529 | 1.995423 |
| ENSG00000125870 | 228.1979 | 0.155053 | 0.053705 | 2.887144 | 0.003888 | 0.035608 | 2.225762 |
| ENSG00000009413 | 1896.855 | -0.09784 | 0.034461 | -2.8393  | 0.004521 | 0.035663 | 2.583187 |
| ENSG00000110429 | 951.4273 | 0.103997 | 0.036039 | 2.885691 | 0.003906 | 0.035733 | 2.225762 |
| ENSG00000177889 | 993.2696 | 0.166184 | 0.057792 | 2.875551 | 0.004033 | 0.035768 | 2.293762 |
| ENSG00000111481 | 518.6756 | 0.123696 | 0.04302  | 2.875289 | 0.004037 | 0.035768 | 2.29693  |
| ENSG00000254330 | 14.07231 | -0.47659 | 0.145985 | -3.26466 | 0.001096 | 0.035789 | 0.622589 |
| ENSG00000286705 | 28.69788 | 0.281499 | 0.090452 | 3.112136 | 0.001857 | 0.035808 | 1.053218 |
| ENSG00000153956 | 1937.269 | 0.14835  | 0.052136 | 2.845446 | 0.004435 | 0.035808 | 2.514347 |
| ENSG00000158186 | 2292.428 | 0.216473 | 0.076082 | 2.845242 | 0.004438 | 0.035808 | 2.514347 |
| ENSG00000152078 | 742.3767 | 0.174361 | 0.061282 | 2.84521  | 0.004438 | 0.035808 | 2.514347 |
| ENSG00000107771 | 2458.554 | 0.11814  | 0.041526 | 2.844963 | 0.004442 | 0.035816 | 2.514347 |
| ENSG00000102900 | 1302.77  | -0.13533 | 0.047723 | -2.83571 | 0.004572 | 0.035868 | 2.583187 |
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| ENSG00000115963 | 144.453  | 0.393827 | 0.136436 | 2.886525 | 0.003895 | 0.035943 | 2.189833 |
| ENSG00000119242 | 1428.998 | -0.11921 | 0.041373 | -2.8813  | 0.00396  | 0.035943 | 2.225762 |

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| ENSG00000129055 | 267.7538 | 0.180696 | 0.062926 | 2.871582 | 0.004084 | 0.035943 | 2.295759 |
| ENSG00000068305 | 1949.133 | 0.120383 | 0.042349 | 2.842619 | 0.004474 | 0.035943 | 2.514347 |
| ENSG00000106460 | 1557.736 | 0.138511 | 0.048736 | 2.842089 | 0.004482 | 0.035983 | 2.514347 |
| ENSG00000126267 | 823.6183 | 0.160569 | 0.055958 | 2.869448 | 0.004112 | 0.036167 | 2.293762 |
| ENSG00000259258 | 26.06214 | -0.3569  | 0.114875 | -3.1068  | 0.001891 | 0.036169 | 1.053218 |
| ENSG00000112981 | 168.2387 | 0.2149   | 0.074653 | 2.878647 | 0.003994 | 0.036169 | 2.225762 |
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| ENSG00000238273 | 45.93471 | -0.29843 | 0.094209 | -3.16775 | 0.001536 | 0.036339 | 0.848718 |
| ENSG00000150540 | 181.9867 | 0.23186  | 0.079663 | 2.910531 | 0.003608 | 0.036339 | 1.995423 |
| ENSG00000156011 | 8672.975 | 0.127255 | 0.044399 | 2.866189 | 0.004154 | 0.036339 | 2.295759 |
| ENSG00000102038 | 965.1648 | 0.120096 | 0.042455 | 2.828765 | 0.004673 | 0.036339 | 2.583187 |
| ENSG00000152778 | 378.9102 | 0.165875 | 0.057892 | 2.865265 | 0.004167 | 0.036405 | 2.295759 |
| ENSG00000166974 | 3304.298 | 0.128456 | 0.04529  | 2.83628  | 0.004564 | 0.036405 | 2.514347 |
| ENSG00000166908 | 911.9851 | 0.127363 | 0.04433  | 2.873036 | 0.004065 | 0.036608 | 2.225762 |
| ENSG00000166479 | 970.8161 | 0.12798  | 0.045294 | 2.825514 | 0.00472  | 0.036608 | 2.583187 |
| ENSG00000185800 | 776.9501 | -0.13377 | 0.04735  | -2.82509 | 0.004727 | 0.036637 | 2.583187 |
| ENSG00000079785 | 1216.422 | 0.138863 | 0.048515 | 2.862265 | 0.004206 | 0.036648 | 2.295759 |
| ENSG00000128872 | 11146.72 | 0.126795 | 0.044636 | 2.840686 | 0.004502 | 0.036648 | 2.456745 |
| ENSG00000233038 | 51.60703 | -0.41449 | 0.133308 | -3.10928 | 0.001875 | 0.036723 | 1.020896 |
| ENSG00000153310 | 1266.116 | 0.169409 | 0.059204 | 2.861437 | 0.004217 | 0.036733 | 2.293762 |
| ENSG00000157833 | 476.9827 | 0.334069 | 0.116405 | 2.869897 | 0.004106 | 0.036837 | 2.225762 |
| ENSG00000117500 | 508.956  | 0.186538 | 0.065009 | 2.869399 | 0.004113 | 0.036875 | 2.225762 |
| ENSG00000143379 | 458.6732 | -0.11162 | 0.038909 | -2.86883 | 0.00412  | 0.036921 | 2.225762 |
| ENSG00000162639 | 136.5191 | 0.2128   | 0.07421  | 2.867549 | 0.004137 | 0.037031 | 2.225762 |
| ENSG00000113163 | 1157.188 | 0.109406 | 0.038284 | 2.857746 | 0.004267 | 0.037031 | 2.295759 |
| ENSG00000243927 | 167.5551 | 0.298451 | 0.102852 | 2.901733 | 0.003711 | 0.037036 | 1.995423 |
| ENSG00000139874 | 212.0812 | 0.238952 | 0.082365 | 2.901132 | 0.003718 | 0.037087 | 1.995423 |
| ENSG00000286230 | 9.761666 | 0.687175 | 0.182255 | 3.770396 | 0.000163 | 0.03717  | 0.087091 |

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| ENSG00000213693 | 50.95375 | -0.30519 | 0.098335 | -3.1036  | 0.001912 | 0.03717  | 1.020896 |
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| ENSG00000167703 | 871.6301 | -0.18097 | 0.063382 | -2.85519 | 0.004301 | 0.03717  | 2.295759 |
| ENSG00000162066 | 158.4919 | -0.21008 | 0.073713 | -2.85002 | 0.004372 | 0.03717  | 2.338927 |
| ENSG00000163161 | 683.6368 | -0.1161  | 0.04108  | -2.82628 | 0.004709 | 0.03717  | 2.514347 |
| ENSG00000197150 | 829.4143 | -0.13998 | 0.049044 | -2.85424 | 0.004314 | 0.037241 | 2.295759 |
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| ENSG00000163516 | 647.3384 | -0.16717 | 0.058606 | -2.85241 | 0.004339 | 0.03737  | 2.293762 |
| ENSG00000079313 | 742.3081 | -0.15904 | 0.056504 | -2.81465 | 0.004883 | 0.03737  | 2.583187 |
| ENSG00000185352 | 1773.134 | 0.183856 | 0.065331 | 2.814243 | 0.004889 | 0.03737  | 2.583187 |
| ENSG00000143742 | 1108.817 | 0.152514 | 0.054194 | 2.814241 | 0.004889 | 0.03737  | 2.583187 |
| ENSG00000228526 | 243.3922 | -0.37237 | 0.130139 | -2.86135 | 0.004218 | 0.0374   | 2.225762 |
| ENSG00000184154 | 104.9341 | -0.22997 | 0.074974 | -3.06729 | 0.00216  | 0.037469 | 1.136415 |
| ENSG00000137642 | 9781.591 | 0.146122 | 0.051785 | 2.821671 | 0.004777 | 0.037469 | 2.514347 |
| ENSG00000236830 | 63.52558 | -0.27724 | 0.089462 | -3.09901 | 0.001942 | 0.037471 | 1.020896 |
| ENSG00000167552 | 4463.836 | 0.262726 | 0.093127 | 2.821147 | 0.004785 | 0.037476 | 2.514347 |
| ENSG00000103335 | 711.1824 | -0.18677 | 0.065549 | -2.84932 | 0.004381 | 0.037592 | 2.293762 |
| ENSG00000124207 | 909.5797 | 0.158596 | 0.055672 | 2.848785 | 0.004389 | 0.037598 | 2.295759 |
| ENSG00000160216 | 2173.4   | -0.10405 | 0.036526 | -2.84865 | 0.00439  | 0.037598 | 2.295759 |
| ENSG00000198176 | 390.8933 | -0.12226 | 0.042338 | -2.88777 | 0.00388  | 0.037613 | 2.025126 |
| ENSG00000144228 | 486.4083 | 0.11642  | 0.040873 | 2.848343 | 0.004395 | 0.037613 | 2.295759 |
| ENSG00000113448 | 1779.015 | 0.106419 | 0.037868 | 2.810269 | 0.00495  | 0.037613 | 2.583187 |
| ENSG00000136404 | 126.3655 | 0.211391 | 0.07439  | 2.841681 | 0.004488 | 0.037641 | 2.338927 |
| ENSG00000101213 | 63.58819 | -0.36586 | 0.117813 | -3.10539 | 0.0019   | 0.03767  | 0.989117 |
| ENSG00000268205 | 928.45   | 0.114534 | 0.040246 | 2.845814 | 0.00443  | 0.037814 | 2.295759 |
| ENSG00000189339 | 1147.633 | -0.21069 | 0.074036 | -2.84573 | 0.004431 | 0.037837 | 2.293762 |
| ENSG00000094804 | 68.38706 | 0.297754 | 0.096286 | 3.092407 | 0.001985 | 0.037991 | 1.023066 |

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| ENSG00000004799 | 913.3573 | -0.3637  |  |  |  | 0.12791  | -2.84337 | 0.004464 | 0.038045 | 2.295759 |
| ENSG00000176920 | 105.5614 | -0.24463 |  |  |  | 0.080255 | -3.04814 | 0.002303 | 0.038067 | 1.182918 |
| ENSG00000182512 | 251.6916 | 0.168752 |  |  |  | 0.05936  | 2.842842 | 0.004471 | 0.038068 | 2.295759 |
| ENSG00000196700 | 869.4698 | -0.13331 |  |  |  | 0.046897 | -2.84256 | 0.004475 | 0.038074 | 2.293762 |
| ENSG00000232354 | 125.1282 | -0.23301 |  |  |  | 0.082149 | -2.83642 | 0.004562 | 0.038074 | 2.338927 |
| ENSG00000088367 | 6319.371 | -0.13523 |  |  |  | 0.047939 | -2.82085 | 0.00479  | 0.038074 | 2.456745 |
| ENSG00000077454 | 150.1934 | -0.19681 |  |  |  | 0.069396 | -2.83608 | 0.004567 | 0.038085 | 2.338927 |
| ENSG00000101958 | 72.68901 | 0.32763  |  |  |  | 0.111554 | 2.936962 | 0.003314 | 0.038094 | 1.695647 |
| ENSG00000135047 | 483.6839 | 0.194468 |  |  |  | 0.069359 | 2.803788 | 0.005051 | 0.038094 | 2.583187 |
| ENSG00000084444 | 1483.911 | 0.156036 |  |  |  | 0.054912 | 2.841565 | 0.004489 | 0.038113 | 2.293762 |
| ENSG00000274461 | 128.2899 | -0.20342 |  |  |  | 0.070923 | -2.86818 | 0.004128 | 0.038117 | 2.108016 |
| ENSG00000274220 | 42.06186 | -0.30005 |  |  |  | 0.09543  | -3.14419 | 0.001665 | 0.038173 | 0.848718 |
| ENSG00000245526 | 1138.177 | -0.13198 |  |  |  | 0.046952 | -2.81102 | 0.004938 | 0.038187 | 2.514347 |
| ENSG00000133958 | 2110.575 | -0.10809 |  |  |  | 0.038065 | -2.83974 | 0.004515 | 0.038218 | 2.295759 |
| ENSG00000127586 | 161.9316 | -0.23985 |  |  |  | 0.083684 | -2.86613 | 0.004155 | 0.038284 | 2.108016 |
| ENSG00000066084 | 2872.777 | 0.159279 |  |  |  | 0.056695 | 2.809374 | 0.004964 | 0.038323 | 2.514347 |
| ENSG00000008952 | 2279.345 | 0.105728 |  |  |  | 0.037647 | 2.808385 | 0.004979 | 0.038421 | 2.514347 |
| ENSG00000196353 | 507.3655 | 0.204827 |  |  |  | 0.073178 | 2.799034 | 0.005126 | 0.038477 | 2.583187 |
| ENSG00000162931 | 251.6508 | -0.18452 |  |  |  | 0.063987 | -2.8838  | 0.003929 | 0.038517 | 1.977088 |
| ENSG00000001036 | 144.0811 | 0.15478  |  |  |  | 0.054289 | 2.851033 | 0.004358 | 0.038549 | 2.189833 |
| ENSG00000068976 | 327.5919 | 0.313036 |  |  |  | 0.108578 | 2.883051 | 0.003938 | 0.038558 | 1.977088 |
| ENSG00000101182 | 586.3023 | 0.136454 |  |  |  | 0.048774 | 2.797674 | 0.005147 | 0.038558 | 2.583187 |
| ENSG00000110330 | 665.4547 | 0.126127 |  |  |  | 0.044334 | 2.844941 | 0.004442 | 0.038586 | 2.225762 |
| ENSG00000107362 | 532.6375 | 0.177117 |  |  |  | 0.062265 | 2.84457  | 0.004447 | 0.038586 | 2.225762 |
| ENSG00000068903 | 1760.343 | 0.127642 |  |  |  | 0.045377 | 2.812945 | 0.004909 | 0.038586 | 2.456745 |
| ENSG00000123560 | 19894.54 | 0.368889 |  |  |  | 0.131348 | 2.808483 | 0.004978 | 0.038586 | 2.492774 |
| ENSG00000274180 | 232.2151 | -0.19495 |  |  |  | 0.06856  | -2.8435  | 0.004462 | 0.038693 | 2.225762 |
| ENSG00000103227 | 389.8901 | -0.21207 |  |  |  | 0.07381  | -2.87316 | 0.004064 | 0.038695 | 2.025126 |
| ENSG00000162694 | 482.5391 | 0.204884 |  |  |  | 0.072062 | 2.843146 | 0.004467 | 0.038695 | 2.225762 |
| ENSG00000158290 | 1107.724 | 0.104896 |  |  |  | 0.037412 | 2.803791 | 0.005051 | 0.038708 | 2.514347 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000067365 | 259.3878 | -0.14604 | 0.051378 | -2.84244 | 0.004477 | 0.038721 | 2.225762 |
| ENSG00000121769 | 553.2756 | 0.180989 | 0.063674 | 2.842435 | 0.004477 | 0.038721 | 2.225762 |
| ENSG00000250329 | 39.13512 | -0.31099 | 0.100927 | -3.08137 | 0.002061 | 0.0388   | 1.020896 |
| ENSG00000141564 | 1147.975 | -0.11809 | 0.041562 | -2.84129 | 0.004493 | 0.0388   | 2.225762 |
| ENSG00000113319 | 2749.865 | 0.184751 | 0.065861 | 2.805163 | 0.005029 | 0.0388   | 2.492774 |
| ENSG00000206418 | 401.8977 | 0.138303 | 0.048179 | 2.870636 | 0.004096 | 0.038859 | 2.025126 |
| ENSG00000004961 | 165.804  | 0.172282 | 0.060673 | 2.839504 | 0.004518 | 0.03892  | 2.225762 |
| ENSG00000125912 | 551.2229 | -0.13719 | 0.048318 | -2.83934 | 0.004521 | 0.03892  | 2.225762 |
| ENSG00000099954 | 490.5089 | -0.20128 | 0.07113  | -2.82969 | 0.004659 | 0.03892  | 2.293762 |
| ENSG00000145425 | 1023.092 | 0.171966 | 0.061597 | 2.79181  | 0.005241 | 0.03892  | 2.583187 |
| ENSG00000151067 | 2354.944 | -0.13102 | 0.046936 | -2.79146 | 0.005247 | 0.03892  | 2.583187 |
| ENSG00000170745 | 80.28362 | 0.323261 | 0.106505 | 3.035158 | 0.002404 | 0.03892  | 1.182918 |
| ENSG00000198894 | 1352.926 | 0.103953 | 0.036746 | 2.828944 | 0.00467  | 0.038937 | 2.295759 |
| ENSG00000163466 | 1136.943 | 0.12624  | 0.044625 | 2.828879 | 0.004671 | 0.038958 | 2.293762 |
| ENSG00000116266 | 678.4346 | 0.119999 | 0.043016 | 2.789628 | 0.005277 | 0.039059 | 2.583187 |
| ENSG00000128284 | 117.5661 | -0.34005 | 0.117555 | -2.8927  | 0.00382  | 0.039093 | 1.867169 |
| ENSG00000135637 | 197.4955 | -0.1493  | 0.052633 | -2.83665 | 0.004559 | 0.039124 | 2.225762 |
| ENSG00000146830 | 1409.312 | -0.14116 | 0.050462 | -2.79725 | 0.005154 | 0.039133 | 2.514347 |
| ENSG00000147164 | 618.0612 | 0.106679 | 0.03826  | 2.788273 | 0.005299 | 0.039142 | 2.583187 |
| ENSG00000235944 | 175.5485 | -0.20892 | 0.072783 | -2.87048 | 0.004099 | 0.039166 | 1.995423 |
| ENSG00000157306 | 117.0735 | -0.21671 | 0.075963 | -2.8528  | 0.004334 | 0.039166 | 2.108016 |
| ENSG00000117425 | 208.4538 | -0.21967 | 0.077743 | -2.82559 | 0.004719 | 0.039166 | 2.295759 |
| ENSG00000250490 | 27.55062 | -0.39494 | 0.1262   | -3.12946 | 0.001751 | 0.03919  | 0.848718 |
| ENSG00000185245 | 39.32373 | -0.37079 | 0.120735 | -3.07106 | 0.002133 | 0.03919  | 1.035363 |
| ENSG00000280157 | 78.24464 | -0.24094 | 0.079178 | -3.04304 | 0.002342 | 0.03919  | 1.136415 |
| ENSG00000124562 | 166.5828 | 0.180187 | 0.06356  | 2.83493  | 0.004584 | 0.03919  | 2.225762 |
| ENSG00000128917 | 140.8701 | -0.40151 | 0.142448 | -2.81866 | 0.004822 | 0.03919  | 2.338927 |
| ENSG00000139687 | 658.086  | 0.135352 | 0.048574 | 2.786494 | 0.005328 | 0.03919  | 2.583187 |
| ENSG00000162591 | 161.5425 | -0.29528 | 0.102197 | -2.88928 | 0.003861 | 0.039256 | 1.867169 |
| ENSG00000136273 | 263.865  | -0.12802 | 0.044715 | -2.86297 | 0.004197 | 0.039321 | 2.025126 |

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| ENSG00000139174 | 365.4681 | 0.127566 | 0.045194 | 2.822625 | 0.004763 | 0.039345 | 2.295759 |
| ENSG00000107560 | 1027.994 | 0.107935 | 0.038643 | 2.793134 | 0.00522  | 0.03935  | 2.514347 |
| ENSG00000095951 | 1210.522 | -0.10651 | 0.037611 | -2.8319  | 0.004627 | 0.039368 | 2.225762 |
| ENSG00000188807 | 333.4477 | -0.16441 | 0.058261 | -2.82195 | 0.004773 | 0.039368 | 2.295759 |
| ENSG00000105171 | 222.9151 | 0.142744 | 0.050593 | 2.821392 | 0.004782 | 0.039416 | 2.295759 |
| ENSG00000061337 | 1104.233 | -0.16292 | 0.058566 | -2.78187 | 0.005405 | 0.039575 | 2.583187 |
| ENSG00000286388 | 193.031  | -0.27203 | 0.095027 | -2.86264 | 0.004201 | 0.039784 | 1.995423 |
| ENSG00000106624 | 712.7249 | 0.470795 | 0.167051 | 2.818271 | 0.004828 | 0.039784 | 2.293762 |
| ENSG00000243433 | 16.94645 | -0.40891 | 0.126861 | -3.22329 | 0.001267 | 0.039858 | 0.600464 |
| ENSG00000152402 | 3401.368 | 0.179768 | 0.064691 | 2.778894 | 0.005454 | 0.039858 | 2.583187 |
| ENSG00000259660 | 49.7354  | -0.47151 | 0.153716 | -3.06739 | 0.002159 | 0.039907 | 1.020896 |
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| ENSG00000106028 | 361.3722 | 0.151602 | 0.053662 | 2.825105 | 0.004727 | 0.039983 | 2.225762 |
| ENSG00000033800 | 996.46   | 0.109875 | 0.039561 | 2.777359 | 0.00548  | 0.039983 | 2.583187 |
| ENSG00000267287 | 16.10793 | -0.68514 | 0.212726 | -3.22075 | 0.001279 | 0.040024 | 0.600464 |
| ENSG00000006128 | 92.35826 | 0.481884 | 0.158876 | 3.033085 | 0.002421 | 0.040024 | 1.136415 |
| ENSG00000061794 | 405.2961 | 0.162043 | 0.056672 | 2.859316 | 0.004246 | 0.040024 | 1.995423 |
| ENSG00000164434 | 241.678  | 0.37388  | 0.130783 | 2.85879  | 0.004253 | 0.040024 | 1.995423 |
| ENSG00000116580 | 1374.425 | -0.11802 | 0.041787 | -2.82426 | 0.004739 | 0.040024 | 2.225762 |
| ENSG00000110011 | 157.5225 | -0.15631 | 0.055387 | -2.82206 | 0.004772 | 0.040241 | 2.225762 |
| ENSG00000247708 | 496.3999 | -0.13387 | 0.047612 | -2.81165 | 0.004929 | 0.040259 | 2.29693  |
| ENSG00000138834 | 6879.904 | -0.12878 | 0.046161 | -2.78974 | 0.005275 | 0.040263 | 2.456745 |
| ENSG00000186908 | 1472.127 | 0.126978 | 0.045795 | 2.77276  | 0.005558 | 0.040328 | 2.583187 |
| ENSG00000122641 | 45.05972 | 0.436966 | 0.140277 | 3.115027 | 0.001839 | 0.040372 | 0.848718 |
| ENSG00000266538 | 35.71681 | -0.30224 | 0.099053 | -3.05132 | 0.002278 | 0.040372 | 1.053218 |
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| ENSG00000105053 | 404.7811 | -0.09132 | 0.031864 | -2.86597 | 0.004157 | 0.040372 | 1.918337 |
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| ENSG00000119729 | 701.1779 | 0.157601 | 0.056089 | 2.809856 | 0.004956 | 0.040372 | 2.293762 |



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| ENSG00000164985 | 1734.517 | 0.119043 | 0.042367 | 2.809829 | 0.004957 | 0.040372 | 2.293762 |
| ENSG00000125977 | 546.9499 | 0.133169 | 0.047406 | 2.80913  | 0.004968 | 0.040372 | 2.295759 |
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| ENSG00000074842 | 143.1217 | 0.166722 | 0.059487 | 2.802673 | 0.005068 | 0.040372 | 2.338927 |
| ENSG00000065923 | 1524.422 | 0.135739 | 0.048976 | 2.771538 | 0.005579 | 0.040372 | 2.583187 |
| ENSG00000076928 | 641.2218 | -0.19079 | 0.068859 | -2.77072 | 0.005593 | 0.040372 | 2.583187 |
| ENSG00000113389 | 36.71627 | 0.416562 | 0.136452 | 3.05281  | 0.002267 | 0.040396 | 1.044965 |
| ENSG00000155011 | 36.52553 | 0.605377 | 0.19787  | 3.05947  | 0.002217 | 0.040399 | 1.020896 |
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| ENSG00000206432 | 223.089  | 0.181254 | 0.063093 | 2.872785 | 0.004069 | 0.040475 | 1.867169 |
| ENSG00000140990 | 472.5097 | 0.160585 | 0.056075 | 2.863751 | 0.004187 | 0.040475 | 1.918337 |
| ENSG00000213741 | 733.6902 | 0.172602 | 0.061499 | 2.806591 | 0.005007 | 0.040475 | 2.295759 |
| ENSG00000172009 | 732.142  | -0.12582 | 0.044833 | -2.80635 | 0.005011 | 0.040475 | 2.295759 |
| ENSG00000164076 | 1856.164 | 0.186882 | 0.067106 | 2.784901 | 0.005354 | 0.040475 | 2.456745 |
| ENSG00000184786 | 51.96966 | 0.267493 | 0.087505 | 3.056901 | 0.002236 | 0.040496 | 1.023066 |
| ENSG00000070444 | 489.9923 | -0.15511 | 0.055277 | -2.80597 | 0.005016 | 0.040496 | 2.293762 |
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| ENSG00000253641 | 354.2268 | -0.15211 | 0.053373 | -2.84999 | 0.004372 | 0.040511 | 1.995423 |
| ENSG00000197121 | 1184.78  | 0.165934 | 0.059146 | 2.805473 | 0.005024 | 0.040511 | 2.293762 |
| ENSG00000177707 | 573.4629 | 0.15236  | 0.05506  | 2.767175 | 0.005654 | 0.040511 | 2.583187 |
| ENSG00000146729 | 627.0916 | 0.142124 | 0.050672 | 2.804753 | 0.005036 | 0.040513 | 2.29693  |
| ENSG00000183576 | 1235.827 | 0.105568 | 0.03764  | 2.804627 | 0.005037 | 0.040529 | 2.295759 |
| ENSG00000156026 | 216.5875 | 0.145893 | 0.051298 | 2.844015 | 0.004455 | 0.040568 | 2.025126 |
| ENSG00000204217 | 4338.751 | 0.139658 | 0.050205 | 2.781745 | 0.005407 | 0.040568 | 2.456745 |
| ENSG00000129353 | 1132.086 | -0.18285 | 0.065901 | -2.77459 | 0.005527 | 0.040568 | 2.514347 |
| ENSG00000197603 | 2494.639 | -0.09736 | 0.03509  | -2.77452 | 0.005528 | 0.040568 | 2.514347 |
| ENSG00000187741 | 118.1181 | -0.19868 | 0.070492 | -2.81847 | 0.004825 | 0.040599 | 2.189833 |
| ENSG00000082482 | 126.6771 | 0.272947 | 0.097031 | 2.813    | 0.004908 | 0.040609 | 2.225762 |
| ENSG00000255317 | 37.34229 | -0.34674 | 0.113879 | -3.04478 | 0.002328 | 0.040693 | 1.053218 |

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| ENSG00000279382 | 90.23316 | -0.2455  | 0.081308 | -3.01944 | 0.002532 | 0.040735 | 1.142898 |
| ENSG00000165476 | 618.2933 | 0.183216 | 0.065389 | 2.801941 | 0.00508  | 0.040735 | 2.293762 |
| ENSG00000138669 | 167.5103 | 0.209947 | 0.074948 | 2.801222 | 0.005091 | 0.040735 | 2.295759 |
| ENSG00000134042 | 751.6863 | -0.31373 | 0.11319  | -2.77175 | 0.005576 | 0.040735 | 2.514347 |
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| ENSG00000171824 | 797.2749 | -0.1394  | 0.049776 | -2.80047 | 0.005103 | 0.040789 | 2.295759 |
| ENSG00000155380 | 1010.539 | -0.41172 | 0.147064 | -2.7996  | 0.005117 | 0.040879 | 2.295759 |
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| ENSG00000254839 | 35.31735 | -0.33409 | 0.109681 | -3.04603 | 0.002319 | 0.041039 | 1.035363 |
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| ENSG00000123983 | 2902.884 | 0.147862 | 0.053627 | 2.757237 | 0.005829 | 0.041309 | 2.583187 |
| ENSG00000160214 | 394.8107 | -0.1339  | 0.047731 | -2.80527 | 0.005027 | 0.041328 | 2.225762 |
| ENSG00000154736 | 49.16235 | 0.30035  | 0.098278 | 3.056132 | 0.002242 | 0.041454 | 0.989117 |
| ENSG00000134013 | 84.60044 | -0.2618  | 0.087351 | -2.99709 | 0.002726 | 0.041454 | 1.201846 |
| ENSG00000160051 | 95.68122 | -0.18008 | 0.060093 | -2.99676 | 0.002729 | 0.041458 | 1.201846 |
| ENSG00000280798 | 442.4488 | 0.1214   | 0.043299 | 2.803767 | 0.005051 | 0.041458 | 2.225762 |
| ENSG00000132938 | 885.9001 | -0.17661 | 0.063007 | -2.80311 | 0.005061 | 0.041471 | 2.225762 |
| ENSG00000151413 | 191.4218 | 0.156715 | 0.056107 | 2.793152 | 0.00522  | 0.041471 | 2.295759 |
| ENSG00000110435 | 723.0004 | 0.136482 | 0.048865 | 2.793039 | 0.005222 | 0.041471 | 2.295759 |
| ENSG00000166206 | 2569.932 | 0.151333 | 0.054621 | 2.770619 | 0.005595 | 0.041504 | 2.456745 |
| ENSG00000100380 | 1971.772 | 0.12574  | 0.045031 | 2.792289 | 0.005234 | 0.041526 | 2.295759 |
| ENSG00000231458 | 12.63738 | -0.54533 | 0.170614 | -3.19627 | 0.001392 | 0.0416   | 0.60691  |
| ENSG00000154188 | 70.87527 | 0.421046 | 0.138322 | 3.043963 | 0.002335 | 0.0416   | 1.020896 |
| ENSG00000287537 | 53.55788 | -0.3359  | 0.11038  | -3.04314 | 0.002341 | 0.0416   | 1.020896 |
| ENSG00000254995 | 82.13551 | -0.30869 | 0.102528 | -3.01083 | 0.002605 | 0.0416   | 1.136415 |
| ENSG00000243679 | 141.7697 | -0.2217  | 0.077582 | -2.85763 | 0.004268 | 0.0416   | 1.867169 |
| ENSG00000198276 | 309.6021 | -0.17426 | 0.06222  | -2.80067 | 0.0051   | 0.0416   | 2.225762 |
| ENSG00000124733 | 248.9436 | 0.166667 | 0.059729 | 2.790385 | 0.005265 | 0.0416   | 2.295759 |
| ENSG00000170027 | 10013.48 | 0.168789 | 0.061125 | 2.761348 | 0.005756 | 0.0416   | 2.514347 |
| ENSG00000116005 | 1273.676 | 0.119794 | 0.043529 | 2.752052 | 0.005922 | 0.0416   | 2.583187 |

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| ENSG00000223959 | 347.7701 | -0.18651 | 0.066848 | -2.79006 | 0.00527  | 0.041608 | 2.295759 |
| ENSG00000268307 | 4.890967 | -0.92324 | 0.246108 | -3.75136 | 0.000176 | 0.041623 | 0.076553 |
| ENSG00000162923 | 1625.287 | 0.084635 | 0.030339 | 2.78965  | 0.005277 | 0.041635 | 2.293762 |
| ENSG00000160392 | 280.1785 | -0.12953 | 0.046437 | -2.78942 | 0.00528  | 0.041635 | 2.295759 |
| ENSG00000089063 | 595.3755 | 0.129175 | 0.046311 | 2.789275 | 0.005283 | 0.041663 | 2.293762 |
| ENSG00000198945 | 125.829  | -0.16912 | 0.060432 | -2.79849 | 0.005134 | 0.0417   | 2.225762 |
| ENSG00000103174 | 617.834  | -0.12789 | 0.045865 | -2.78839 | 0.005297 | 0.0417   | 2.295759 |
| ENSG00000148481 | 738.7804 | 0.142826 | 0.051223 | 2.788317 | 0.005298 | 0.041725 | 2.293762 |
| ENSG00000252835 | 187.2047 | 0.245935 | 0.086879 | 2.830769 | 0.004644 | 0.041955 | 1.995423 |
| ENSG00000213465 | 285.9192 | 0.152122 | 0.053826 | 2.826192 | 0.004711 | 0.041955 | 2.025126 |
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| ENSG00000085872 | 284.004  | -0.17529 | 0.062701 | -2.79567 | 0.005179 | 0.041955 | 2.225762 |
| ENSG00000152595 | 82.2275  | 0.469184 | 0.156746 | 2.993284 | 0.00276  | 0.042043 | 1.182918 |
| ENSG00000101439 | 5829.223 | -0.2667  | 0.095792 | -2.78418 | 0.005366 | 0.042091 | 2.295759 |
| ENSG00000113456 | 370.142  | 0.128866 | 0.04629  | 2.783906 | 0.005371 | 0.042091 | 2.295759 |
| ENSG00000126368 | 541.9208 | -0.20753 | 0.074553 | -2.78362 | 0.005376 | 0.042091 | 2.29693  |
| ENSG00000162409 | 894.6202 | 0.128835 | 0.046929 | 2.745325 | 0.006045 | 0.042091 | 2.583187 |
| ENSG00000167721 | 335.9179 | -0.1115  | 0.039484 | -2.82401 | 0.004743 | 0.042098 | 2.025126 |
| ENSG00000227533 | 67.55321 | -0.28659 | 0.094423 | -3.03513 | 0.002404 | 0.042225 | 1.023066 |
| ENSG00000169933 | 1668.538 | 0.151005 | 0.054275 | 2.782217 | 0.005399 | 0.042264 | 2.293762 |
| ENSG00000081791 | 961.2561 | -0.08731 | 0.031723 | -2.75217 | 0.00592  | 0.042264 | 2.514347 |
| ENSG00000099769 | 24.58502 | -0.42013 | 0.13768  | -3.05153 | 0.002277 | 0.042316 | 0.963911 |
| ENSG00000197608 | 440.7752 | -0.12823 | 0.045449 | -2.8214  | 0.004781 | 0.042316 | 2.025126 |
| ENSG00000083937 | 432.2323 | 0.153897 | 0.055141 | 2.790982 | 0.005255 | 0.042316 | 2.225762 |
| ENSG00000189043 | 2339.606 | 0.226172 | 0.08133  | 2.780926 | 0.00542  | 0.042316 | 2.295759 |
| ENSG00000205089 | 74.53184 | -0.20286 | 0.067624 | -2.99974 | 0.002702 | 0.042335 | 1.142898 |
| ENSG00000104859 | 533.711  | -0.18061 | 0.064964 | -2.7801  | 0.005434 | 0.042381 | 2.293762 |
| ENSG00000131459 | 336.5869 | -0.16461 | 0.059213 | -2.77992 | 0.005437 | 0.042381 | 2.295759 |
| ENSG00000165006 | 678.0993 | 0.10187  | 0.036649 | 2.779581 | 0.005443 | 0.042392 | 2.295759 |
| ENSG00000141337 | 191.2628 | -0.18099 | 0.065134 | -2.77868 | 0.005458 | 0.042487 | 2.295759 |

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| ENSG00000117461 | 544.4621 | 0.23626  | 0.085035 | 2.778377 | 0.005463 | 0.042487 | 2.29693  |
| ENSG00000084234 | 4740.88  | 0.111255 | 0.040051 | 2.777802 | 0.005473 | 0.042542 | 2.295759 |
| ENSG00000061938 | 3138.819 | -0.17977 | 0.065236 | -2.75574 | 0.005856 | 0.042542 | 2.456745 |
| ENSG00000128791 | 264.7272 | 0.142599 | 0.051339 | 2.777622 | 0.005476 | 0.042545 | 2.295759 |
| ENSG00000175764 | 822.4437 | -0.14934 | 0.053773 | -2.7773  | 0.005481 | 0.042566 | 2.295759 |
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| ENSG00000137857 | 251.3902 | -0.20752 | 0.073538 | -2.8219  | 0.004774 | 0.042582 | 1.995423 |
| ENSG00000065970 | 367.8429 | -0.10993 | 0.039444 | -2.78705 | 0.005319 | 0.042582 | 2.225762 |
| ENSG00000113312 | 796.8335 | 0.111672 | 0.040218 | 2.776666 | 0.005492 | 0.042582 | 2.295759 |
| ENSG00000174456 | 562.9081 | 0.164016 | 0.059079 | 2.776238 | 0.005499 | 0.042582 | 2.29693  |
| ENSG00000149679 | 240.2445 | -0.13542 | 0.048779 | -2.77617 | 0.0055   | 0.042592 | 2.295759 |
| ENSG00000100568 | 683.1616 | 0.105959 | 0.038583 | 2.746228 | 0.006028 | 0.042603 | 2.514347 |
| ENSG00000177947 | 27.94063 | -0.4221  | 0.138557 | -3.04642 | 0.002316 | 0.042669 | 0.963911 |
| ENSG00000253771 | 244.0608 | -0.18834 | 0.066721 | -2.82285 | 0.00476  | 0.042737 | 1.977088 |
| ENSG00000056291 | 18.30388 | 0.586152 | 0.183564 | 3.193167 | 0.001407 | 0.042759 | 0.583933 |
| ENSG00000122705 | 959.8604 | 0.133396 | 0.048086 | 2.774126 | 0.005535 | 0.042774 | 2.293762 |
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| ENSG00000172461 | 3847.192 | 0.142414 | 0.051904 | 2.743821 | 0.006073 | 0.042793 | 2.514347 |
| ENSG00000111364 | 287.2765 | -0.14775 | 0.053275 | -2.77328 | 0.005549 | 0.042803 | 2.295759 |
| ENSG00000174437 | 7686.714 | 0.111653 | 0.040698 | 2.743427 | 0.00608  | 0.042803 | 2.514347 |
| ENSG00000133103 | 624.5411 | 0.112031 | 0.040972 | 2.734351 | 0.00625  | 0.042808 | 2.583187 |
| ENSG00000204392 | 86.55173 | 0.21079  | 0.07346  | 2.869438 | 0.004112 | 0.04287  | 1.695647 |
| ENSG00000018189 | 4362.899 | 0.125218 | 0.045808 | 2.733559 | 0.006265 | 0.04287  | 2.583187 |
| ENSG00000260790 | 15.35271 | -0.38826 | 0.12326  | -3.14995 | 0.001633 | 0.042987 | 0.670508 |
| ENSG00000139200 | 465.9396 | -0.23595 | 0.084841 | -2.78103 | 0.005419 | 0.042987 | 2.225762 |
| ENSG00000064419 | 900.2666 | 0.091583 | 0.033411 | 2.741076 | 0.006124 | 0.042987 | 2.514347 |
| ENSG00000238230 | 37.19389 | -0.41839 | 0.138646 | -3.0177  | 0.002547 | 0.042999 | 1.044965 |
| ENSG00000275052 | 1186.724 | 0.089031 | 0.032489 | 2.740302 | 0.006138 | 0.043047 | 2.514347 |
| ENSG00000147874 | 369.1887 | 0.120912 | 0.043663 | 2.769205 | 0.005619 | 0.043139 | 2.295759 |
| ENSG00000128655 | 40.82547 | 0.34239  | 0.11353  | 3.015857 | 0.002563 | 0.0432   | 1.044965 |

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| ENSG00000120942 | 194.6802 | -0.1269  | 0.045192 | -2.80804 | 0.004984 | 0.043318 | 2.025126 |
| ENSG00000179818 | 1432.504 | -0.12663 | 0.045756 | -2.76739 | 0.005651 | 0.043318 | 2.295759 |
| ENSG00000107643 | 1022.132 | 0.123093 | 0.044967 | 2.737403 | 0.006193 | 0.043325 | 2.514347 |
| ENSG00000180611 | 137.7006 | 0.223868 | 0.080467 | 2.782117 | 0.005401 | 0.043358 | 2.189833 |
| ENSG00000204977 | 519.7104 | 0.119516 | 0.043042 | 2.776707 | 0.005491 | 0.043358 | 2.225762 |
| ENSG00000158545 | 511.5692 | -0.13614 | 0.049235 | -2.76502 | 0.005692 | 0.043551 | 2.295759 |
| ENSG00000142599 | 3213.065 | -0.10736 | 0.039382 | -2.72602 | 0.00641  | 0.04357  | 2.583187 |
| ENSG00000172270 | 3788.797 | -0.16192 | 0.059152 | -2.73731 | 0.006194 | 0.043609 | 2.492774 |
| ENSG00000147162 | 4633.564 | 0.103254 | 0.037732 | 2.73647  | 0.00621  | 0.043699 | 2.492774 |
| ENSG00000090020 | 520.588  | -0.15543 | 0.056252 | -2.76308 | 0.005726 | 0.043728 | 2.295759 |
| ENSG00000138190 | 536.8146 | 0.137665 | 0.049648 | 2.772812 | 0.005557 | 0.043756 | 2.225762 |
| ENSG00000167395 | 469.6678 | -0.13647 | 0.048403 | -2.81954 | 0.004809 | 0.04383  | 1.918337 |
| ENSG00000159840 | 907.6068 | -0.1622  | 0.058513 | -2.77198 | 0.005572 | 0.04383  | 2.225762 |
| ENSG00000100632 | 269.6313 | 0.157338 | 0.056764 | 2.771766 | 0.005575 | 0.04383  | 2.225762 |
| ENSG00000134817 | 532.9572 | 0.561512 | 0.203289 | 2.762131 | 0.005743 | 0.04383  | 2.293762 |
| ENSG00000132382 | 893.2925 | -0.13021 | 0.047823 | -2.72265 | 0.006476 | 0.04383  | 2.583187 |
| ENSG00000128654 | 330.0993 | 0.176331 | 0.062779 | 2.808774 | 0.004973 | 0.043933 | 1.977088 |
| ENSG00000171204 | 262.1815 | 0.170756 | 0.061635 | 2.770456 | 0.005598 | 0.043933 | 2.225762 |
| ENSG00000114120 | 1321.02  | 0.13951  | 0.050542 | 2.760261 | 0.005776 | 0.043958 | 2.293762 |
| ENSG00000163848 | 1495.627 | 0.101197 | 0.036666 | 2.759988 | 0.00578  | 0.043974 | 2.293762 |
| ENSG00000134318 | 3246.416 | 0.102198 | 0.037564 | 2.720635 | 0.006516 | 0.043993 | 2.583187 |
| ENSG00000136261 | 230.1664 | 0.163065 | 0.058889 | 2.76903  | 0.005622 | 0.044037 | 2.225762 |
| ENSG00000241769 | 38.61223 | -0.28812 | 0.095645 | -3.01239 | 0.002592 | 0.044117 | 1.020896 |
| ENSG00000230715 | 103.3414 | -0.23032 | 0.077607 | -2.96778 | 0.003    | 0.044117 | 1.182918 |
| ENSG00000119318 | 1349.955 | 0.115937 | 0.042042 | 2.757616 | 0.005822 | 0.044117 | 2.295759 |
| ENSG00000166411 | 593.7212 | 0.146162 | 0.053009 | 2.757305 | 0.005828 | 0.044117 | 2.295759 |
| ENSG00000151883 | 689.6353 | 0.123662 | 0.045336 | 2.727707 | 0.006378 | 0.044117 | 2.514347 |
| ENSG00000112062 | 910.5785 | 0.089452 | 0.032895 | 2.719348 | 0.006541 | 0.044117 | 2.583187 |
| ENSG00000111669 | 3890.345 | 0.188451 | 0.069321 | 2.718531 | 0.006557 | 0.044117 | 2.583187 |
| ENSG00000236333 | 335.1843 | 0.165344 | 0.059098 | 2.79779  | 0.005145 | 0.044117 | 2.025126 |

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| ENSG00000144134 | 252.2364 | -0.1394  | 0.050378 | -2.76706 | 0.005657 | 0.044117 | 2.225762 |
| ENSG00000187446 | 1245.283 | 0.121827 | 0.044194 | 2.756636 | 0.00584  | 0.044138 | 2.295759 |
| ENSG00000188848 | 93.48271 | 0.281161 | 0.094792 | 2.966081 | 0.003016 | 0.044222 | 1.182918 |
| ENSG00000231211 | 15.20688 | 0.450148 | 0.14257  | 3.157383 | 0.001592 | 0.044262 | 0.622589 |
| ENSG00000273218 | 41.53761 | -0.33436 | 0.111421 | -3.00089 | 0.002692 | 0.044262 | 1.053218 |
| ENSG00000171798 | 3609.106 | -0.14896 | 0.054063 | -2.75529 | 0.005864 | 0.044262 | 2.295759 |
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| ENSG00000144559 | 273.3159 | -0.14811 | 0.052902 | -2.79973 | 0.005115 | 0.044349 | 1.995423 |
| ENSG00000105357 | 868.2038 | -0.17834 | 0.064759 | -2.75386 | 0.00589  | 0.044368 | 2.295759 |
| ENSG00000171451 | 477.8517 | 0.162338 | 0.058964 | 2.753178 | 0.005902 | 0.04444  | 2.295759 |
| ENSG00000100307 | 1635.509 | -0.11421 | 0.041349 | -2.76204 | 0.005744 | 0.044591 | 2.225762 |
| ENSG00000100813 | 1768.775 | -0.10779 | 0.039499 | -2.7289  | 0.006355 | 0.044671 | 2.456745 |
| ENSG00000106546 | 191.2554 | 0.168391 | 0.060327 | 2.791316 | 0.005249 | 0.044725 | 2.025126 |
| ENSG00000165169 | 679.3021 | 0.219637 | 0.079854 | 2.750473 | 0.005951 | 0.044725 | 2.295759 |
| ENSG00000270171 | 32.91348 | -0.32584 | 0.107788 | -3.02295 | 0.002503 | 0.044766 | 0.963911 |
| ENSG00000183662 | 254.332  | 0.189926 | 0.068812 | 2.76008  | 0.005779 | 0.044766 | 2.225762 |
| ENSG00000273682 | 5.183653 | -0.8435  | 0.226723 | -3.72039 | 0.000199 | 0.04477  | 0.076553 |
| ENSG00000105325 | 849.5797 | -0.12888 | 0.046703 | -2.75946 | 0.00579  | 0.044777 | 2.225762 |
| ENSG00000197857 | 380.1597 | -0.11441 | 0.041612 | -2.74936 | 0.005971 | 0.044777 | 2.295759 |
| ENSG00000118596 | 865.1768 | 0.152116 | 0.055341 | 2.74873  | 0.005983 | 0.044877 | 2.293762 |
| ENSG00000093144 | 359.6945 | 0.125465 | 0.04491  | 2.793671 | 0.005211 | 0.044915 | 1.995423 |
| ENSG00000171847 | 279.0209 | -0.21244 | 0.07598  | -2.79601 | 0.005174 | 0.044968 | 1.977088 |
| ENSG00000100220 | 553.0729 | 0.129738 | 0.047902 | 2.708412 | 0.006761 | 0.044968 | 2.583187 |
| ENSG00000074071 | 206.1492 | 0.147886 | 0.053048 | 2.787784 | 0.005307 | 0.045005 | 2.025126 |
| ENSG00000100372 | 169.1693 | 0.159751 | 0.056774 | 2.813791 | 0.004896 | 0.045013 | 1.867169 |
| ENSG00000188185 | 129.5196 | -0.21925 | 0.079566 | -2.7556  | 0.005859 | 0.045141 | 2.225762 |
| ENSG00000139737 | 1865.447 | 0.183703 | 0.067872 | 2.706598 | 0.006798 | 0.045141 | 2.583187 |
| ENSG00000196535 | 3289.773 | -0.14025 | 0.051517 | -2.72236 | 0.006482 | 0.045226 | 2.456745 |
| ENSG00000229122 | 28.51836 | -0.33698 | 0.111479 | -3.02285 | 0.002504 | 0.045274 | 0.947688 |
| ENSG00000277534 | 150.8057 | 0.171231 | 0.062076 | 2.758412 | 0.005808 | 0.045425 | 2.189833 |

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|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000178177 | 401.0055 | 0.125285 | 0.04474  | 2.800304 | 0.005105 | 0.045537 | 1.918337 |
| ENSG00000159202 | 1073.8   | 0.09013  | 0.033235 | 2.711884 | 0.00669  | 0.045537 | 2.514347 |
| ENSG00000247516 | 94.46122 | 0.247315 | 0.087111 | 2.839074 | 0.004524 | 0.045605 | 1.695647 |
| ENSG00000198862 | 1148.189 | 0.129994 | 0.047248 | 2.751316 | 0.005936 | 0.045605 | 2.225762 |
| ENSG00000187325 | 459.5455 | 0.151986 | 0.055452 | 2.740878 | 0.006128 | 0.045605 | 2.295759 |
| ENSG00000150990 | 315.5525 | -0.14927 | 0.053579 | -2.78603 | 0.005336 | 0.045655 | 1.995423 |
| ENSG00000272391 | 442.5816 | -0.15114 | 0.054252 | -2.78591 | 0.005338 | 0.045655 | 1.995423 |
| ENSG00000230084 | 275.7311 | 0.175622 | 0.06315  | 2.781034 | 0.005419 | 0.045655 | 2.025126 |
| ENSG00000165861 | 465.19   | -0.08747 | 0.031461 | -2.78038 | 0.005429 | 0.045704 | 2.025126 |
| ENSG00000114796 | 2987.376 | 0.12637  | 0.046128 | 2.739547 | 0.006152 | 0.045704 | 2.295759 |
| ENSG00000164051 | 100.6464 | 0.184479 | 0.06265  | 2.944604 | 0.003234 | 0.045719 | 1.201846 |
| ENSG00000188542 | 122.4901 | -0.15541 | 0.055396 | -2.80544 | 0.005025 | 0.045719 | 1.867169 |
| ENSG00000185532 | 314.4158 | 0.244677 | 0.08788  | 2.784231 | 0.005365 | 0.045719 | 1.995423 |
| ENSG00000095209 | 123.6711 | 0.179351 | 0.065249 | 2.748717 | 0.005983 | 0.045719 | 2.225762 |
| ENSG00000160685 | 296.7249 | 0.181884 | 0.066411 | 2.738745 | 0.006167 | 0.045719 | 2.295759 |
| ENSG00000104946 | 575.6406 | -0.1277  | 0.046641 | -2.73784 | 0.006184 | 0.045719 | 2.29693  |
| ENSG00000174173 | 151.8813 | 0.180612 | 0.066115 | 2.731801 | 0.006299 | 0.045719 | 2.338927 |
| ENSG00000006831 | 1287.879 | 0.15923  | 0.058793 | 2.708319 | 0.006763 | 0.045719 | 2.514347 |
| ENSG00000099219 | 838.177  | 0.139149 | 0.05139  | 2.707737 | 0.006774 | 0.045719 | 2.514347 |
| ENSG00000198015 | 1339.524 | 0.123051 | 0.045578 | 2.69977  | 0.006939 | 0.045719 | 2.583187 |
| ENSG00000279693 | 29.71279 | -0.31048 | 0.1018   | -3.04994 | 0.002289 | 0.045741 | 0.848718 |
| ENSG00000166004 | 721.4014 | -0.14027 | 0.051244 | -2.73733 | 0.006194 | 0.045741 | 2.293762 |
| ENSG00000177189 | 864.4917 | 0.143205 | 0.052324 | 2.736884 | 0.006202 | 0.045741 | 2.295759 |
| ENSG00000143819 | 716.1745 | -0.18904 | 0.069073 | -2.73687 | 0.006203 | 0.045741 | 2.295759 |
| ENSG00000063046 | 2577.837 | 0.144877 | 0.053371 | 2.714551 | 0.006637 | 0.045741 | 2.456745 |
| ENSG00000125743 | 353.0934 | 0.163683 | 0.059592 | 2.746751 | 0.006019 | 0.045761 | 2.225762 |
| ENSG00000119661 | 686.937  | 0.120164 | 0.043911 | 2.736563 | 0.006208 | 0.045782 | 2.293762 |
| ENSG00000241837 | 216.5498 | 0.177777 | 0.064035 | 2.776242 | 0.005499 | 0.045909 | 2.025126 |
| ENSG00000278873 | 88.83804 | -0.27456 | 0.093194 | -2.94612 | 0.003218 | 0.04597  | 1.182918 |
| ENSG00000169057 | 2745.275 | -0.07981 | 0.029485 | -2.70671 | 0.006795 | 0.046046 | 2.492774 |

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| ENSG00000196976 | 157.7063 | 0.196853 | 0.070295 | 2.800389 | 0.005104 | 0.046153 | 1.867169 |
| ENSG00000111845 | 143.9056 | 0.170145 | 0.062405 | 2.726476 | 0.006401 | 0.046188 | 2.338927 |
| ENSG00000161692 | 294.5683 | -0.18201 | 0.065463 | -2.78028 | 0.005431 | 0.046337 | 1.977088 |
| ENSG00000169718 | 532.9898 | -0.11932 | 0.043692 | -2.73086 | 0.006317 | 0.046348 | 2.29693  |
| ENSG00000093000 | 765.966  | 0.090972 | 0.033681 | 2.700987 | 0.006913 | 0.046348 | 2.514347 |
| ENSG00000173692 | 1730.575 | 0.120907 | 0.044919 | 2.691671 | 0.00711  | 0.046361 | 2.583187 |
| ENSG00000117528 | 703.8799 | 0.137229 | 0.050081 | 2.740136 | 0.006141 | 0.046449 | 2.225762 |
| ENSG00000104695 | 1225.681 | 0.129468 | 0.048116 | 2.690731 | 0.00713  | 0.046449 | 2.583187 |
| ENSG00000154429 | 1611.044 | 0.112167 | 0.04157  | 2.698288 | 0.00697  | 0.04663  | 2.514347 |
| ENSG00000184939 | 898.867  | -0.0845  | 0.030975 | -2.72802 | 0.006372 | 0.046666 | 2.295759 |
| ENSG00000283199 | 48.86707 | -0.35332 | 0.118664 | -2.97746 | 0.002907 | 0.046704 | 1.044965 |
| ENSG00000196428 | 1348.348 | 0.101071 | 0.03692  | 2.737566 | 0.00619  | 0.046704 | 2.225762 |
| ENSG00000122484 | 1512.989 | -0.14074 | 0.051602 | -2.72742 | 0.006383 | 0.046704 | 2.295759 |
| ENSG00000134440 | 1942.096 | 0.157238 | 0.058512 | 2.687288 | 0.007203 | 0.046803 | 2.583187 |
| ENSG00000165238 | 2604.149 | -0.18742 | 0.069516 | -2.69606 | 0.007016 | 0.046815 | 2.514347 |
| ENSG00000206077 | 1163.749 | -0.36772 | 0.134936 | -2.72518 | 0.006427 | 0.046941 | 2.295759 |
| ENSG00000152467 | 82.85541 | -0.23263 | 0.079361 | -2.93129 | 0.003376 | 0.047074 | 1.201846 |
| ENSG00000184867 | 625.9047 | 0.129569 | 0.047567 | 2.723945 | 0.006451 | 0.047074 | 2.295759 |
| ENSG00000167962 | 256.646  | -0.13417 | 0.049086 | -2.73345 | 0.006267 | 0.047154 | 2.225762 |
| ENSG00000184752 | 378.3928 | 0.190075 | 0.068786 | 2.763279 | 0.005722 | 0.047297 | 2.025126 |
| ENSG00000152620 | 696.2127 | 0.16014  | 0.059494 | 2.691687 | 0.007109 | 0.047305 | 2.514347 |
| ENSG00000100138 | 1033.759 | 0.136911 | 0.050124 | 2.731429 | 0.006306 | 0.04738  | 2.225762 |
| ENSG00000233579 | 110.6046 | -0.23501 | 0.085893 | -2.73602 | 0.006219 | 0.047469 | 2.189833 |
| ENSG00000131437 | 2792.491 | 0.139539 | 0.051735 | 2.697179 | 0.006993 | 0.047558 | 2.456745 |
| ENSG00000145832 | 187.9567 | 0.329392 | 0.119315 | 2.760691 | 0.005768 | 0.047565 | 2.025126 |
| ENSG00000268879 | 8.948407 | -0.64028 | 0.174931 | -3.66019 | 0.000252 | 0.047631 | 0.088325 |
| ENSG00000169885 | 12.52127 | -0.52892 | 0.168861 | -3.13228 | 0.001735 | 0.047687 | 0.60691  |
| ENSG00000221978 | 1572.712 | -0.11522 | 0.042387 | -2.71828 | 0.006562 | 0.047713 | 2.293762 |
| ENSG00000171055 | 961.6799 | 0.116274 | 0.042782 | 2.717856 | 0.006571 | 0.047753 | 2.293762 |
| ENSG00000063169 | 206.3337 | -0.26101 | 0.09464  | -2.75792 | 0.005817 | 0.047819 | 2.025126 |

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| ENSG00000090266 | 308.976  | 0.160687 | 0.058923 | 2.727055 | 0.00639  | 0.047819 | 2.225762 |
| ENSG00000085185 | 226.6518 | -0.17707 | 0.064939 | -2.72675 | 0.006396 | 0.047819 | 2.225762 |
| ENSG00000161791 | 828.4861 | -0.16591 | 0.061063 | -2.71709 | 0.006586 | 0.047819 | 2.293762 |
| ENSG00000100077 | 2130.679 | 0.139525 | 0.051374 | 2.715848 | 0.006611 | 0.047893 | 2.295759 |
| ENSG00000137124 | 153.588  | 0.196491 | 0.072083 | 2.725899 | 0.006413 | 0.047899 | 2.225762 |
| ENSG00000161800 | 169.1926 | 0.155309 | 0.057198 | 2.715287 | 0.006622 | 0.047931 | 2.295759 |
| ENSG00000091140 | 760.5788 | 0.164439 | 0.060563 | 2.715162 | 0.006624 | 0.047951 | 2.293762 |
| ENSG00000120913 | 117.4042 | -0.24242 | 0.089498 | -2.70868 | 0.006755 | 0.047951 | 2.338927 |
| ENSG00000279315 | 34.07536 | -0.32673 | 0.11026  | -2.96328 | 0.003044 | 0.04796  | 1.053218 |
| ENSG00000158528 | 2932.421 | 0.137454 | 0.051167 | 2.686402 | 0.007223 | 0.048062 | 2.492774 |
| ENSG00000124074 | 136.8065 | -0.18335 | 0.06732  | -2.72354 | 0.006459 | 0.048091 | 2.225762 |
| ENSG00000198794 | 3737.129 | 0.103793 | 0.038253 | 2.713309 | 0.006662 | 0.048091 | 2.295759 |
| ENSG00000078747 | 1801.846 | 0.106152 | 0.039701 | 2.673802 | 0.0075   | 0.048094 | 2.583187 |
| ENSG00000234361 | 18.22198 | 0.381936 | 0.122451 | 3.119109 | 0.001814 | 0.048214 | 0.622231 |
| ENSG00000183291 | 477.6339 | 0.148473 | 0.054742 | 2.712238 | 0.006683 | 0.048214 | 2.293762 |
| ENSG00000113583 | 277.7214 | 0.148151 | 0.054629 | 2.71196  | 0.006689 | 0.048214 | 2.295759 |
| ENSG00000065150 | 2184.367 | 0.111151 | 0.041452 | 2.681414 | 0.007331 | 0.048214 | 2.514347 |
| ENSG00000183696 | 579.5305 | -0.15432 | 0.056721 | -2.72072 | 0.006514 | 0.048322 | 2.225762 |
| ENSG00000213676 | 545.7635 | -0.12658 | 0.046696 | -2.71066 | 0.006715 | 0.048322 | 2.293762 |
| ENSG00000100591 | 868.4526 | 0.212924 | 0.078555 | 2.710528 | 0.006718 | 0.048322 | 2.295759 |
| ENSG00000171853 | 1125.621 | -0.11926 | 0.044498 | -2.68008 | 0.00736  | 0.048322 | 2.514347 |
| ENSG00000197647 | 76.24979 | -0.20551 | 0.070052 | -2.93359 | 0.003351 | 0.048349 | 1.142898 |
| ENSG00000244968 | 108.7516 | -0.29013 | 0.099262 | -2.92289 | 0.003468 | 0.048349 | 1.182918 |
| ENSG00000275427 | 211.7495 | -0.20138 | 0.074319 | -2.70965 | 0.006735 | 0.048363 | 2.295759 |
| ENSG00000125814 | 6215.799 | 0.241406 | 0.089104 | 2.709246 | 0.006744 | 0.048378 | 2.295759 |
| ENSG00000111540 | 2446.007 | 0.077262 | 0.028937 | 2.670025 | 0.007585 | 0.048378 | 2.583187 |
| ENSG00000073150 | 521.7799 | -0.233   | 0.086023 | -2.70854 | 0.006758 | 0.048459 | 2.295759 |
| ENSG00000287168 | 47.78899 | -0.36948 | 0.124128 | -2.97661 | 0.002915 | 0.048486 | 0.989117 |
| ENSG00000229593 | 19.82581 | -0.4271  | 0.136153 | -3.13693 | 0.001707 | 0.048525 | 0.578677 |
| ENSG00000261292 | 108.8244 | 0.31188  | 0.112382 | 2.775178 | 0.005517 | 0.048556 | 1.867169 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000181315 | 151.4645 | 0.158182 | 0.05856  | 2.701178 | 0.006909 | 0.048556 | 2.338927 |
| ENSG00000276975 | 764.426  | -0.19981 | 0.073538 | -2.71714 | 0.006585 | 0.048585 | 2.225762 |
| ENSG00000156860 | 694.0718 | -0.14098 | 0.052852 | -2.66739 | 0.007644 | 0.048585 | 2.583187 |
| ENSG00000181610 | 596.6427 | 0.121948 | 0.045056 | 2.706572 | 0.006798 | 0.048596 | 2.295759 |
| ENSG00000026036 | 135.9406 | -0.22823 | 0.084026 | -2.71616 | 0.006604 | 0.048656 | 2.225762 |
| ENSG00000111371 | 2769.755 | 0.161287 | 0.060218 | 2.678408 | 0.007397 | 0.048656 | 2.492774 |
| ENSG00000119698 | 495.0256 | 0.208093 | 0.076912 | 2.705592 | 0.006818 | 0.048675 | 2.295759 |
| ENSG00000184319 | 123.2338 | 0.184715 | 0.067577 | 2.7334   | 0.006268 | 0.048698 | 2.108016 |
| ENSG00000197816 | 180.8666 | -0.16355 | 0.060231 | -2.7154  | 0.006619 | 0.048698 | 2.225762 |
| ENSG00000232611 | 145.709  | -0.1605  | 0.059117 | -2.71496 | 0.006628 | 0.048743 | 2.225762 |
| ENSG00000248394 | 19.57346 | -0.39231 | 0.125283 | -3.13134 | 0.00174  | 0.048752 | 0.583933 |
| ENSG00000165055 | 368.3391 | -0.12359 | 0.044723 | -2.76341 | 0.00572  | 0.048761 | 1.918337 |
| ENSG00000203666 | 180.1998 | -0.18438 | 0.067941 | -2.71388 | 0.00665  | 0.048815 | 2.225762 |
| ENSG00000146005 | 1777.003 | 0.220517 | 0.082398 | 2.67625  | 0.007445 | 0.048815 | 2.492774 |
| ENSG00000163864 | 269.9807 | -0.15102 | 0.055038 | -2.74393 | 0.006071 | 0.048957 | 2.025126 |
| ENSG00000120805 | 930.8098 | 0.151714 | 0.056782 | 2.671863 | 0.007543 | 0.048972 | 2.514347 |
| ENSG00000232928 | 114.0656 | -0.23014 | 0.084682 | -2.7177  | 0.006574 | 0.048981 | 2.189833 |
| ENSG00000149575 | 2164.343 | 0.142542 | 0.05276  | 2.701713 | 0.006898 | 0.049007 | 2.295759 |
| ENSG00000133135 | 89.66591 | 0.2807   | 0.09595  | 2.925468 | 0.003439 | 0.049059 | 1.142898 |
| ENSG00000100426 | 438.3397 | -0.121   | 0.044133 | -2.74164 | 0.006113 | 0.049191 | 2.025126 |
| ENSG00000185158 | 469.1116 | -0.14819 | 0.054072 | -2.74064 | 0.006132 | 0.049315 | 2.025126 |
| ENSG00000164951 | 2922.917 | 0.162426 | 0.061073 | 2.659546 | 0.007825 | 0.049315 | 2.583187 |
| ENSG00000175701 | 140.9395 | 0.19005  | 0.070581 | 2.692656 | 0.007089 | 0.04932  | 2.338927 |
| ENSG00000156521 | 273.7173 | -0.13623 | 0.049722 | -2.73972 | 0.006149 | 0.049392 | 2.025126 |
| ENSG00000103811 | 576.049  | 0.195123 | 0.072331 | 2.697642 | 0.006983 | 0.04946  | 2.293762 |
| ENSG00000182504 | 955.9076 | 0.123382 | 0.046423 | 2.657767 | 0.007866 | 0.04946  | 2.583187 |
| ENSG00000198420 | 859.3353 | 0.11657  | 0.043861 | 2.657721 | 0.007867 | 0.04946  | 2.583187 |
| ENSG00000138944 | 1251.8   | 0.199056 | 0.074899 | 2.65767  | 0.007868 | 0.04946  | 2.583187 |
| ENSG00000187566 | 48.62118 | -0.26257 | 0.089058 | -2.94828 | 0.003196 | 0.049554 | 1.044965 |
| ENSG00000114982 | 1161.327 | -0.07942 | 0.029347 | -2.70626 | 0.006804 | 0.049554 | 2.225762 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000198836 | 2457.036 | 0.142547 | 0.052866 | 2.696382 | 0.00701  | 0.049554 | 2.295759 |
| ENSG00000168488 | 1193.865 | -0.14671 | 0.054418 | -2.69595 | 0.007019 | 0.049554 | 2.295759 |
| ENSG00000102780 | 1197.059 | 0.138076 | 0.051981 | 2.656285 | 0.007901 | 0.049554 | 2.583187 |
| ENSG00000286998 | 35.62473 | -0.30505 | 0.103586 | -2.94492 | 0.00323  | 0.049646 | 1.053218 |
| ENSG00000165186 | 498.5419 | 0.217647 | 0.080758 | 2.695055 | 0.007038 | 0.049646 | 2.293762 |
| ENSG00000083642 | 2149.284 | 0.122382 | 0.045929 | 2.664603 | 0.007708 | 0.049646 | 2.514347 |
| ENSG00000181458 | 15.16927 | 0.541463 | 0.175704 | 3.08167  | 0.002058 | 0.049653 | 0.670508 |
| ENSG00000279138 | 58.65614 | 0.304809 | 0.102849 | 2.963656 | 0.00304  | 0.049689 | 0.989117 |
| ENSG00000150471 | 3708.509 | 0.096855 | 0.036327 | 2.666222 | 0.007671 | 0.049727 | 2.492774 |
| ENSG00000120733 | 1803.283 | -0.07524 | 0.028227 | -2.66543 | 0.007689 | 0.049823 | 2.492774 |
| ENSG00000081870 | 138.9408 | 0.146965 | 0.054381 | 2.702519 | 0.006882 | 0.049919 | 2.225762 |
| ENSG00000164651 | 22.83151 | 0.445477 | 0.143502 | 3.104325 | 0.001907 | 0.049923 | 0.616514 |
| ENSG00000179144 | 39.87324 | -0.44708 | 0.151465 | -2.95172 | 0.00316  | 0.049933 | 1.020896 |

*Table A15. Differential gene expression results of the 2,290 identified significant genes in KCL BrainBank (112 cases and 59 controls) using DESeq2.*

| Gene ID         | Mean     | log2Fold Change (lfc) | lfcSE    | stat     | p-value  | p-value adjusted | weight   |
|-----------------|----------|-----------------------|----------|----------|----------|------------------|----------|
| ENSG00000110492 | 133.5512 | -1.25677              | 0.1436   | -8.75189 | 2.10E-18 | 6.25E-14         | 1.351128 |
| ENSG00000074410 | 162.787  | -1.30137              | 0.166754 | -7.80414 | 5.99E-15 | 5.22E-11         | 2.309341 |
| ENSG00000263503 | 31.6298  | 6.539068              | 0.863893 | 7.5693   | 3.75E-14 | 4.13E-10         | 1.217444 |
| ENSG00000280022 | 64.22935 | 2.697014              | 0.380911 | 7.080425 | 1.44E-12 | 6.49E-09         | 2.226625 |
| ENSG00000156510 | 27.18357 | -1.12371              | 0.161379 | -6.96317 | 3.33E-12 | 2.49E-08         | 1.07387  |
| ENSG00000225972 | 2196.419 | -3.3143               | 0.491492 | -6.74334 | 1.55E-11 | 8.16E-08         | 1.270767 |
| ENSG00000262539 | 25.23384 | 3.854736              | 0.582695 | 6.615364 | 3.71E-11 | 3.85E-07         | 0.553372 |
| ENSG00000188803 | 1015.372 | -0.7648               | 0.122788 | -6.22864 | 4.71E-10 | 1.61E-06         | 1.466075 |
| ENSG00000253661 | 120.3669 | -0.71605              | 0.119247 | -6.00477 | 1.92E-09 | 4.43E-06         | 1.931656 |
| ENSG00000147256 | 67.66208 | -1.14947              | 0.194808 | -5.90055 | 3.62E-09 | 1.08E-05         | 1.351128 |
| ENSG00000260604 | 28.83856 | 1.160571              | 0.197831 | 5.866472 | 4.45E-09 | 1.52E-05         | 1.07387  |
| ENSG00000133067 | 38.37801 | -1.20298              | 0.208847 | -5.76011 | 8.41E-09 | 2.22E-05         | 1.269879 |
| ENSG00000186407 | 8.641325 | -1.56512              | 0.266986 | -5.8622  | 4.57E-09 | 2.27E-05         | 0.612254 |
| ENSG00000162654 | 231.2506 | -0.6389               | 0.111933 | -5.70785 | 1.14E-08 | 2.27E-05         | 1.445883 |
| ENSG00000274370 | 12.58547 | -0.99811              | 0.172466 | -5.78728 | 7.15E-09 | 3.25E-05         | 0.553372 |
| ENSG00000118292 | 81.89972 | -0.60244              | 0.106764 | -5.6427  | 1.67E-08 | 3.25E-05         | 1.351128 |
| ENSG00000115138 | 48.39594 | -1.12311              | 0.200235 | -5.60898 | 2.04E-08 | 3.56E-05         | 1.351128 |
| ENSG00000206192 | 10.5623  | -1.81807              | 0.318041 | -5.71646 | 1.09E-08 | 3.78E-05         | 0.64362  |
| ENSG00000129521 | 1134.879 | -0.42475              | 0.076375 | -5.56138 | 2.68E-08 | 3.92E-05         | 1.445883 |
| ENSG00000262500 | 4.009117 | 3.444991              | 0.595785 | 5.782269 | 7.37E-09 | 5.48E-05         | 0.27027  |
| ENSG00000266918 | 41.36129 | 0.887806              | 0.161954 | 5.48183  | 4.21E-08 | 6.29E-05         | 1.280812 |
| ENSG00000179869 | 12.62954 | -1.47936              | 0.275509 | -5.36955 | 7.89E-08 | 0.000261         | 0.553372 |
| ENSG00000074803 | 127.8479 | -0.70928              | 0.137265 | -5.16723 | 2.38E-07 | 0.0003           | 1.351128 |
| ENSG00000144115 | 407.3358 | -1.01487              | 0.203547 | -4.98594 | 6.17E-07 | 0.0003           | 3.446452 |
| ENSG00000279082 | 252.0769 | -0.90238              | 0.17868  | -5.05028 | 4.41E-07 | 0.000367         | 1.931656 |
| ENSG00000185710 | 30.70662 | -1.84991              | 0.351971 | -5.25585 | 1.47E-07 | 0.000399         | 0.553372 |
| ENSG00000084628 | 267.3802 | 0.54497               | 0.10711  | 5.087939 | 3.62E-07 | 0.000399         | 1.351128 |
| ENSG00000154188 | 195.4752 | 0.66512               | 0.133414 | 4.985373 | 6.18E-07 | 0.000399         | 2.226625 |
| ENSG00000183196 | 1153.305 | 0.624723              | 0.12347  | 5.059718 | 4.20E-07 | 0.000491         | 1.185475 |

|                 |          |          |  |          |          |          |          |          |
|-----------------|----------|----------|--|----------|----------|----------|----------|----------|
| ENSG00000231305 | 38.75656 | -0.55757 |  | 0.112071 | -4.97512 | 6.52E-07 | 0.000679 | 1.269879 |
| ENSG00000183484 | 39.24346 | -0.62651 |  | 0.126021 | -4.97149 | 6.64E-07 | 0.000679 | 1.269879 |
| ENSG00000237840 | 19.1028  | -0.59121 |  | 0.116147 | -5.09022 | 3.58E-07 | 0.000751 | 0.598245 |
| ENSG00000170412 | 219.343  | -0.53373 |  | 0.111314 | -4.7948  | 1.63E-06 | 0.000891 | 2.226625 |
| ENSG00000270547 | 19.4663  | 1.315129 |  | 0.260464 | 5.049185 | 4.44E-07 | 0.000948 | 0.553372 |
| ENSG00000170927 | 13.05592 | 0.848056 |  | 0.168494 | 5.033151 | 4.82E-07 | 0.001002 | 0.553372 |
| ENSG00000283503 | 268.4364 | 0.457918 |  | 0.095856 | 4.777159 | 1.78E-06 | 0.001028 | 1.931656 |
| ENSG00000121858 | 77.60314 | -0.768   |  | 0.160318 | -4.79051 | 1.66E-06 | 0.001338 | 1.351128 |
| ENSG00000170160 | 657.6304 | 0.696677 |  | 0.146314 | 4.761516 | 1.92E-06 | 0.001387 | 1.466075 |
| ENSG00000132967 | 11.86973 | -1.13069 |  | 0.225967 | -5.00377 | 5.62E-07 | 0.001575 | 0.368099 |
| ENSG00000211896 | 6.758291 | -1.99604 |  | 0.400981 | -4.9779  | 6.43E-07 | 0.001756 | 0.368099 |
| ENSG00000185829 | 102.7036 | 0.615767 |  | 0.133811 | 4.601762 | 4.19E-06 | 0.001779 | 2.309341 |
| ENSG00000270098 | 21.55012 | -0.69135 |  | 0.141873 | -4.87304 | 1.10E-06 | 0.001902 | 0.553372 |
| ENSG00000259781 | 29.17013 | -0.83118 |  | 0.170963 | -4.86178 | 1.16E-06 | 0.001937 | 0.553372 |
| ENSG00000261888 | 24.23126 | -0.81265 |  | 0.1684   | -4.82569 | 1.40E-06 | 0.001937 | 0.64362  |
| ENSG00000173402 | 2968.423 | -0.28583 |  | 0.061093 | -4.67867 | 2.89E-06 | 0.001937 | 1.351128 |
| ENSG00000134817 | 2248.8   | 0.901673 |  | 0.192572 | 4.682257 | 2.84E-06 | 0.001952 | 1.270767 |
| ENSG00000100033 | 8.439501 | -1.18645 |  | 0.243723 | -4.86802 | 1.13E-06 | 0.001964 | 0.471379 |
| ENSG00000259433 | 39.11882 | 1.083201 |  | 0.232    | 4.668964 | 3.03E-06 | 0.001964 | 1.280812 |
| ENSG00000135094 | 186.3328 | -0.64649 |  | 0.138866 | -4.65547 | 3.23E-06 | 0.001964 | 1.351128 |
| ENSG00000169248 | 6.231895 | -1.81811 |  | 0.369668 | -4.91821 | 8.73E-07 | 0.001993 | 0.351128 |
| ENSG00000077327 | 74.43465 | -0.6953  |  | 0.149717 | -4.64411 | 3.42E-06 | 0.001993 | 1.351128 |
| ENSG00000228570 | 32.89021 | -0.70408 |  | 0.149957 | -4.69521 | 2.66E-06 | 0.002064 | 0.998163 |
| ENSG00000280096 | 3.556621 | 1.38743  |  | 0.281933 | 4.921134 | 8.60E-07 | 0.002094 | 0.311788 |
| ENSG00000110090 | 1614.559 | -0.34875 |  | 0.075808 | -4.60039 | 4.22E-06 | 0.002133 | 1.445883 |
| ENSG00000082175 | 108.7168 | -0.65746 |  | 0.145695 | -4.51257 | 6.40E-06 | 0.002133 | 2.226625 |
| ENSG00000156076 | 960.124  | -0.91799 |  | 0.198526 | -4.62404 | 3.76E-06 | 0.00214  | 1.26296  |
| ENSG00000104368 | 408.7614 | -0.43574 |  | 0.096938 | -4.49503 | 6.96E-06 | 0.002204 | 2.226625 |
| ENSG00000115556 | 107.5359 | -0.45069 |  | 0.098722 | -4.56526 | 4.99E-06 | 0.002392 | 1.445883 |
| ENSG00000162595 | 99.51092 | -0.69272 |  | 0.151429 | -4.57453 | 4.77E-06 | 0.002408 | 1.351128 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000163586 | 5.960733 | -1.59193 | 0.326897 | -4.86983 | 1.12E-06 | 0.002439 | 0.301937 |
| ENSG00000166603 | 74.26673 | 0.75271  | 0.168728 | 4.461093 | 8.15E-06 | 0.002439 | 2.226625 |
| ENSG00000134042 | 2461.257 | -0.47493 | 0.103553 | -4.58637 | 4.51E-06 | 0.002442 | 1.185475 |
| ENSG00000167703 | 1800.358 | -0.42574 | 0.09285  | -4.58523 | 4.53E-06 | 0.002442 | 1.185475 |
| ENSG00000131095 | 162600.1 | 0.644156 | 0.141639 | 4.547887 | 5.42E-06 | 0.002481 | 1.351128 |
| ENSG00000226320 | 88.01614 | 0.387915 | 0.086689 | 4.474763 | 7.65E-06 | 0.002481 | 1.931656 |
| ENSG00000181019 | 657.8029 | -0.72136 | 0.15906  | -4.53515 | 5.76E-06 | 0.002557 | 1.351128 |
| ENSG00000061455 | 74.93929 | 0.395185 | 0.088616 | 4.459513 | 8.21E-06 | 0.002557 | 1.931656 |
| ENSG00000085265 | 14.40145 | -1.172   | 0.2506   | -4.67678 | 2.91E-06 | 0.002799 | 0.598245 |
| ENSG00000026508 | 1969.677 | 1.010434 | 0.223539 | 4.520171 | 6.18E-06 | 0.002799 | 1.270767 |
| ENSG00000127328 | 2738.296 | 0.292084 | 0.064709 | 4.513833 | 6.37E-06 | 0.002799 | 1.315447 |
| ENSG00000286602 | 135.1801 | 0.525448 | 0.117445 | 4.473996 | 7.68E-06 | 0.003008 | 1.445883 |
| ENSG00000285668 | 10.5989  | 1.666001 | 0.360527 | 4.621016 | 3.82E-06 | 0.00314  | 0.64362  |
| ENSG00000228459 | 41.9649  | 0.774618 | 0.172102 | 4.500935 | 6.77E-06 | 0.00314  | 1.152902 |
| ENSG00000149480 | 1432.899 | -0.25949 | 0.058012 | -4.47306 | 7.71E-06 | 0.00314  | 1.315447 |
| ENSG00000105643 | 1488.917 | 0.46359  | 0.104086 | 4.453917 | 8.43E-06 | 0.00314  | 1.466075 |
| ENSG00000228696 | 190.8604 | 1.059703 | 0.242611 | 4.367906 | 1.25E-05 | 0.00314  | 2.226625 |
| ENSG00000015133 | 350.929  | -0.52627 | 0.120667 | -4.36135 | 1.29E-05 | 0.003205 | 2.106768 |
| ENSG00000154451 | 22.0554  | -0.61722 | 0.133901 | -4.60957 | 4.04E-06 | 0.003233 | 0.64362  |
| ENSG00000259383 | 1.313792 | 22.19183 | 4.433095 | 5.005944 | 5.56E-07 | 0.00329  | 0.083834 |
| ENSG00000249170 | 31.75053 | -0.72108 | 0.161649 | -4.46077 | 8.17E-06 | 0.00329  | 1.217444 |
| ENSG00000143641 | 1496.256 | -0.21772 | 0.048933 | -4.44931 | 8.61E-06 | 0.00329  | 1.315447 |
| ENSG00000271447 | 362.7948 | -0.58346 | 0.131675 | -4.43106 | 9.38E-06 | 0.00329  | 1.445883 |
| ENSG00000239961 | 37.76158 | 1.02089  | 0.22997  | 4.439232 | 9.03E-06 | 0.003415 | 1.280812 |
| ENSG00000136235 | 869.0736 | 0.827179 | 0.186543 | 4.434259 | 9.24E-06 | 0.003502 | 1.26296  |
| ENSG00000273382 | 38.83502 | -0.47881 | 0.107853 | -4.43951 | 9.02E-06 | 0.003647 | 1.16988  |
| ENSG00000273259 | 21.68011 | 1.61979  | 0.355889 | 4.551388 | 5.33E-06 | 0.003863 | 0.64362  |
| ENSG00000204758 | 27.26221 | -0.38753 | 0.087271 | -4.44055 | 8.97E-06 | 0.003863 | 1.07387  |
| ENSG00000261159 | 17.76737 | -0.62163 | 0.141765 | -4.38496 | 1.16E-05 | 0.004299 | 1.217444 |
| ENSG00000133106 | 101.5349 | -0.47511 | 0.108967 | -4.36015 | 1.30E-05 | 0.004299 | 1.351128 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000160606 | 77.60832 | -0.44054 | 0.103572 | -4.2535  | 2.10E-05 | 0.004299 | 2.226625 |
| ENSG00000188133 | 53.35818 | -0.78253 | 0.179791 | -4.35247 | 1.35E-05 | 0.004416 | 1.347187 |
| ENSG00000179761 | 260.5534 | -0.43082 | 0.099393 | -4.33448 | 1.46E-05 | 0.004417 | 1.445883 |
| ENSG00000125337 | 82.02922 | 1.109148 | 0.256271 | 4.328026 | 1.50E-05 | 0.0045   | 1.445883 |
| ENSG00000153446 | 274.2878 | -0.44856 | 0.103389 | -4.33859 | 1.43E-05 | 0.004541 | 1.351128 |
| ENSG00000186638 | 153.5907 | -0.31581 | 0.07476  | -4.22431 | 2.40E-05 | 0.004557 | 2.226625 |
| ENSG00000157601 | 983.4162 | -0.32967 | 0.076469 | -4.3111  | 1.62E-05 | 0.004607 | 1.466075 |
| ENSG00000164326 | 166.9693 | -1.18004 | 0.280367 | -4.20889 | 2.57E-05 | 0.004607 | 2.309341 |
| ENSG00000237686 | 28.78739 | -0.64995 | 0.148066 | -4.38957 | 1.14E-05 | 0.004656 | 0.998163 |
| ENSG00000176641 | 1306.538 | 0.329762 | 0.075838 | 4.348229 | 1.37E-05 | 0.004656 | 1.185475 |
| ENSG00000176845 | 242.6388 | -0.51397 | 0.11895  | -4.32088 | 1.55E-05 | 0.004656 | 1.351128 |
| ENSG00000135407 | 412.0547 | -0.19298 | 0.04702  | -4.10419 | 4.06E-05 | 0.004688 | 3.446452 |
| ENSG00000115902 | 3113.24  | -0.29678 | 0.06886  | -4.30986 | 1.63E-05 | 0.005069 | 1.270767 |
| ENSG00000160602 | 59.47598 | -0.56416 | 0.131803 | -4.2803  | 1.87E-05 | 0.005394 | 1.351128 |
| ENSG00000129657 | 5811.898 | -0.33541 | 0.07829  | -4.28417 | 1.83E-05 | 0.005617 | 1.262783 |
| ENSG00000251381 | 29.56053 | -0.68706 | 0.157406 | -4.36489 | 1.27E-05 | 0.006045 | 0.798279 |
| ENSG00000198740 | 4190.632 | 0.339745 | 0.080236 | 4.234335 | 2.29E-05 | 0.006045 | 1.445883 |
| ENSG00000288235 | 57.05243 | 0.698918 | 0.164415 | 4.250948 | 2.13E-05 | 0.006477 | 1.212648 |
| ENSG00000257277 | 41.38851 | 0.547955 | 0.129146 | 4.242927 | 2.21E-05 | 0.006477 | 1.269879 |
| ENSG00000187634 | 90.00486 | 0.718748 | 0.1733   | 4.147417 | 3.36E-05 | 0.006477 | 1.931656 |
| ENSG00000186188 | 69.49396 | -0.58405 | 0.140982 | -4.14271 | 3.43E-05 | 0.006496 | 1.931656 |
| ENSG00000108774 | 437.3061 | -0.26668 | 0.064978 | -4.10411 | 4.06E-05 | 0.006604 | 2.226625 |
| ENSG00000143171 | 160.9837 | -0.50558 | 0.11997  | -4.21423 | 2.51E-05 | 0.006661 | 1.351128 |
| ENSG00000211592 | 7.7389   | -1.67945 | 0.377869 | -4.44453 | 8.81E-06 | 0.006674 | 0.469722 |
| ENSG00000166033 | 6082.421 | -0.27753 | 0.064505 | -4.30252 | 1.69E-05 | 0.007039 | 0.84637  |
| ENSG00000286870 | 29.73585 | 1.248447 | 0.290311 | 4.300375 | 1.71E-05 | 0.007381 | 0.798279 |
| ENSG00000159348 | 637.5377 | -0.19755 | 0.047076 | -4.19641 | 2.71E-05 | 0.007381 | 1.26296  |
| ENSG00000286215 | 279.1383 | 0.315662 | 0.07571  | 4.169345 | 3.05E-05 | 0.007381 | 1.445883 |
| ENSG00000137573 | 571.0085 | 0.419139 | 0.100391 | 4.17505  | 2.98E-05 | 0.007719 | 1.315447 |
| ENSG00000173678 | 3.049237 | -1.8528  | 0.413925 | -4.47618 | 7.60E-06 | 0.008169 | 0.311788 |



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| ENSG00000184678 | 797.6461 | -0.29649 | 0.071281 | -4.15947 | 3.19E-05 | 0.008169 | 1.315447 |
| ENSG00000162174 | 1101.206 | -0.31854 | 0.077168 | -4.12791 | 3.66E-05 | 0.008299 | 1.466075 |
| ENSG00000196208 | 1709.461 | -0.25425 | 0.061696 | -4.12108 | 3.77E-05 | 0.008528 | 1.445883 |
| ENSG00000188933 | 150.5036 | 0.669884 | 0.165196 | 4.055081 | 5.01E-05 | 0.008528 | 1.931656 |
| ENSG00000255542 | 34.45218 | -0.58034 | 0.139342 | -4.16488 | 3.12E-05 | 0.008636 | 1.16988  |
| ENSG00000215367 | 28.38202 | 0.494061 | 0.119144 | 4.146771 | 3.37E-05 | 0.008911 | 1.217444 |
| ENSG00000280350 | 16.15258 | -0.82054 | 0.193691 | -4.23634 | 2.27E-05 | 0.009084 | 0.798279 |
| ENSG00000138798 | 147.1282 | 0.420264 | 0.102145 | 4.114383 | 3.88E-05 | 0.009099 | 1.351128 |
| ENSG00000031081 | 1878.174 | -0.37193 | 0.090271 | -4.12015 | 3.79E-05 | 0.009362 | 1.270767 |
| ENSG00000166341 | 1313.541 | -0.36471 | 0.088907 | -4.10213 | 4.09E-05 | 0.009702 | 1.315447 |
| ENSG00000241015 | 169.1738 | 0.402388 | 0.098304 | 4.093321 | 4.25E-05 | 0.009737 | 1.351128 |
| ENSG00000286117 | 40.44825 | -0.83557 | 0.20378  | -4.10037 | 4.12E-05 | 0.009887 | 1.280812 |
| ENSG00000010310 | 69.86611 | 0.729416 | 0.184509 | 3.95328  | 7.71E-05 | 0.010548 | 2.226625 |
| ENSG00000172137 | 421.3868 | -0.64533 | 0.168066 | -3.83976 | 0.000123 | 0.010806 | 3.446452 |
| ENSG00000183347 | 20.8462  | -0.62634 | 0.147483 | -4.24684 | 2.17E-05 | 0.010877 | 0.598245 |
| ENSG00000012223 | 132.9679 | 1.43223  | 0.365193 | 3.92184  | 8.79E-05 | 0.011336 | 2.309341 |
| ENSG00000114547 | 62.21449 | -0.33997 | 0.083556 | -4.06874 | 4.73E-05 | 0.01136  | 1.230506 |
| ENSG00000004939 | 16.0025  | -1.13386 | 0.267934 | -4.23185 | 2.32E-05 | 0.011373 | 0.598245 |
| ENSG00000162711 | 161.3007 | -0.38052 | 0.094121 | -4.04292 | 5.28E-05 | 0.011387 | 1.351128 |
| ENSG00000279673 | 34.33318 | -0.51956 | 0.12666  | -4.10205 | 4.10E-05 | 0.011796 | 0.998163 |
| ENSG00000283307 | 12.95121 | 1.260601 | 0.310824 | 4.055679 | 5.00E-05 | 0.011796 | 1.217444 |
| ENSG00000080493 | 6421.253 | -0.4725  | 0.117823 | -4.01023 | 6.07E-05 | 0.011944 | 1.445883 |
| ENSG00000158270 | 646.7901 | 0.528726 | 0.131993 | 4.005724 | 6.18E-05 | 0.011944 | 1.466075 |
| ENSG00000004948 | 8.498729 | -1.29393 | 0.303751 | -4.25984 | 2.05E-05 | 0.012206 | 0.471379 |
| ENSG00000154529 | 241.1537 | 0.549681 | 0.137548 | 3.996291 | 6.43E-05 | 0.012429 | 1.445883 |
| ENSG00000091656 | 2839.561 | -0.27895 | 0.069615 | -4.007   | 6.15E-05 | 0.012537 | 1.351128 |
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| ENSG00000150551 | 163.1567 | -0.46228 | 0.115911 | -3.98825 | 6.66E-05 | 0.012595 | 1.445883 |
| ENSG00000140287 | 11.03146 | -1.34846 | 0.326967 | -4.12414 | 3.72E-05 | 0.012654 | 0.798279 |
| ENSG00000189238 | 29.84552 | -0.63177 | 0.153236 | -4.12284 | 3.74E-05 | 0.012654 | 0.798279 |

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| ENSG00000185052 | 529.6451 | -0.37884 | 0.094833 | -3.9948  | 6.47E-05 | 0.012849 | 1.351128 |
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| ENSG00000154040 | 384.0765 | 0.306081 | 0.077195 | 3.965023 | 7.34E-05 | 0.014024 | 1.351128 |
| ENSG00000214717 | 1267.272 | -0.21815 | 0.05525  | -3.94846 | 7.87E-05 | 0.014024 | 1.445883 |
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| ENSG00000028277 | 284.2344 | -0.38867 | 0.102038 | -3.80902 | 0.00014  | 0.015217 | 2.309341 |
| ENSG00000072694 | 19.69931 | 1.283341 | 0.309756 | 4.143075 | 3.43E-05 | 0.015391 | 0.553372 |
| ENSG00000225265 | 38.16861 | -0.40966 | 0.103812 | -3.94619 | 7.94E-05 | 0.015391 | 1.280812 |
| ENSG00000134202 | 2154.804 | -0.39564 | 0.099975 | -3.95742 | 7.58E-05 | 0.015486 | 1.185475 |
| ENSG00000127993 | 1045.042 | 0.292956 | 0.074913 | 3.910632 | 9.21E-05 | 0.015486 | 1.445883 |
| ENSG00000198342 | 148.8905 | -0.37676 | 0.099219 | -3.79724 | 0.000146 | 0.015486 | 2.309341 |
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| ENSG00000180644 | 14.27254 | -0.81081 | 0.198454 | -4.08564 | 4.40E-05 | 0.016425 | 0.64362  |
| ENSG00000135114 | 10.08749 | -0.81916 | 0.200618 | -4.08319 | 4.44E-05 | 0.016425 | 0.64362  |
| ENSG00000136870 | 2413.658 | 0.283105 | 0.072311 | 3.915109 | 9.04E-05 | 0.016425 | 1.315447 |
| ENSG00000227992 | 9.752316 | 0.556297 | 0.135953 | 4.091831 | 4.28E-05 | 0.016537 | 0.612254 |
| ENSG00000261770 | 166.2669 | 0.407494 | 0.10466  | 3.893486 | 9.88E-05 | 0.017201 | 1.351128 |
| ENSG00000170498 | 4.282905 | -1.45934 | 0.344781 | -4.23267 | 2.31E-05 | 0.01764  | 0.301937 |
| ENSG00000261603 | 3.138347 | -1.02595 | 0.244402 | -4.1978  | 2.70E-05 | 0.01764  | 0.351128 |
| ENSG00000277987 | 22.59759 | 0.77975  | 0.191242 | 4.077292 | 4.56E-05 | 0.01764  | 0.598245 |
| ENSG00000110063 | 367.4512 | -0.20671 | 0.054966 | -3.76061 | 0.000169 | 0.01764  | 2.226625 |
| ENSG00000156804 | 3148.913 | 0.252824 | 0.065087 | 3.884416 | 0.000103 | 0.01815  | 1.262783 |
| ENSG00000052795 | 3789.35  | 0.204287 | 0.052768 | 3.871432 | 0.000108 | 0.01815  | 1.351128 |
| ENSG00000184260 | 638.1467 | -0.37157 | 0.096025 | -3.86956 | 0.000109 | 0.01815  | 1.351128 |
| ENSG00000137959 | 430.302  | -0.58221 | 0.150487 | -3.86882 | 0.000109 | 0.01815  | 1.351128 |

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| ENSG00000105251 | 327.6787 | -0.44306 | 0.115114 | -3.84883 | 0.000119 | 0.019304 | 1.351128 |
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| ENSG00000286653 | 71.04917 | 0.610517 | 0.160125 | 3.812744 | 0.000137 | 0.020552 | 1.445883 |
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| ENSG00000225178 | 37.15403 | 0.914494 | 0.238594 | 3.832842 | 0.000127 | 0.020825 | 1.280812 |
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| ENSG00000183908 | 522.5764 | 0.370554 | 0.096771 | 3.829186 | 0.000129 | 0.021324 | 1.26296  |
| ENSG00000242756 | 1.867762 | -1.39689 | 0.319581 | -4.371   | 1.24E-05 | 0.021705 | 0.117166 |
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| ENSG00000268087 | 82.10616 | -0.2333  | 0.061184 | -3.81307 | 0.000137 | 0.021705 | 1.299739 |
| ENSG00000103710 | 425.4441 | 0.629235 | 0.165476 | 3.802582 | 0.000143 | 0.021705 | 1.351128 |
| ENSG00000276043 | 127.2902 | 0.484191 | 0.127948 | 3.784279 | 0.000154 | 0.021705 | 1.445883 |
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| ENSG00000248079 | 87.41768 | 0.388263 | 0.102676 | 3.781436 | 0.000156 | 0.021705 | 1.445883 |
| ENSG00000078098 | 115.8441 | 0.407826 | 0.109971 | 3.708488 | 0.000209 | 0.021705 | 1.931656 |
| ENSG00000135046 | 480.182  | 0.417268 | 0.117416 | 3.553746 | 0.00038  | 0.022049 | 3.446452 |
| ENSG00000121742 | 1200.898 | -0.65128 | 0.173051 | -3.76351 | 0.000168 | 0.022754 | 1.466075 |
| ENSG00000285825 | 51.76019 | -0.43887 | 0.115369 | -3.80403 | 0.000142 | 0.022863 | 1.230506 |
| ENSG00000261087 | 1028.43  | 0.235676 | 0.062069 | 3.796987 | 0.000146 | 0.022863 | 1.26296  |
| ENSG00000196502 | 444.7595 | -0.36178 | 0.096215 | -3.76019 | 0.00017  | 0.023038 | 1.445883 |
| ENSG00000234177 | 268.2376 | -0.24153 | 0.06621  | -3.64796 | 0.000264 | 0.023177 | 2.226625 |
| ENSG00000109111 | 4710.721 | -0.11247 | 0.029839 | -3.76935 | 0.000164 | 0.023536 | 1.351128 |
| ENSG00000273706 | 10.65592 | -1.15257 | 0.282607 | -4.07836 | 4.54E-05 | 0.023824 | 0.368099 |
| ENSG00000118257 | 708.2095 | -0.38204 | 0.101066 | -3.78013 | 0.000157 | 0.023882 | 1.26296  |

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| ENSG00000198774 | 49.24417 | 1.051707 | 0.279676 | 3.760443 | 0.00017  | 0.024112 | 1.347187 |
| ENSG00000154856 | 1290.505 | -0.36526 | 0.097031 | -3.76437 | 0.000167 | 0.024189 | 1.315447 |
| ENSG00000170989 | 1726.666 | -0.37153 | 0.098726 | -3.76323 | 0.000168 | 0.024189 | 1.315447 |
| ENSG00000288574 | 61.83671 | 0.47351  | 0.125493 | 3.773198 | 0.000161 | 0.024417 | 1.230506 |
| ENSG00000140450 | 2273.99  | 0.438904 | 0.117056 | 3.749508 | 0.000177 | 0.024417 | 1.351128 |
| ENSG00000117362 | 854.1133 | -0.18171 | 0.048657 | -3.7344  | 0.000188 | 0.024417 | 1.445883 |
| ENSG00000272505 | 866.2084 | 0.214767 | 0.057553 | 3.731649 | 0.00019  | 0.024417 | 1.466075 |
| ENSG00000133121 | 2397.617 | 0.179147 | 0.047649 | 3.759694 | 0.00017  | 0.024812 | 1.270767 |
| ENSG00000273407 | 15.74309 | 0.505796 | 0.127915 | 3.954146 | 7.68E-05 | 0.024921 | 0.553372 |
| ENSG00000286241 | 18.21282 | 0.825528 | 0.213289 | 3.870467 | 0.000109 | 0.024921 | 0.798279 |
| ENSG00000165370 | 20.02107 | -0.91745 | 0.243813 | -3.76294 | 0.000168 | 0.024921 | 1.217444 |
| ENSG00000130287 | 7218.267 | -0.34119 | 0.09088  | -3.75428 | 0.000174 | 0.024921 | 1.262783 |
| ENSG00000180104 | 2101.531 | -0.19141 | 0.051003 | -3.75291 | 0.000175 | 0.024921 | 1.270767 |
| ENSG00000188064 | 186.2337 | -0.58686 | 0.157823 | -3.71844 | 0.0002   | 0.024921 | 1.445883 |
| ENSG00000137965 | 184.1171 | -0.36518 | 0.101478 | -3.59856 | 0.00032  | 0.024921 | 2.309341 |
| ENSG00000283378 | 11.04495 | 0.653433 | 0.169136 | 3.863351 | 0.000112 | 0.025043 | 0.798279 |
| ENSG00000102445 | 347.4989 | -0.25816 | 0.069187 | -3.73129 | 0.00019  | 0.02509  | 1.351128 |
| ENSG00000159261 | 4.8448   | -1.07902 | 0.264454 | -4.08018 | 4.50E-05 | 0.025572 | 0.311788 |
| ENSG00000254858 | 130.8154 | -0.28886 | 0.079568 | -3.63033 | 0.000283 | 0.025848 | 1.931656 |
| ENSG00000261575 | 8.796402 | 0.940395 | 0.24038  | 3.912113 | 9.15E-05 | 0.026098 | 0.612254 |
| ENSG00000183486 | 104.4597 | -0.47759 | 0.128521 | -3.71603 | 0.000202 | 0.026098 | 1.351128 |
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| ENSG00000172965 | 465.6063 | 0.213438 | 0.059534 | 3.585129 | 0.000337 | 0.02623  | 2.226625 |
| ENSG00000227243 | 14.37327 | 0.886214 | 0.22664  | 3.910234 | 9.22E-05 | 0.026604 | 0.598245 |
| ENSG00000100450 | 1.413186 | -1.81526 | 0.449796 | -4.03575 | 5.44E-05 | 0.026614 | 0.351128 |
| ENSG00000254031 | 17.30413 | 0.736052 | 0.187443 | 3.926812 | 8.61E-05 | 0.026614 | 0.553372 |
| ENSG00000149357 | 1160.527 | -0.17137 | 0.045859 | -3.73691 | 0.000186 | 0.026614 | 1.185475 |
| ENSG00000164309 | 1869.177 | -0.29287 | 0.078446 | -3.7334  | 0.000189 | 0.026614 | 1.185475 |
| ENSG00000109501 | 2064.288 | -0.30931 | 0.083476 | -3.70542 | 0.000211 | 0.026614 | 1.351128 |
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| ENSG00000285908 | 115.3032 | 0.660109 | 0.17915  | 3.68468  | 0.000229 | 0.026614 | 1.445883 |
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| ENSG00000261465 | 6.933466 | 0.841256 | 0.209542 | 4.014738 | 5.95E-05 | 0.026869 | 0.368099 |
| ENSG00000175283 | 199.2821 | -0.24517 | 0.068124 | -3.5988  | 0.00032  | 0.027391 | 1.931656 |
| ENSG00000257408 | 1.334011 | -1.40549 | 0.354746 | -3.96196 | 7.43E-05 | 0.02748  | 0.445883 |
| ENSG00000162415 | 528.6921 | -0.14763 | 0.039962 | -3.69421 | 0.000221 | 0.027525 | 1.315447 |
| ENSG00000226478 | 7.693835 | -0.68929 | 0.172192 | -4.00301 | 6.25E-05 | 0.027665 | 0.368099 |
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| ENSG00000212371 | 7.486317 | 0.963045 | 0.244438 | 3.939831 | 8.15E-05 | 0.028151 | 0.469722 |
| ENSG00000116833 | 8.701728 | -1.05398 | 0.263793 | -3.9955  | 6.46E-05 | 0.028214 | 0.368099 |
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| ENSG00000204396 | 349.1062 | -0.46743 | 0.127242 | -3.67353 | 0.000239 | 0.02837  | 1.351128 |
| ENSG00000161955 | 174.1592 | -0.39167 | 0.106708 | -3.67046 | 0.000242 | 0.028599 | 1.351128 |
| ENSG00000261839 | 47.65689 | 0.400185 | 0.103563 | 3.864157 | 0.000111 | 0.028625 | 0.61906  |
| ENSG00000287907 | 22.74844 | 0.789943 | 0.205057 | 3.852315 | 0.000117 | 0.028785 | 0.64362  |
| ENSG00000144182 | 95.58521 | 0.303238 | 0.082748 | 3.664593 | 0.000248 | 0.028918 | 1.351128 |
| ENSG00000019991 | 665.3317 | 0.582619 | 0.158296 | 3.680558 | 0.000233 | 0.028949 | 1.26296  |
| ENSG00000139410 | 132.718  | -0.40864 | 0.115701 | -3.53186 | 0.000413 | 0.029001 | 2.226625 |
| ENSG00000196436 | 36.19548 | 0.842614 | 0.228813 | 3.682544 | 0.000231 | 0.03065  | 1.16988  |
| ENSG00000267904 | 112.3894 | -0.2138  | 0.060813 | -3.51579 | 0.000438 | 0.03065  | 2.226625 |
| ENSG00000121406 | 598.4298 | 0.153519 | 0.042147 | 3.642498 | 0.00027  | 0.030912 | 1.351128 |
| ENSG00000274588 | 17.27518 | -0.92253 | 0.240188 | -3.84085 | 0.000123 | 0.031484 | 0.598245 |
| ENSG00000168386 | 690.4881 | 0.248009 | 0.06789  | 3.653095 | 0.000259 | 0.031484 | 1.26296  |
| ENSG00000127472 | 98.93731 | -0.57163 | 0.157265 | -3.63482 | 0.000278 | 0.031484 | 1.351128 |
| ENSG00000159723 | 24.9255  | -0.82794 | 0.219978 | -3.76374 | 0.000167 | 0.03162  | 0.798279 |
| ENSG00000164736 | 41.83361 | -0.69283 | 0.186926 | -3.70643 | 0.00021  | 0.03162  | 0.998163 |
| ENSG00000087085 | 796.5464 | -0.44231 | 0.12236  | -3.61478 | 0.000301 | 0.03162  | 1.445883 |
| ENSG00000206195 | 87.39852 | 0.605936 | 0.167759 | 3.611944 | 0.000304 | 0.03162  | 1.445883 |
| ENSG00000164972 | 221.3599 | -0.37826 | 0.104743 | -3.6113  | 0.000305 | 0.03162  | 1.445883 |
| ENSG00000251093 | 2.338633 | 2.266637 | 0.521155 | 4.349253 | 1.37E-05 | 0.0321   | 0.063389 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000143819 | 2330.961 | -0.37165 | 0.102563 | -3.62365 | 0.00029  | 0.0321   | 1.351128 |
| ENSG00000170509 | 34.25606 | 0.511837 | 0.139943 | 3.657472 | 0.000255 | 0.032193 | 1.16988  |
| ENSG00000171551 | 35.70253 | -1.01844 | 0.280219 | -3.63443 | 0.000279 | 0.032193 | 1.280812 |
| ENSG00000117305 | 421.1037 | -0.16998 | 0.050457 | -3.36873 | 0.000755 | 0.032279 | 3.446452 |
| ENSG00000253875 | 129.7744 | 0.329449 | 0.094825 | 3.474278 | 0.000512 | 0.032557 | 2.309341 |
| ENSG00000255998 | 3.876123 | -1.01663 | 0.25745  | -3.94884 | 7.85E-05 | 0.032709 | 0.351128 |
| ENSG00000284726 | 42.42487 | 0.331716 | 0.090899 | 3.649292 | 0.000263 | 0.032754 | 1.16988  |
| ENSG00000260018 | 21.63167 | -0.44727 | 0.122987 | -3.63674 | 0.000276 | 0.032928 | 1.217444 |
| ENSG00000239467 | 112.1888 | -0.25414 | 0.070437 | -3.60811 | 0.000308 | 0.033025 | 1.351128 |
| ENSG00000165474 | 41.18608 | -0.69217 | 0.189951 | -3.64392 | 0.000269 | 0.033086 | 1.16988  |
| ENSG00000255550 | 12.85642 | 0.651055 | 0.179321 | 3.630664 | 0.000283 | 0.033268 | 1.217444 |
| ENSG00000259417 | 617.987  | -0.41902 | 0.115722 | -3.62091 | 0.000294 | 0.033268 | 1.26296  |
| ENSG00000286712 | 8.61979  | 0.934669 | 0.245844 | 3.801883 | 0.000144 | 0.033352 | 0.614045 |
| ENSG00000224511 | 14.21789 | -0.75407 | 0.201995 | -3.73309 | 0.000189 | 0.033404 | 0.798279 |
| ENSG00000182492 | 964.3747 | 0.419885 | 0.117255 | 3.580952 | 0.000342 | 0.033404 | 1.445883 |
| ENSG00000156218 | 542.9067 | 0.310795 | 0.086873 | 3.577602 | 0.000347 | 0.033404 | 1.466075 |
| ENSG00000203808 | 152.144  | 0.393065 | 0.113417 | 3.465668 | 0.000529 | 0.033404 | 2.226625 |
| ENSG00000169860 | 810.3534 | -0.43442 | 0.121636 | -3.5715  | 0.000355 | 0.033926 | 1.466075 |
| ENSG00000144136 | 2000.849 | -0.21687 | 0.060436 | -3.58845 | 0.000333 | 0.034084 | 1.351128 |
| ENSG00000259868 | 82.59178 | 0.36914  | 0.102882 | 3.58801  | 0.000333 | 0.034084 | 1.351128 |
| ENSG00000169836 | 78.6486  | -0.54238 | 0.151813 | -3.5727  | 0.000353 | 0.034084 | 1.445883 |
| ENSG00000172428 | 1081.066 | -0.26521 | 0.074277 | -3.57059 | 0.000356 | 0.034084 | 1.445883 |
| ENSG00000273456 | 37.98449 | -0.31275 | 0.086259 | -3.62575 | 0.000288 | 0.034304 | 1.152902 |
| ENSG00000262039 | 17.05034 | 0.736791 | 0.203985 | 3.61198  | 0.000304 | 0.034304 | 1.217444 |
| ENSG00000224738 | 40.86304 | 0.30735  | 0.084816 | 3.623734 | 0.00029  | 0.034455 | 1.152902 |
| ENSG00000134595 | 20.07541 | -0.66657 | 0.176914 | -3.76778 | 0.000165 | 0.034681 | 0.64362  |
| ENSG00000107738 | 1276.307 | -0.52464 | 0.145292 | -3.61095 | 0.000305 | 0.034681 | 1.185475 |
| ENSG00000172270 | 8410.822 | -0.30184 | 0.084397 | -3.57639 | 0.000348 | 0.034681 | 1.351128 |
| ENSG00000141449 | 589.2182 | -0.3394  | 0.095362 | -3.55905 | 0.000372 | 0.034681 | 1.445883 |
| ENSG00000184898 | 239.4005 | -0.29045 | 0.084582 | -3.43398 | 0.000595 | 0.034681 | 2.309341 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000118503 | 175.3402 | -0.43606 | 0.126838 | -3.43795 | 0.000586 | 0.035289 | 2.226625 |
| ENSG00000013573 | 201.623  | 0.530101 | 0.154724 | 3.426096 | 0.000612 | 0.035428 | 2.309341 |
| ENSG00000136872 | 183.9155 | 0.459344 | 0.134143 | 3.424278 | 0.000616 | 0.035548 | 2.309341 |
| ENSG00000205609 | 1.776186 | -1.181   | 0.307129 | -3.84527 | 0.00012  | 0.03575  | 0.445883 |
| ENSG00000170275 | 3135.171 | 0.186438 | 0.052084 | 3.579567 | 0.000344 | 0.03575  | 1.270767 |
| ENSG00000145476 | 1590.1   | -0.23147 | 0.065288 | -3.54541 | 0.000392 | 0.03575  | 1.445883 |
| ENSG00000288075 | 498.1664 | -0.27435 | 0.080009 | -3.42904 | 0.000606 | 0.035754 | 2.226625 |
| ENSG00000235310 | 154.3131 | 0.377218 | 0.110075 | 3.426913 | 0.00061  | 0.035918 | 2.226625 |
| ENSG00000196767 | 99.68631 | -0.4495  | 0.126985 | -3.53976 | 0.0004   | 0.036168 | 1.445883 |
| ENSG00000280107 | 86.97176 | 0.361388 | 0.105601 | 3.422213 | 0.000621 | 0.036308 | 2.226625 |
| ENSG00000205106 | 23.69501 | -0.5534  | 0.147089 | -3.76233 | 0.000168 | 0.036491 | 0.598245 |
| ENSG00000204525 | 2054.375 | -0.38554 | 0.109068 | -3.53485 | 0.000408 | 0.036491 | 1.445883 |
| ENSG00000132164 | 1688.176 | -0.41439 | 0.115575 | -3.58543 | 0.000337 | 0.036525 | 1.185475 |
| ENSG00000109610 | 405.8953 | -0.48964 | 0.138593 | -3.53292 | 0.000411 | 0.036525 | 1.445883 |
| ENSG00000138083 | 11.47923 | -1.20631 | 0.327554 | -3.68277 | 0.000231 | 0.037018 | 0.798279 |
| ENSG00000243007 | 1.796855 | 1.565414 | 0.403757 | 3.877123 | 0.000106 | 0.037785 | 0.351128 |
| ENSG00000281248 | 9.728692 | 0.859806 | 0.225795 | 3.807913 | 0.00014  | 0.037785 | 0.471379 |
| ENSG00000150764 | 3291.995 | 0.233446 | 0.065822 | 3.546657 | 0.00039  | 0.037785 | 1.315447 |
| ENSG00000167766 | 1438.076 | 0.284514 | 0.080295 | 3.54336  | 0.000395 | 0.037785 | 1.315447 |
| ENSG00000184232 | 704.3398 | -0.41993 | 0.118542 | -3.54244 | 0.000396 | 0.037785 | 1.315447 |
| ENSG00000161896 | 287.3565 | 0.655516 | 0.185424 | 3.535231 | 0.000407 | 0.037785 | 1.351128 |
| ENSG00000141485 | 304.7288 | -0.52213 | 0.147695 | -3.5352  | 0.000407 | 0.037785 | 1.351128 |
| ENSG00000186815 | 2558.343 | -0.28108 | 0.079186 | -3.54957 | 0.000386 | 0.037926 | 1.270767 |
| ENSG00000229828 | 11.23487 | -0.92014 | 0.245058 | -3.75478 | 0.000173 | 0.038678 | 0.553372 |
| ENSG00000250948 | 10.22919 | 0.818093 | 0.223402 | 3.661979 | 0.00025  | 0.038678 | 0.798279 |
| ENSG00000101439 | 18894.46 | -0.40958 | 0.116135 | -3.52678 | 0.000421 | 0.038678 | 1.351128 |
| ENSG00000253854 | 142.5921 | 0.198387 | 0.058662 | 3.381876 | 0.00072  | 0.038678 | 2.309341 |
| ENSG00000288052 | 13.15503 | 0.618358 | 0.168973 | 3.659513 | 0.000253 | 0.038923 | 0.798279 |
| ENSG00000141349 | 638.7688 | -0.1873  | 0.053116 | -3.52631 | 0.000421 | 0.038923 | 1.315447 |
| ENSG00000134864 | 74.05516 | -0.33815 | 0.096535 | -3.50292 | 0.00046  | 0.038923 | 1.445883 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000132768 | 287.477  | -0.19189 | 0.054804 | -3.50142 | 0.000463 | 0.038923 | 1.445883 |
| ENSG00000171169 | 123.1967 | -0.24471 | 0.071474 | -3.42382 | 0.000617 | 0.038923 | 1.931656 |
| ENSG00000175832 | 78.67042 | -0.4713  | 0.133642 | -3.52659 | 0.000421 | 0.039116 | 1.299739 |
| ENSG00000286330 | 95.64693 | -0.48822 | 0.144362 | -3.3819  | 0.00072  | 0.039116 | 2.226625 |
| ENSG00000269825 | 279.7401 | 0.419812 | 0.124706 | 3.366397 | 0.000762 | 0.03971  | 2.309341 |
| ENSG00000120215 | 108.8079 | 0.341788 | 0.097871 | 3.492227 | 0.000479 | 0.039773 | 1.445883 |
| ENSG00000246089 | 88.53114 | -0.25925 | 0.073656 | -3.51967 | 0.000432 | 0.039791 | 1.299739 |
| ENSG00000137285 | 3400.25  | -0.4419  | 0.125904 | -3.50978 | 0.000448 | 0.040567 | 1.315447 |
| ENSG00000278970 | 93.13204 | -0.23905 | 0.068588 | -3.48523 | 0.000492 | 0.040567 | 1.445883 |
| ENSG00000286300 | 32.62895 | 0.404785 | 0.114716 | 3.52858  | 0.000418 | 0.040713 | 1.217444 |
| ENSG00000261451 | 973.9347 | 0.205772 | 0.058819 | 3.498402 | 0.000468 | 0.040857 | 1.351128 |
| ENSG00000268996 | 98.60553 | -0.38314 | 0.114276 | -3.3528  | 0.0008   | 0.040857 | 2.309341 |
| ENSG00000007129 | 16.71484 | -0.71615 | 0.194197 | -3.68774 | 0.000226 | 0.041119 | 0.64362  |
| ENSG00000135597 | 2957.747 | -0.15162 | 0.043153 | -3.51358 | 0.000442 | 0.041119 | 1.262783 |
| ENSG00000163346 | 4387.389 | -0.37711 | 0.108484 | -3.47623 | 0.000509 | 0.041119 | 1.445883 |
| ENSG00000152049 | 170.46   | 0.633742 | 0.189001 | 3.353118 | 0.000799 | 0.041835 | 2.226625 |
| ENSG00000236796 | 24.50437 | -0.55575 | 0.153253 | -3.62638 | 0.000287 | 0.041851 | 0.798279 |
| ENSG00000158578 | 35.11793 | -0.87797 | 0.250696 | -3.50214 | 0.000462 | 0.042003 | 1.269879 |
| ENSG00000198574 | 73.27962 | 0.635186 | 0.183183 | 3.467487 | 0.000525 | 0.042003 | 1.445883 |
| ENSG00000231193 | 6.608506 | -0.8149  | 0.218277 | -3.7333  | 0.000189 | 0.042339 | 0.514262 |
| ENSG00000115112 | 187.5358 | -0.70128 | 0.201406 | -3.48192 | 0.000498 | 0.042339 | 1.351128 |
| ENSG00000088543 | 799.6962 | -0.24279 | 0.069417 | -3.49753 | 0.00047  | 0.042482 | 1.26296  |
| ENSG00000003400 | 140.941  | -0.35824 | 0.103485 | -3.4618  | 0.000537 | 0.042482 | 1.445883 |
| ENSG00000196335 | 79.50753 | -0.42042 | 0.125889 | -3.33959 | 0.000839 | 0.042931 | 2.226625 |
| ENSG00000285549 | 9.012423 | 0.565697 | 0.152707 | 3.704462 | 0.000212 | 0.043248 | 0.551111 |
| ENSG00000189431 | 31.64362 | -0.61607 | 0.174383 | -3.53285 | 0.000411 | 0.043248 | 1.07387  |
| ENSG00000172554 | 63.03614 | -0.52115 | 0.150037 | -3.47346 | 0.000514 | 0.043248 | 1.347187 |
| ENSG00000219607 | 197.9717 | -0.4158  | 0.120482 | -3.45116 | 0.000558 | 0.043248 | 1.445883 |
| ENSG00000132530 | 240.9373 | -0.34699 | 0.102861 | -3.37335 | 0.000743 | 0.043248 | 1.931656 |
| ENSG00000278291 | 138.3737 | -0.30418 | 0.091254 | -3.33334 | 0.000858 | 0.043248 | 2.226625 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000255052 | 665.1259 | 0.438941 | 0.127423 | 3.444764 | 0.000572 | 0.043553 | 1.466075 |
| ENSG00000099995 | 2777.045 | -0.16922 | 0.048586 | -3.4829  | 0.000496 | 0.04365  | 1.262783 |
| ENSG00000100342 | 137.2116 | -0.43382 | 0.130416 | -3.32643 | 0.00088  | 0.04365  | 2.226625 |
| ENSG00000287225 | 120.5658 | -0.39861 | 0.120148 | -3.31763 | 0.000908 | 0.04365  | 2.309341 |
| ENSG00000146374 | 137.1924 | 0.486791 | 0.146775 | 3.31658  | 0.000911 | 0.04365  | 2.309341 |
| ENSG00000249119 | 11.70589 | -1.30715 | 0.357513 | -3.65624 | 0.000256 | 0.043724 | 0.64362  |
| ENSG00000111331 | 492.6771 | -0.34892 | 0.101363 | -3.44232 | 0.000577 | 0.043724 | 1.445883 |
| ENSG00000134321 | 215.8309 | -0.31697 | 0.094249 | -3.3631  | 0.000771 | 0.043724 | 1.931656 |
| ENSG00000229921 | 26.97223 | 1.057625 | 0.303246 | 3.487674 | 0.000487 | 0.043739 | 1.217444 |
| ENSG00000144026 | 1230.21  | 0.232783 | 0.06718  | 3.465047 | 0.00053  | 0.043925 | 1.315447 |
| ENSG00000162692 | 82.66317 | -0.74618 | 0.215288 | -3.46594 | 0.000528 | 0.044188 | 1.299739 |
| ENSG00000286695 | 87.23677 | 0.530285 | 0.158269 | 3.350538 | 0.000807 | 0.045263 | 1.931656 |
| ENSG00000109794 | 645.0499 | -0.22677 | 0.066205 | -3.4252  | 0.000614 | 0.045304 | 1.466075 |
| ENSG00000255503 | 19.52915 | 0.477414 | 0.133143 | 3.585729 | 0.000336 | 0.045402 | 0.798279 |
| ENSG00000251639 | 6.375982 | 0.73175  | 0.196774 | 3.718733 | 0.0002   | 0.045484 | 0.469722 |
| ENSG00000271646 | 72.7062  | -0.38465 | 0.111673 | -3.44443 | 0.000572 | 0.045484 | 1.351128 |
| ENSG00000164104 | 661.6875 | -0.26668 | 0.077855 | -3.42538 | 0.000614 | 0.045484 | 1.445883 |
| ENSG00000183798 | 198.0727 | -0.39447 | 0.119352 | -3.30512 | 0.000949 | 0.045484 | 2.226625 |
| ENSG00000203435 | 43.86957 | -0.41377 | 0.118767 | -3.4839  | 0.000494 | 0.045604 | 1.152902 |
| ENSG00000287876 | 5.840832 | 1.459035 | 0.382149 | 3.817969 | 0.000135 | 0.045795 | 0.311788 |
| ENSG00000005882 | 1215.111 | -0.2091  | 0.060833 | -3.43725 | 0.000588 | 0.046032 | 1.351128 |
| ENSG00000140545 | 1012.628 | -0.36957 | 0.108151 | -3.41714 | 0.000633 | 0.046157 | 1.445883 |
| ENSG00000196605 | 685.5106 | 0.168638 | 0.049412 | 3.412903 | 0.000643 | 0.046157 | 1.466075 |
| ENSG00000244155 | 1.444926 | -1.561   | 0.412647 | -3.7829  | 0.000155 | 0.046237 | 0.351128 |
| ENSG00000151623 | 2563.873 | -0.20121 | 0.058321 | -3.44997 | 0.000561 | 0.046237 | 1.270767 |
| ENSG00000233013 | 4.54267  | 0.981193 | 0.25959  | 3.779785 | 0.000157 | 0.046456 | 0.351128 |
| ENSG00000244731 | 246.4866 | 0.768251 | 0.225191 | 3.411559 | 0.000646 | 0.046456 | 1.445883 |
| ENSG00000271714 | 108.485  | -0.26607 | 0.079848 | -3.33227 | 0.000861 | 0.046456 | 1.931656 |
| ENSG00000271287 | 2.845935 | 7.209205 | 1.730007 | 4.167153 | 3.08E-05 | 0.046597 | 0.06861  |
| ENSG00000287347 | 35.65952 | 0.455621 | 0.129971 | 3.505567 | 0.000456 | 0.047194 | 0.998163 |

|                 |          |          |          |          |          |          |          |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| ENSG00000182141 | 2613.924 | 0.352603 | 0.10366  | 3.401533 | 0.00067  | 0.047792 | 1.445883 |
| ENSG00000215154 | 182.7251 | -0.27851 | 0.085222 | -3.26809 | 0.001083 | 0.048227 | 2.309341 |
| ENSG00000174640 | 143.0272 | -0.44708 | 0.136962 | -3.26428 | 0.001097 | 0.048755 | 2.309341 |
| ENSG00000091986 | 507.2881 | 0.412469 | 0.12606  | 3.272011 | 0.001068 | 0.049079 | 2.226625 |
| ENSG00000164694 | 10.20439 | -0.7918  | 0.219679 | -3.60435 | 0.000313 | 0.0492   | 0.64362  |
| ENSG00000280079 | 24.92972 | 0.411046 | 0.115853 | 3.547991 | 0.000388 | 0.0492   | 0.798279 |
| ENSG00000226490 | 19.15065 | -0.66838 | 0.194454 | -3.43719 | 0.000588 | 0.0492   | 1.217444 |
| ENSG00000072210 | 3174.636 | 0.210905 | 0.061596 | 3.424017 | 0.000617 | 0.0492   | 1.262783 |
| ENSG00000165959 | 4026.907 | 0.422124 | 0.123295 | 3.423682 | 0.000618 | 0.0492   | 1.262783 |
| ENSG00000287593 | 44.44002 | 0.581016 | 0.169787 | 3.422034 | 0.000622 | 0.0492   | 1.280812 |
| ENSG00000255020 | 53.56483 | -0.40827 | 0.119867 | -3.406   | 0.000659 | 0.0492   | 1.347187 |
| ENSG00000270966 | 13.0287  | -0.43829 | 0.121719 | -3.60085 | 0.000317 | 0.049302 | 0.64362  |
| ENSG00000003989 | 1929.228 | 0.557115 | 0.162869 | 3.420629 | 0.000625 | 0.049302 | 1.270767 |

*Table A16. Differential gene expression results of the 402 identified significant genes in TargetALS (112 cases and 20 controls) using DESeq2.*

| # | Term Name  | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names  |
|---|--|-----------|-----------|------------------------|-------------------|--|
| 1 | Protein folding_Folding in normal condition              | 119       | 3.774E-06 | 4.667E-04              | 18                | HSP90, Alpha crystallin B, HSP70, HSPA4, Aha1, TCP1-theta, VBP-1, PPID, TCP1-delta, HSP90 beta, TCP1-eta, Calcineurin A (catalytic), Hdj-2, DNAJA2, HSC70, Calcineurin A (beta), TCP1-alpha, TCP1-epsilon  |
| 2 | Neurophysiological process_Transmission of nerve impulse | 213       | 6.101E-06 | 4.667E-04              | 25                | PRKAR2B, GABA-A receptor alpha-1 subunit, PKC-beta, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, CaMK IV, GLRA, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, cPKC (conventional), Serotonin receptor, PKA-reg (cAMP-dependent), GRM6, Galpha(i)-specific amine GPCRs, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, Glycine receptor beta chain, Kv4.2 channel, Calmodulin, ERK1/2, HTR2A, ERK2 (MAPK1), PRKAR1A |
| 3 | Signal transduction_Neuropeptide signaling pathways      | 156       | 4.897E-05 | 2.497E-03              | 19                | NPY, PAM, NPFF receptor 2, MC4R, Substance P extracellular region, GPR124, Galpha(i)-specific peptide GPCRs, CRH receptor 2, Secretogranin V, PKA-reg (cAMP-dependent), Substance P, Galpha(q)-specific peptide GPCRs, PKD1L1, Calmodulin, ERK1/2, SSTR2, ERK2 (MAPK1), SSTR1, Galpha(s)-specific peptide GPCRs  |
| 4 | Cytoskeleton_Regulation of cytoskeleton rearrangement    | 183       | 1.447E-04 | 3.724E-03              | 20                | Tubulin alpha 1A, MELC, 14-3-3 beta/alpha, G-protein beta/gamma, ECT2, Galpha(i)-specific amine GPCRs, Protein kinase G1, Calponin-1, Zeta-sarcoglycan, Destrin, CAPZA, Tubulin alpha, MRLC, ERK1/2, PKC, Protein kinase G, ERK2 (MAPK1), ARP3, 14-3-3, 14-3-3 eta   |
| 5 | Reproduction_Gonadotropin regulation                     | 199       | 1.630E-04 | 3.724E-03              | 21                | GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, GABA-A receptor alpha-4 subunit, PKA-reg (cAMP-dependent), Protein kinase G1, GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, PKC-beta2, G-protein gamma 3, Protein kinase G 2, PKC-beta1, Calmodulin, ERK1/2, Guanylate Cyclase 1, soluble, Protein kinase G, MEK4(MAP2K4), PI3K reg class IA  |
| 6 | Development_Neurogenesis_Axonal guidance                 | 229       | 1.691E-04 | 3.724E-03              | 23                | Semaphorin 3C, NckAP1, MELC, Ephrin-A receptor 5, Semaphorin 5A, Ephrin-A receptor 4, Semaphorin 3E, cPKC (conventional), PKA-reg (cAMP-dependent), PP1-cat, Ephrin-A receptors, CDK5, Selenoprotein P, Calcineurin A (catalytic), ENC1, Calmodulin, Calcyclin, Syntenin 1, ERK1/2, Mindin, Guanine deaminase, PI3K reg class IA, 14-3-3 eta   |

|    |  |     |           |           |    |   |
|----|--|-----|-----------|-----------|----|---|
| 7  | Muscle contraction   | 171 | 1.704E-04 | 3.724E-03 | 19 | Alpha crystallin B, Smooth muscle myosin, MELC, HCN2, Galpha(i)-specific peptide GPCRs, CaMK IV, Myotrophin, cPKC (conventional), Galpha(q)-specific amine GPCRs, NCX1, Protein kinase G1, Calponin-1, Galpha(q)-specific peptide GPCRs, PP2A catalytic, MRLC, Calmodulin, PKC, Guanylate Cyclase 1, soluble, Protein kinase G  |
| 8  | Reproduction_GnRH signaling pathway                                    | 166 | 3.416E-04 | 6.534E-03 | 18 | GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, GABA-A receptor alpha-4 subunit, PKA-reg (cAMP-dependent), Protein kinase G1, GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, PKC-beta2, Protein kinase G 2, Calmodulin, ERK1/2, Guanylate Cyclase 1, soluble, Protein kinase G, PI3K reg class IA |
| 9  | Development_Blood vessel morphogenesis                                 | 227 | 9.665E-04 | 1.586E-02 | 21 | Galpha(s)-specific nucleotide-like GPCRs, Angiopietin 1, APJ, Endothelin-1, PDE, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, CRH receptor 2, EGF, DLL4, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Protein kinase G1, Galpha(q)-specific peptide GPCRs, CEACAM1, Galpha(s)-specific CRF GPCRs, ERK1/2, Protein kinase G, ERK2 (MAPK1), MEK4(MAP2K4), PI3K reg class IA |
| 10 | Muscle contraction_Nitric oxide signaling in the cardiovascular system | 124 | 1.036E-03 | 1.586E-02 | 14 | HSP90, Endothelin-1, G-protein beta/gamma, PKA-reg type II (cAMP-dependent), PKA-reg (cAMP-dependent), PP1-cat, Protein kinase G1, Calcineurin A (catalytic), PP2A catalytic, PDE4A, Calmodulin, Guanylate Cyclase 1, soluble, MEF2C, PI3K reg class IA   |
| 11 | Neurophysiological process_GABAergic neurotransmission                 | 140 | 1.193E-03 | 1.660E-02 | 15 | GLSK, GAD1, ALDR, Synaptotagmin I, GABA-A receptor alpha-1 subunit, G-protein beta/gamma, P/Q-type calcium channel alpha-1A subunit, NSF, GABA-A receptor beta-2 subunit, PP1-cat, Clathrin heavy chain, MDH1, Calmodulin, AATC, GAD2   |
| 12 | Development_Melanocyte development and pigmentation                    | 50  | 1.368E-03 | 1.744E-02 | 8  | MGF, PKC-beta, PKA-reg (cAMP-dependent), Protein kinase G1, Guanylate cyclase (alpha-1/beta-1), ERK1/2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs   |
| 13 | Translation_Regulation of initiation                                   | 127 | 3.730E-03 | 4.390E-02 | 13 | PP2A cat (alpha), PP1-cat gamma, EGF, PP1-cat, PP2A catalytic, eIF4A, eIF2S1, RHEB2, ERK1/2, PI3K reg class IA (p55-gamma), ERK2 (MAPK1), MEK4(MAP2K4), PI3K reg class IA   |
| 14 | Signal transduction_Oxytocin signaling                                 | 86  | 4.272E-03 | 4.647E-02 | 10 | PKC-beta, G-protein beta/gamma, cPKC (conventional), Protein kinase G1, PP2A catalytic, Calmodulin, ERK1/2, PKC, Guanylate Cyclase 1, soluble, MEF2C  |
| 15 | Reproduction_Male sex differentiation                                  | 241 | 4.556E-03 | 4.647E-02 | 20 | Cadherin 8, PTCH2, HSP70, PKC-beta, PAFAH gamma, EGF, BMPR1A, PKA-reg (cAMP-dependent), HMDH, Clathrin heavy chain, Histone H2, Histone H2A, Selenoprotein P, NCOA4 (ARA70), Patched, Calmodulin, ERK1/2, PKC, Ran, TCP1-alpha  |

|    |   |     |           |           |    |   |
|----|---|-----|-----------|-----------|----|---|
| 16 | Reproduction_Feeding and Neurohormone signaling       | 210 | 4.994E-03 | 4.775E-02 | 18 | PAM, IRF1, Endothelin-1, MGF, HSP70, Substance P extracellular region, Galpha(q)-specific Class A Orphan/other GPCRs, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, PKA-reg (cAMP-dependent), Substance P, CDK5, Galpha(q)-specific peptide GPCRs, PP2A catalytic, Galpha(s)-specific CRF GPCRs, RHEB2, Calmodulin, PI3K reg class IA |
| 17 | Signal Transduction_Cholecystokinin signaling         | 106 | 6.672E-03 | 5.671E-02 | 11 | PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, Pro-CCK, M-Ras, PKA-reg (cAMP-dependent), PKC-beta2, Galpha(q)-specific peptide GPCRs, Calmodulin, ERK1/2, ERK2 (MAPK1)   |
| 18 | Cell cycle_Meiosis                                    | 106 | 6.672E-03 | 5.671E-02 | 11 | HSP70, 14-3-3 beta/alpha, EGF, PP1-cat, Tubulin alpha, PP2A catalytic, STAG3, Securin, PI3K reg class IA, 14-3-3, 14-3-3 eta  |
| 19 | Transport_Calcium transport                           | 192 | 1.025E-02 | 8.258E-02 | 16 | HPCA, Pannexin-1, Synaptotagmin I, TRPC5, PKC-beta, P/Q-type calcium channel alpha-1A subunit, TRPV1, cPKC (conventional), TRPC4, PMCA1, NCX1, Calcineurin A (catalytic), MPTP complex, Calmodulin, SAP102, CALB1   |
| 20 | Cell cycle_G1-S Growth factor regulation              | 195 | 1.179E-02 | 9.021E-02 | 16 | PP2A cat (alpha), IRF1, Activin A, PKC-beta, EGF, cPKC (conventional), Activin beta A, MEK4/7, PP2A catalytic, Activin, ERK1/2, PI3K reg class IA (p55-gamma), PKC, ERK2 (MAPK1), MEK4(MAP2K4), PI3K reg class IA   |
| 21 | Protein folding_Protein folding nucleus               | 58  | 1.305E-02 | 9.213E-02 | 7  | HSP90, HSP70, HSPA4, Calcineurin A (catalytic), HSC70, Calcineurin A (beta), Glutaredoxin 1   |
| 22 | Protein folding_Response to unfolded proteins         | 72  | 1.325E-02 | 9.213E-02 | 8  | HSP90, HSP70, HSPA4, HSP90 beta, Hdj-2, Glutaredoxin, HSC70, Glutaredoxin 1   |
| 23 | Neurophysiological process_Corticoliberin signaling   | 49  | 1.964E-02 | 1.306E-01 | 6  | G-protein beta/gamma, CRH receptor 2, cPKC (conventional), PKA-reg (cAMP-dependent), Calmodulin, ERK2 (MAPK1)   |
| 24 | Apoptosis_Apoptotic mitochondria                      | 79  | 2.220E-02 | 1.415E-01 | 8  | HSP70, VDAC 1, Glutaredoxin, ERK2 (MAPK1), MAP1, 14-3-3, 14-3-3 eta, Glutaredoxin 1   |
| 25 | Neurophysiological process_Long-term potentiation     | 82  | 2.711E-02 | 1.659E-01 | 8  | CaMK IV, PKA-reg (cAMP-dependent), Protein kinase G 2, Calmodulin, ERK1/2, Guanylate Cyclase 1, soluble, Protein kinase G, ERK2 (MAPK1)   |
| 26 | Cell cycle_G2-M                                       | 206 | 3.755E-02 | 2.210E-01 | 15 | Cyclin G, 14-3-3 beta/alpha, TCP1-theta, EGF, TCP1-delta, TCP1-eta, Nek8, Cyclin G1, MRLC, Securin, ERK1/2, TCP1-alpha, TCP1-epsilon, 14-3-3, 14-3-3 eta  |
| 27 | Reproduction_Spermatogenesis, motility and copulation | 230 | 4.614E-02 | 2.615E-01 | 16 | HSP70, Tcf5, ODF3, PKC-beta, G-protein beta/gamma, EGF, BMPR1A, PKA-reg (cAMP-dependent), HMDH, Histone H2, Histone H2A, NCOA4 (ARA70), Hdj-2, Calmodulin, PKC, Ran   |



|    |   |     |           |           |    |  |
|----|---|-----|-----------|-----------|----|--|
| 28 | Neurophysiological process_Circadian rhythm                       | 76  | 4.886E-02 | 2.670E-01 | 7  | REV-ERBalpha, cPKC (conventional), PKA-reg (cAMP-dependent), Protein kinase G 2, Calmodulin, ERK1/2, Guanylate Cyclase 1, soluble  |
| 29 | Response to hypoxia and oxidative stress                          | 161 | 5.099E-02 | 2.690E-01 | 12 | Peroxiredoxin, PRDX3, Thioredoxin, PRDX1, TXNRD1, HSP90 beta, Selenoprotein P, Glutaredoxin, ERK2 (MAPK1), MEK4(MAP2K4), SOD1, Glutaredoxin 1  |
| 30 | Reproduction_Progesterone signaling                               | 216 | 5.308E-02 | 2.707E-01 | 15 | GABA-A receptor alpha-1 subunit, GABA-A receptor beta-2 subunit, EGF, GABA-A receptor alpha-4 subunit, PKA-reg (cAMP-dependent), GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, Galpha(q)-specific peptide GPCRs, DLC1 (Dynein LC8a), Calmodulin, PGRMC1, CLIC4, ERK2 (MAPK1), TFIIB, PI3K reg class IA |
| 31 | Apoptosis_Anti-Apoptosis mediated by external signals by Estrogen | 95  | 5.700E-02 | 2.813E-01 | 8  | Thioredoxin, G-protein beta/gamma, Protein kinase G1, ERK1/2, Guanylate Cyclase 1, soluble, MEK4(MAP2K4), SOD1, PI3K reg class IA  |
| 32 | Muscle contraction_Relaxin signaling                              | 82  | 6.827E-02 | 3.264E-01 | 7  | Endothelin-1, G-protein beta/gamma, PKA-reg (cAMP-dependent), Protein kinase G1, PDE4A, ERK1/2, Guanylate Cyclase 1, soluble   |
| 33 | Signal transduction_WNT signaling                                 | 176 | 8.682E-02 | 3.795E-01 | 12 | PP2A cat (alpha), PKC-beta, EGF, PKA-reg type II (cAMP-dependent), PKA-reg (cAMP-dependent), PKC-beta2, Calcineurin A (catalytic), PP2A catalytic, Calmodulin, CaMK II delta, Calcineurin A (beta), MEK4(MAP2K4)   |
| 34 | Cell adhesion_Synaptic contact                                    | 176 | 8.682E-02 | 3.795E-01 | 12 | Synaptotagmin I, Synaptotagmin, CNTN1 (F3), GABA-A receptor alpha-1 subunit, GABA-A receptor beta-2 subunit, GABA-A receptor alpha-4 subunit, GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, Syntenin 1, CaMK II delta, SAP102, 14-3-3 eta  |
| 35 | Cytoskeleton_Actin filaments                                      | 176 | 8.682E-02 | 3.795E-01 | 12 | MELC, Protein kinase G1, Calponin-1, Zeta-sarcoglycan, Destrin, CAPZA, MRLC, ERK1/2, Protein kinase G, ERK2 (MAPK1), Nephrocystin-4, ARP3  |
| 36 | Development_Skeletal muscle development                           | 144 | 1.019E-01 | 3.929E-01 | 10 | Alpha crystallin B, Smooth muscle myosin, MELC, CaMK IV, Elastin, Myotrophin, MEF2, MRLC, Calmodulin, MEF2C  |
| 37 | Transport_Manganese transport                                     | 108 | 1.023E-01 | 3.929E-01 | 8  | PP2A cat (alpha), ARG2, PPM1E, TRPC5, TRPC4, NCX1, IDI1, PRNP  |
| 38 | Cell adhesion_Cadherins   | 182 | 1.047E-01 | 3.929E-01 | 12 | Cadherin 8, PKC-beta, DKK2, WIF1, PP1-cat, Vinexin, PKC-beta2, PP2A catalytic, PKC-beta1, PKC, K-cadherin (CDH6), DKK1   |
| 39 | Cytoskeleton_Spindle microtubules                                 | 109 | 1.064E-01 | 3.929E-01 | 8  | Tubulin alpha 1A, Importin (karyopherin)-alpha, Karyopherin alpha 2, Tubulin alpha, DLC1 (Dynein LC8a), Securin, Ran, TCP1-alpha   |

|    |   |     |           |           |    |  |
|----|---|-----|-----------|-----------|----|--|
| 40 | Proliferation_Positive regulation cell proliferation                          | 221 | 1.077E-01 | 3.929E-01 | 14 | Endothelin-1, MGF, Galpha(i)-specific peptide GPCRs, MTG16 (CBFA2T3), EGF, Serotonin receptor, PKA-reg (cAMP-dependent), Galpha(i)-specific amine GPCRs, MRLC, ERK1/2, ERK2 (MAPK1), MEK4(MAP2K4), PRKAR1A, PI3K reg class IA                  |
| 41 | Development_Regulation of angiogenesis  | 221 | 1.077E-01 | 3.929E-01 | 14 | Angiopoietin 1, Endothelin-1, Galpha(i)-specific peptide GPCRs, Semaphorin 5A, Ephrin-A receptor 4, HMDH, Ephrin-A receptors, Galpha(q)-specific peptide GPCRs, Patched, CEACAM1, ERK1/2, PKC, ERK2 (MAPK1), PI3K reg class IA                 |
| 42 | Proliferation_Negative regulation of cell proliferation                       | 183 | 1.079E-01 | 3.929E-01 | 12 | CNOT7, CDC18L (CDC6), Tcf15, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, Securin, ERK1/2, SSTR2, Guanylate Cyclase 1, soluble, ERK2 (MAPK1), SSTR1, SAP102   |
| 43 | Cardiac development_Wnt_beta-catenin, Notch, VEGF, IP3 and integrin signaling | 151 | 1.280E-01 | 4.556E-01 | 10 | Semaphorin 3C, G-protein beta/gamma, DLL4, Calcineurin A (catalytic), MEF2, Kv4.2 channel, Calmodulin, MEF2C, Calcineurin A (beta), DKK1   |
| 44 | Protein folding_ER and cytoplasm  | 45  | 1.344E-01 | 4.675E-01 | 4  | HSP90, HSP70, Glutaredoxin, HSC70  |
| 45 | Signal transduction_CREM pathway  | 98  | 1.395E-01 | 4.696E-01 | 7  | ODF3, CaMK IV, EGF, CREB4, PKA-reg (cAMP-dependent), ERK1/2, ERK2 (MAPK1)  |
| 46 | Cell adhesion_Attractive and repulsive receptors                              | 174 | 1.439E-01 | 4.696E-01 | 11 | Semaphorin 3C, Ephrin-A receptor 5, Semaphorin 5A, Ephrin-A receptor 4, Semaphorin 3E, Ephrin-A receptors, CDK5, Destrin, ERK1/2, PI3K reg class IA (p55-gamma), PI3K reg class IA   |
| 47 | Development_Hemopoiesis, Erythropoietin pathway                               | 136 | 1.442E-01 | 4.696E-01 | 9  | PAK3, MGF, G-protein beta/gamma, PKC-beta2, Calmodulin, ERK1/2, PI3K reg class IA (p55-gamma), ERK2 (MAPK1), PI3K reg class IA   |
| 48 | Inflammation_Histamine signaling  | 215 | 1.519E-01 | 4.842E-01 | 13 | Guanylate cyclase, Guanylate cyclase alpha, GUCY1B1, G-protein beta/gamma, PKA-reg (cAMP-dependent), GUCY1A3, Guanylate cyclase beta, Calcineurin A (catalytic), Calmodulin, ERK1/2, CaMK II delta, Guanylate Cyclase 1, soluble, ERK2 (MAPK1) |
| 49 | Development_Neurogenesis_Synaptogenesis                                       | 178 | 1.603E-01 | 5.005E-01 | 11 | Synaptotagmin I, Synaptotagmin, TRPC5, KIS, P/Q-type calcium channel alpha-1A subunit, NSF, SYP, Calmodulin, Endophilin A1, SAP102, 14-3-3 eta   |
| 50 | Inflammation_MIF signaling  | 141 | 1.679E-01 | 5.133E-01 | 9  | PRDX1, G-protein beta/gamma, PKA-reg (cAMP-dependent), CDK5, PP2A catalytic, Galpha(s)-specific CRF GPCRs, ERK1/2, PKC, ERK2 (MAPK1)   |

Table A17. Top 50 KCL BrainBank Process Networks enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| #  | Term Name   | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|----|---|-----------|-----------|------------------------|-------------------|---|
| 1  | Signal transduction_Neuropeptide signaling pathways   | 139       | 1.458E-16 | 1.618E-14              | 25                | CLIP, ACTH, alpha-MSH, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, MC4R, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Joining peptide (JP), N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, Calcitonin receptor, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, Galpha(s)-specific peptide GPCRs, AGRP, beta-MSH, CART |
| 2  | Development_Blood vessel morphogenesis                | 208       | 6.720E-04 | 3.730E-02              | 13                | Angiopoietin 1, APJ, Neuropilin-2, VCAM1, HIF-prolyl hydroxylase, Galpha(q)-specific peptide GPCRs, PLAT (TPA), Galpha(i)-specific peptide GPCRs, S1P1 receptor, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, Galpha(i)-specific EDG GPCRs, EGF   |
| 3  | Reproduction_Progesterone signaling                   | 187       | 8.481E-03 | 2.490E-01              | 10                | HGF, PLA2, Galpha(s)-specific calcitonin GPCRs, Galpha(q)-specific peptide GPCRs, PLC-delta, EGF, PR (membrane), Oct-2, WNT, PR (nuclear)   |
| 4  | Inflammation_Interferon signaling                     | 106       | 9.021E-03 | 2.490E-01              | 7                 | MxB, ILT4, IFI27, I-TAC, Apo-2L(TNFSF10), MxA, IFI44  |
| 5  | Reproduction_Spermatogenesis, motility and copulation | 195       | 1.122E-02 | 2.490E-01              | 10                | Histone H2, Histone H2A, SPAG6, MFGE8, Galpha(s)-specific calcitonin GPCRs, Connexin 26, Calcitonin receptor, EGF, SOX3, Oct-2  |
| 6  | Transport_Sodium transport                            | 153       | 2.024E-02 | 3.744E-01              | 8                 | SLC6A11, ASCT1 (SLC1A4), NCKX3, SLC13A5, GLVR1, SLC4A4, Aquaporin 1, SLC12A1  |
| 7  | Transport_Bile acids transport and its regulation     | 33        | 3.611E-02 | 5.146E-01              | 3                 | HYEP, L-FABP, LRH1  |
| 8  | Inflammation_NK cell cytotoxicity                     | 141       | 3.709E-02 | 5.146E-01              | 7                 | Caspase-10, EAT-2, Histone H2B, HMGB2, Perforin, Apo-2L(TNFSF10), HLAC  |
| 9  | Inflammation_Complement system                        | 60        | 4.379E-02 | 5.401E-01              | 4                 | C4, Ficolin, C4a, C4b   |
| 10 | Development_Melanocyte development and pigmentation   | 39        | 5.498E-02 | 5.908E-01              | 3                 | ACTH, alpha-MSH, Galpha(s)-specific peptide GPCRs   |

|    |   |     |           |           |   |  |
|----|---|-----|-----------|-----------|---|--|
| 11 | Immune response_Innate immune response to RNA viral infection | 66  | 5.855E-02 | 5.908E-01 | 4 | Caspase-10, I-TAC, 2'-5'-oligoadenylate synthetase, MxA  |
| 12 | Signal transduction_ESR1-nuclear pathway                      | 204 | 8.375E-02 | 7.747E-01 | 8 | HMG1,2, APJ, LRH1, Lactoferrin, SUPT6H, EGF, MTA2, PR (nuclear)                                |
| 13 | Inflammation_Histamine signaling                              | 167 | 1.672E-01 | 9.915E-01 | 6 | HDC, Kappa chain (Ig light chain), VCAM1, PLA2, IGHG1, PLA2G5                                  |
| 14 | Development_Neurogenesis in general                           | 180 | 2.111E-01 | 9.915E-01 | 6 | LHX1, SIX3, POU class III, SOX3, WNT, Midkine  |
| 15 | Transcription_Nuclear receptors transcriptional regulation    | 181 | 2.147E-01 | 9.915E-01 | 6 | HMG1,2, HMGB2, EGF, RXR, RXRG, PR (nuclear)  |
| 16 | Signal transduction_ESR1-membrane pathway                     | 77  | 2.447E-01 | 9.915E-01 | 3 | EGF, PR (membrane), PR (nuclear)   |
| 17 | Apoptosis_Apoptotic nucleus                                   | 155 | 2.620E-01 | 9.915E-01 | 5 | Caspase-10, Histone H2B, HMGB2, Perforin, Proline oxidase 1                                    |
| 18 | Cell adhesion_Cell-matrix interactions                        | 195 | 2.663E-01 | 9.915E-01 | 6 | CD44, CD44 soluble, CD44 (ICD), Neurocan, Biglycan, CD44 (EXT)                                 |
| 19 | Apoptosis_Death Domain receptors & caspases in apoptosis      | 118 | 2.675E-01 | 9.915E-01 | 4 | A20, Caspase-10, Apo-2L(TNFSF10), NALP3  |
| 20 | Immune response_BCR pathway                                   | 118 | 2.675E-01 | 9.915E-01 | 4 | Kappa chain (Ig light chain), IGHG1, Fc gamma RII beta, Oct-2                                  |
| 21 | Blood coagulation   | 82  | 2.748E-01 | 9.915E-01 | 3 | PLAT (TPA), Galpha(q)-specific nucleotide-like GPCRs, P2Y1                                     |
| 22 | Cell adhesion_Leucocyte chemotaxis                            | 158 | 2.748E-01 | 9.915E-01 | 5 | Tubulin beta, VCAM1, Galpha(q)-specific peptide GPCRs, Galpha(i)-specific peptide GPCRs, I-TAC |
| 23 | Transport_Iron transport                                      | 85  | 2.931E-01 | 9.915E-01 | 3 | HIF-prolyl hydroxylase, EGLN3, Lactoferrin   |
| 24 | Transcription_Chromatin modification                          | 124 | 2.975E-01 | 9.915E-01 | 4 | Histone H2, Histone H2A, Histone H2B, MTA2   |

|    |  |     |           |           |   |   |
|----|--|-----|-----------|-----------|---|---|
| 25 | Cell adhesion_Platelet-endothelium-leucocyte interactions  | 166 | 3.096E-01 | 9.915E-01 | 5 | HGF, VCAM1, CD44, PLAT (TPA), EGF   |
| 26 | Chemotaxis   | 128 | 3.177E-01 | 9.915E-01 | 4 | CD44, Galpha(q)-specific peptide GPCRs, Galpha(i)-specific peptide GPCRs, I-TAC                         |
| 27 | Inflammation_Protein C signaling                           | 93  | 3.421E-01 | 9.915E-01 | 3 | PLAT (TPA), S1P1 receptor, Galpha(i)-specific EDG GPCRs   |
| 28 | Reproduction_Male sex differentiation                      | 220 | 3.646E-01 | 9.915E-01 | 6 | Histone H2, HGF, Histone H2A, Connexin 26, EGF, SOX3  |
| 29 | Signal transduction_Androgen receptor signaling cross-talk | 61  | 3.951E-01 | 9.915E-01 | 2 | EGF, WNT  |
| 30 | Response to hypoxia and oxidative stress                   | 105 | 4.150E-01 | 9.915E-01 | 3 | HIF-prolyl hydroxylase, GSTM3, SOD3 (EC-SOD)  |
| 31 | Reproduction_Feeding and Neurohormone signaling            | 194 | 4.340E-01 | 9.915E-01 | 5 | CD44, Galpha(q)-specific peptide GPCRs, POMC, Galpha(i)-specific peptide GPCRs, PEA3                    |
| 32 | Cytoskeleton_Macropinocytosis and its regulation           | 70  | 4.641E-01 | 9.915E-01 | 2 | HGF, EGF  |
| 33 | Muscle contraction   | 157 | 4.642E-01 | 9.915E-01 | 4 | Galpha(q)-specific peptide GPCRs, Galpha(i)-specific peptide GPCRs, Dystroglycan, ACES                  |
| 34 | Development_Regulation of angiogenesis                     | 202 | 4.691E-01 | 9.915E-01 | 5 | Angiopoietin 1, Galpha(q)-specific peptide GPCRs, Biglycan, Galpha(i)-specific peptide GPCRs, PLC-delta |
| 35 | Transport_Potassium transport                              | 161 | 4.837E-01 | 9.915E-01 | 4 | KCNE4, NCKX3, Aquaporin 1, SLC12A1  |
| 36 | Cytoskeleton_Intermediate filaments                        | 74  | 4.933E-01 | 9.915E-01 | 2 | Tubulin beta, GFAP  |
| 37 | Proteolysis_ECM remodeling                                 | 75  | 5.004E-01 | 9.915E-01 | 2 | Cystatin C, PLAT (TPA)  |

|    |   |     |           |           |   |  |
|----|---|-----|-----------|-----------|---|--|
| 38 | Proteolysis_Proteolysis in cell cycle and apoptosis                           | 120 | 5.022E-01 | 9.915E-01 | 3 | A20, Caspase-10, APH-1A  |
| 39 | Signal transduction_WNT signaling   | 168 | 5.173E-01 | 9.915E-01 | 4 | CD44, WNT7B, EGF, WNT  |
| 40 | Cell adhesion_Platelet aggregation  | 125 | 5.298E-01 | 9.915E-01 | 3 | PLA2, SLC21A2, P2Y1  |
| 41 | Development_Neurogenesis_Synaptogenesis                                       | 175 | 5.498E-01 | 9.915E-01 | 4 | Syntrophin gamma 2, Dystroglycan, ACES, WNT                        |
| 42 | Development_Neuromuscular junction  | 131 | 5.618E-01 | 9.915E-01 | 3 | P2Y1, Dystroglycan, ACES   |
| 43 | Cardiac development_Wnt_beta-catenin, Notch, VEGF, IP3 and integrin signaling | 133 | 5.722E-01 | 9.915E-01 | 3 | Neuropilin-2, Galpha(s)-specific calcitonin GPCRs, WNT             |
| 44 | Cell adhesion_Amyloid proteins  | 180 | 5.724E-01 | 9.915E-01 | 4 | WNT7B, CD147, ACES, WNT  |
| 45 | Signal transduction_Leptin signaling  | 87  | 5.809E-01 | 9.915E-01 | 2 | POMC, CPT-1A   |
| 46 | Signal transduction_CREM pathway  | 87  | 5.809E-01 | 9.915E-01 | 2 | PLAT (TPA), EGF  |
| 47 | Neurophysiological process_Corticoliberin signaling                           | 39  | 5.852E-01 | 9.915E-01 | 1 | POMC   |
| 48 | Signal Transduction_BMP and GDF signaling                                     | 88  | 5.872E-01 | 9.915E-01 | 2 | CD44, PRSS11 (HtrA1)   |
| 49 | Signal Transduction_Cholecystokinin signaling                                 | 93  | 6.175E-01 | 9.915E-01 | 2 | Galpha(q)-specific peptide GPCRs, Galpha(i)-specific peptide GPCRs |
| 50 | Inflammation_Innate inflammatory response                                     | 144 | 6.265E-01 | 9.915E-01 | 3 | PLA2, C4, I-TAC  |

Table A18. Top 50 TargetALS Process Networks enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| # | Term Name                                    | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names  |
|---|--|-----------|-----------|------------------------|-------------------|--|
| 1 | Heredodegenerative Disorders, Nervous System | 3074      | 5.958E-31 | 1.301E-27              | 215               | PLP1, NPY, PRPS1, HSP90, PAK3, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, G3BP2, ILDR2, MAL2, COX VIc, GAD1, MEGF10, THAP11, PTCH2, ELOVL5, Peroxiredoxin, Esterase D, Neuropeptide K, PSMB5, T-plastin, BRSK2, UQCRQPC, DYNLT3, G-protein beta, UQCRH, NDUFAB1, CCK8-Gly, NckAP1, NDUFA1, MGF, PDH E2 subunit N6-lipoyllysine, MELC, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, CNR1, Synaptotagmin IV, Synaptotagmin, PRDX3, Thioredoxin, NDUFA4, PDE, Cystatin C, PPT1, SCF, SDHB, ANKRD36B, NCKP1 subunit, CCK8, TPH2, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, Kv3.3, ORP-family, TRPC5, PKC-beta, TCP1-theta, PRDX1, G-protein beta/gamma, NDUFB6, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, TXNRD1, ORP8, PIMT, TRPV1, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, GRAIL, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, Dysferlin, Elastin, EGF, Pro-CCK, SYTC, Dynein, axonemal, heavy chains, cPKC (conventional), NDUFB1, ELOVL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, COX VIa, CLCN4, SMRT, NHE6, Neurokinin A, PDLIM2, UQCR10, Clathrin heavy chain, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, C9orf5, Galpha(i)-specific amine GPCRs, TRPC4, HCN, RTEL1-TNFRSF6B, HLF, CAP1, MEGF6, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, SYT16, Fatty acid-binding protein, HINT, IZUMO1, GABA-A receptor alpha-3 subunit, DYNLT, SPSY, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPSRs, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, NDUFA5, Tubulin alpha, Creatine kinase, DSCAML1, Azi1, Patched, TNK1, MEF2, NAPB, HNMT, APRI0, MEK4/7, ACSL4, ATF/CREB, GLGB, ODP2, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, ID11, SNAPs, LAMP2, COX VIa-1, YPEL5, Kv4.2 channel, PRNP, HSPC138, RHEB2, NKCC1, Malin, PKC-beta1, LOXL2, NME5, Calcyclin, SCOT, Octanoyl-holo-acp, ERK1/2, AATC, NFIC, CaMK II delta, HSC70, PKC, HTR2A, GS1-124K5.11, MEF2C, ERK2 (MAPK1), OAT, MEK4(MAP2K4), CCK8-GlyArgArg, IMPA1, sKITLG, PRPS, SOD1, TFIIB, SAP102, Cyclophilin A, FOXP1/2/4 proteins, |

|   |                    |      |           |           |     |  |
|---|--------------------|------|-----------|-----------|-----|--|
|   |                    |      |           |           |     | PI3K reg class IA, Galpha(s)-specific peptide GPCRs, ATP6AP2, CALB1, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, Midkine, 14-3-3, RAGE  |
| 2 | Huntington Disease | 984  | 8.344E-30 | 9.107E-27 | 107 | NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, MAL2, COX VIc, GAD1, Peroxiredoxin, Neuropeptide K, UQCRQPC, UQCRH, NDUFAB1, CCK8-Gly, NDUFA1, NDUFB4, NDUFA8, Synaptotagmin I, Substance P extracellular region, CNR1, Synaptotagmin IV, Synaptotagmin, Thioredoxin, NDUFA4, PDE, SDHB, CCK8, Neuropeptide gamma, GABA-A receptor alpha-1 subunit, ORP-family, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, TXNRD1, ORP8, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, CaMK IV, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, Pro-CCK, cPKC (conventional), NDUFB1, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, COX VIa, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, Galpha(i)-specific amine GPCRs, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, SYT16, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Galpha(q)-specific peptide GPCRs, NDUFA5, Tubulin alpha, Creatine kinase, NAPB, HNMT, APRIO, ATF/CREB, SNAPs, COX VIa-1, YPEL5, PRNP, NKCC1, PKC-beta1, SCOT, Octanoyl-holo-acp, CaMK II delta, PKC, HTR2A, OAT, CCK8-GlyArgArg, SOD1, Cyclophilin A, FOXP1/2/4 proteins, CALB1, COX VIIa-2, 14-3-3 |
| 3 | Chorea             | 1029 | 3.633E-28 | 2.644E-25 | 107 | NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, MAL2, COX VIc, GAD1, Peroxiredoxin, Neuropeptide K, UQCRQPC, UQCRH, NDUFAB1, CCK8-Gly, NDUFA1, NDUFB4, NDUFA8, Synaptotagmin I, Substance P extracellular region, CNR1, Synaptotagmin IV, Synaptotagmin, Thioredoxin, NDUFA4, PDE, SDHB, CCK8, Neuropeptide gamma, GABA-A receptor alpha-1 subunit, ORP-family, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, TXNRD1, ORP8, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, CaMK IV, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, Pro-CCK, cPKC (conventional), NDUFB1, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, COX VIa, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, Histone H2, CCK5,  |



|   |                        |      |           |           |     |  |
|---|------------------------|------|-----------|-----------|-----|--|
|   |                        |      |           |           |     | Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, Galpha(i)-specific amine GPCRs, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, SYT16, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, NDUFA5, Tubulin alpha, Creatine kinase, NAPB, HNMT, APRIO, ATF/CREB, SNAPs, COX VIa-1, YPEL5, PRNP, NKCC1, PKC-beta1, SCOT, Octanoyl-holo-acp, CaMK II delta, PKC, HTR2A, OAT, CCK8-GlyArgArg, SOD1, Cyclophilin A, FOXP1/2/4 proteins, CALB1, COX VIIa-2, 14-3-3  |
| 4 | Basal Ganglia Diseases | 2881 | 1.223E-25 | 6.673E-23 | 194 | NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, ET-1, G3BP2, ILDR2, MAL2, COX VIc, GAD1, HPCA, ELOVL5, Peroxiredoxin, Esterase D, Endothelin-1, Neuropeptide K, BRSK2, UQCRQPC, ALDR, UQCRH, PSMA5, NDUFAB1, CCK8-Gly, BTBD12, NDUFA1, MGF, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, CNR1, Synaptotagmin IV, PPM1E, DnaJB9, Synaptotagmin, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, PDE, Cystatin C, SCF, SDHB, SLC39A10, DKK3, CCK8, TPH2, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, ORP-family, LY6G5B, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SUR, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, TXNRD1, ORP8, AMIGO2, LASS6, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, IDUA, SLC2A13, Semaphorin 5A, NSF, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, FBXO2, SYP, Rho GTPase, PDE4, G-protein gamma, Rap1GDS1, Elastin, EGF, Pro-CCK, HIST1H2BN, cPKC (conventional), NDUFB1, AP3S1, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, VDAC 1, COX VIa, Osteopontin, Big ET-1, Lingo1, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, AP-3 sigma subunits, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, C9orf5, Galpha(i)-specific amine GPCRs, DNAJC12, RTEL1-TNFRSF6B, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, FLJ32001, SYT16, Fatty acid-binding protein, IZUMO1, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, B-FABP, MEF2, NAPB, HNMT, APRIO, ATF/CREB, RAI1, LAMP2-C, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, MPTP complex, NKCC1, HIST2H2BE, PKC-beta1, |

|   |                    |      |           |           |     |   |
|---|--------------------|------|-----------|-----------|-----|---|
|   |                    |      |           |           |     | LOXL2, Endophilin A1, Aquaporin 1, NDFIP1, Syntenin 1, SCOT, Octanoyl-holo-acp, ADHX, AATC, CaMK II delta, HSC70, PKC, SUR1, HTR2A, GS1-124K5.11, OAT, CCK8-GlyArgArg, sKITLG, SOD1, GSE1, Cyclophilin A, FOXP1/2/4 proteins, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, MRPL3, COX VIIa-2, ARP3, 14-3-3, RAGE, 14-3-3 eta   |
| 5 | Movement Disorders | 2994 | 5.030E-24 | 2.196E-21 | 195 | NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, ET-1, G3BP2, ILDR2, MAL2, COX VIc, GAD1, HPCA, ELOVL5, Peroxiredoxin, Esterase D, Endothelin-1, Neuropeptide K, BRSK2, UQCRQPC, ALDR, UQCRH, PSMA5, NDUFA1, CCK8-Gly, NDUFA1, MGF, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, CNR1, Synaptotagmin IV, PPM1E, DnaJB9, Synaptotagmin, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, Dynein, axonemal, light chains, PDE, Cystatin C, SCF, SDHB, SLC39A10, DKK3, CCK8, TPH2, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, ORP-family, LY6G5B, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SUR, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, TXNRD1, ORP8, AMIGO2, LASS6, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, IDUA, SLC2A13, Semaphorin 5A, NSF, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, FBXO2, SYP, Rho GTPase, PDE4, G-protein gamma, Elastin, EGF, Pro-CCK, Dynein, axonemal, heavy chains, HIST1H2BN, cPKC (conventional), NDUFB1, AP3S1, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, VDAC 1, COX VIa, Osteopontin, Big ET-1, NHE6, Lingo1, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, AP-3 sigma subunits, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, C9orf5, DOC1, Galpha(i)-specific amine GPCRs, DNAJC12, RTEL1-TNFRSF6B, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, FLJ32001, SYT16, Fatty acid-binding protein, IZUMO1, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, B-FABP, MEF2, NAPB, HNMT, APRIO, ATF/CREB, RAI1, LAMP2-C, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, MPTP complex, NKCC1, HIST2H2BE, PKC-beta1, LOXL2, Endophilin A1, Aquaporin 1, NDFIP1, Syntenin 1, SCOT, Octanoyl-holo-acp, ADHX, AATC, CaMK II delta, HSC70, PKC, SUR1, HTR2A, GS1-124K5.11, OAT, CCK8-GlyArgArg, sKITLG, |

|   |                     |      |           |           |     |  |
|---|---------------------|------|-----------|-----------|-----|--|
|   |                     |      |           |           |     | SOD1, Cyclophilin A, FOXP1/2/4 proteins, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, MRPL3, COX VIIa-2, ARP3, 14-3-3, RAGE, 14-3-3 eta   |
| 6 | Dyskinesias         | 1854 | 3.305E-23 | 1.201E-20 | 141 | NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, MAL2, COX VIc, GAD1, THAP11, HPCA, ELOVL5, Peroxiredoxin, Neuropeptide K, UQCRQPC, KLHL4, UQCRH, NDUFAB1, CCK8-Gly, NDUFA1, NPFF receptor 2, NDUFB4, NDUFA8, Synaptotagmin I, Substance P extracellular region, CNR1, Glycogen phosphorylase, Synaptotagmin IV, Synaptotagmin, PRDX3, Thioredoxin, NDUFA4, Dynein, axonemal, light chains, PDE, Cystatin C, SDHB, SLC39A10, ANKRD36B, CCK8, TPH2, Neuropeptide gamma, GABA-A receptor alpha-1 subunit, Kv3.3, ORP-family, TRPC5, PKC-beta, PAFAH gamma, PRDX1, G-protein beta/gamma, NDUFB6, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, TXNRD1, ORP8, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, IP3KA, CaMK IV, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, Pro-CCK, Dynein, axonemal, heavy chains, cPKC (conventional), NDUFB1, ELOVL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, COX VIa, SMRT, NHE6, Neurokinin A, PDLIM2, UQCR10, Clathrin heavy chain, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, DOC1, Galpha(i)-specific amine GPCRs, HLF, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, SYT16, ASAH, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, SLC25A46, PDH beta, Galpha(q)-specific peptide GPCRs, NDUFA5, Tubulin alpha, Creatine kinase, NAPB, HNMT, APRIO, ATF/CREB, GLGB, LAMP2-C, BMI-1, SNAPs, LAMP2, COX VIa-1, YPEL5, PRNP, NKCC1, PKC-beta1, SCOT, Octanoyl-holo-acp, NFIC, CaMK II delta, PKC, HTR2A, PMM2, OAT, CCK8-GlyArgArg, SOD1, Cyclophilin A, FOXP1/2/4 proteins, CALB1, GAD2, NF-I, COX VIIa-2, 14-3-3 |
| 7 | Cognition Disorders | 1319 | 3.852E-23 | 1.201E-20 | 114 | NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, MAL2, COX VIc, GAD1, Peroxiredoxin, Neuropeptide K, UQCRQPC, UQCRH, NDUFAB1, CCK8-Gly, NDUFA1, NDUFB4, NDUFA8, Synaptotagmin I, Substance P extracellular region, CNR1, Synaptotagmin IV, Synaptotagmin, Thioredoxin, NDUFA4, PDE, Cystatin C, SDHB, CCK8, Neuropeptide gamma, GABA-A receptor alpha-1 subunit, ORP-family, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, NDUFS4, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB,   |

|   |                |      |           |           |     |   |
|---|----------------|------|-----------|-----------|-----|---|
|   |                |      |           |           |     | S100, TXNRD1, ORP8, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, CaMK IV, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, Pro-CCK, cPKC (conventional), NDUFB1, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, COX VIa, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, Galpha(i)-specific amine GPCRs, CAP1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, SYT16, Fatty acid-binding protein, GABA-A receptor alpha-3 subunit, COX Va, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, sRAGE, Galpha(q)-specific peptide GPCRs, NDUFA5, Tubulin alpha, Creatine kinase, B-FABP, TNK1, NAPB, HNMT, APRIO, ATF/CREB, SNAPs, COX VIa-1, YPEL5, PRNP, NKCC1, PKC-beta1, SCOT, Octanoyl-holo-acp, CaMK II delta, PKC, HTR2A, OAT, CCK8-GlyArgArg, SOD1, Cyclophilin A, FOXP1/2/4 proteins, CALB1, COX VIIa-2, 14-3-3, RAGE  |
| 8 | Brain Diseases | 8447 | 7.345E-23 | 2.004E-20 | 400 | PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAM, HMGCLL1, Cadherin 8, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, IRF1, ILDR2, MAL2, GLSK, Rab-3B, COX VIc, GAD1, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, HPCA, APJ, ELOVL5, Peroxiredoxin, Activin A, UBL5, Esterase D, Endothelin-1, Trehalase, Neuropeptide K, Nkpd1, BRSK2, UQCRQPC, G-protein beta, KLHL4, ALDR, UQCRH, Rab-6A, Mucin 5B, PSMA5, NDUFAB1, CCK8-Gly, BTBD12, NDUFA1, DNAH1, MRPL1, Lgi4, Pannexin-1, FAM90A1, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, NPFF receptor 2, NDUFB4, MC4R, NDUFA8, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, Substance P extracellular region, DDX3Y, CNR1, Glycogen phosphorylase, Synaptotagmin IV, PPM1E, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, PDE, Cystatin C, PPT1, SCF, SDHB, SLC39A10, DKK3, LUZP2, ANKRD36B, HCN2, Guanylate cyclase alpha, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, LINC00342, D330028D13Rik, Kv3.3, ORP-family, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, LASS6, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose |

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|--|--|--|--|--|--|
|  |  |  |  |  | <p> reductase, NDUFB3, Rab-3, ATG9B, TM2D3, Ephrin-A receptor 5, LAPT4B, IDUA, CRH receptor 2, SLC2A13, Semaphorin 5A, NSF, CaMK IV, CHCHD2, GLRA, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, G-protein gamma, UBE2D1, ZNF70, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, A830006F12Rik, EGF, Pro-CCK, Dynein, axonemal, heavy chains, MMADHC, HIST1H2BN, PKA-reg type II (cAMP-dependent), cPKC (conventional), NDUFB1, ELOVL4, AP3S1, Serotonin receptor, CHMP5, Apelin, GABA-A receptor alpha-4 subunit, PPID, TRPC, SLC7A5, HTR5A, VDAC 1, C17orf76, WIF1, COX VIa, CLCN4, Osteopontin, SMRT, Big ET-1, NHE6, Rab-3C, M-Ras, PKA-reg (cAMP-dependent), RNF152, Lingo1, PP1-cat, HMDH, Neurokinin A, PDLIM2, UQCR10, GUCY1A3, Clathrin heavy chain, Substance P, AP-3 sigma subunits, StARD4, GRM6, Histone H2, LIPA, MCT1 (SLC16A1), CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, NPR3, C9orf5, GP-IB alpha, Galpha(i)-specific amine GPCRs, Stch, LINGO1-AS1, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, CAP1, HSP90 beta, TXNIP (VDUP1), Vinexin, COL25A1, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PANX2, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Glycine receptor, Fatty acid-binding protein, Synaptoporin, MAML1, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, Glycine receptor beta chain, CAPZA, RTL1, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, sRAGE, SLC25A46, Glyoxalase I, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, SNAP190, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, B-FABP, C17orf72, Patched, TNK1, CHKB-AS1, XK, MEF2, NAPB, ADAR3, HNMT, APRIO, MEK4/7, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, LAMP2-C, Acyl-CoA synthetase, PP2A catalytic, IDI1, AP-4, MRLC, BMI-1, SNAPS, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, HSPC138, MPTP complex, ENC1, STAG3, RHEB2, NKCC1, Neurocalcin delta, Malin, HIST2H2BE, PKC-beta1, Calmodulin, LPL, DIRAS2, Apo-2L(TNFSF10), SET1B, LOXL2, HSPC125, USMG5, Endophilin A1, Activin, Aquaporin 1, NDFIP1, Calcyclin, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ERK1/2, AATC, UGCG, Anks4b, NFIC, CaMK II delta, HSC70, PKC, SSTR2, SUR1, HTR2A, PMM2, MPP7, GS1-124K5.11, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, Protein kinase G, ERK2 (MAPK1), </p> |
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|   |                            |      |           |           |     |   |
|---|----------------------------|------|-----------|-----------|-----|---|
|   |                            |      |           |           |     | DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), TMEM70, PRKAR1A, IGFALS, CCK8-GlyArgArg, UFC1, Nephrocystin-4, DKK1, sKITLG, SSTR1, Guanine deaminase, SOD1, PPP4R2, GSE1, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, DBH-AS1, Galpha(s)-specific peptide GPCRs, ATP5L, ACTR3, OXR1, CALB1, Tubulin alpha-4A, RhoE, Pcdh19, CD166, GAD2, NF-I, MRPL3, Neuroserpin, COX VIIa-2, Midkine, ARP3, PXDN, 14-3-3, RAGE, 14-3-3 eta, SNX10   |
| 9 | Neurodegenerative Diseases | 6726 | 5.305E-22 | 1.287E-19 | 336 | PLP1, NPY, FAM3C, PP2A cat (alpha), PRPS1, HSP90, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, IRF1, ILDR2, MAL2, Rab-3B, COX VIc, GAD1, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, HPCA, ELOVL5, Peroxiredoxin, UBL5, Esterase D, Endothelin-1, Neuropeptide K, PSMB5, T-plastin, Nkpd1, BRSK2, UQCRQPC, DYNLT3, G-protein beta, LAS1L, ALDR, UQCRH, Rab-6A, PSMA5, NDUFAB1, CCK8-Gly, NckAP1, NDUFA1, MGF, PRKAR2B, MELC, NPFF receptor 2, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, DDX3Y, CNR1, Synaptotagmin IV, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, Septin 1, PDE, Cystatin C, PPT1, SCF, SDHB, DKK3, LUZP2, ANKRD36B, NCKP1 subunit, CCK8, TPH2, Neuropeptide gamma, RAB39B, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, ORP-family, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, TCP1-theta, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, Rab-6, TXNRD1, ORP8, AMIGO2, LASS6, PIMT, TRPV1, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, TM2D3, Ephrin-A receptor 5, IDUA, SLC2A13, Semaphorin 5A, RPL9, NSF, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, FBXO2, SYP, Rho GTPase, PDE4, G-protein gamma, UBE2D1, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, A830006F12Rik, EGF, Pro-CCK, SYTC, Dynein, axonemal, heavy chains, HIST1H2BN, PKA-reg type II (cAMP-dependent), NELL1, cPKC (conventional), NDUFB1, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, GABA-A receptor alpha-4 subunit, PPID, TRPC, HTR5A, PDK4, VDAC 1, C17orf76, COX VIa, Osteopontin, SMRT, Big ET-1, NHE6, Rab-3C, PKA-reg (cAMP-dependent), Lingo1, PP1-cat, HMDH, Neurokinin A, PDLIM2, UQCR10, Clathrin heavy chain, Substance P, AP-3 sigma subunits, StARD4, Histone H2, LIPA, ARHGAP18, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, |

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|----|------------------|------|-----------|-----------|-----|---|
|    |                  |      |           |           |     | <p>Histone H2A, C9orf5, Galpha(i)-specific amine GPCRs, TRPC4, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, CAP1, HSP90 beta, Vinexin, COL25A1, MEGF6, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, FLJ32001, SYT16, Fatty acid-binding protein, HINT, Synaptopodin, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, DYNLT, COX Va, ATP5A, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPSRs, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, MAFbx, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, B-FABP, Azi1, Patched, TNK1, MEF2, NAPB, ADAR3, HNMT, APRIO, BTBD10, MEK4/7, Peg10, ACSL4, ATF/CREB, GLGB, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, Kv4.2 channel, PRNP, HSPC138, MPTP complex, STAG3, RHEB2, NKCC1, Neurocalcin delta, Malin, HIST2H2BE, PKC-beta1, LPL, DIRAS2, Apo-2L(TNFSF10), LOXL2, Endophilin A1, Aquaporin 1, NDFIP1, NME5, Calcyclin, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, ADHX, ERK1/2, AATC, UGCG, NFIC, CaMK II delta, HSC70, PKC, SSTR2, SUR1, HTR2A, MPP7, GS1-124K5.11, ARPP-19, K-cadherin (CDH6), MEF2C, Protein kinase G, ERK2 (MAPK1), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), PRKAR1A, CCK8-GlyArgArg, IMPA1, UFC1, DKK1, sKITLG, PRPS, SOD1, TFIIB, FSTL5, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, ATP5L, CALB1, Tubulin alpha-4A, CD166, GAD2, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, Midkine, SAMD10, ARP3, 14-3-3, RAGE, 14-3-3 eta, SNX10</p> |
| 10 | Mental Disorders | 7319 | 5.398E-21 | 1.178E-18 | 354 | <p>PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, ILDR2, MAL2, GLSK, Rab-3B, COX VIc, GAD1, MEGF10, PTCH2, N-chimaerin, APJ, Smooth muscle myosin, ELOVL5, Peroxiredoxin, UBL5, Endothelin-1, Neuropeptide K, AP-1 gamma subunits, Nkpd1, REV-ERBalpha, BRSK2, UQCRQPC, P2Y11, G-protein beta, LAS1L, UQCRH, Rab-6A, PSMA5, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, NDUFA1, DCMC, PRKAR2B, PLD5, NPFF receptor 2, NDUFB4, MC4R, NDUFA8, C12orf62, Synaptotagmin I, Guanylate cyclase, KCNK2, HSP70, Substance P extracellular region, DDX3Y, CNR1, Synaptotagmin IV, HDBP1, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, PDE, Cystatin C, PPT1, SDHB, DKK3, LUZP2, NCKP1 subunit, HCN2, Galpha(q)-</p>   |

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|  |  |  |  |  | <p>specific Class A Orphan/other GPCRs, CCK8, GPR124, TPH2, Neuropeptide gamma, RAB39B, Aha1, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, GUCY1B1, ORP-family, Tenascin-C, CEACAM, TRPC5, PKC-beta, KIS, PAFAH gamma, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, FLJ35776, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, FAM69A, Rab-6, TXNRD1, ORP8, AMIGO2, PIMT, TRPV1, PRR12, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, TM2D3, Ephrin-A receptor 5, CRH receptor 2, Semaphorin 5A, NSF, CaMK IV, CHCHD2, GLRA, GABA-A receptor beta-2 subunit, CECR2, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, G-protein gamma, UBE2D1, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, A830006F12Rik, Secretogranin V, EGF, Pro-CCK, SYTC, Dynein, axonemal, heavy chains, BMPR1A, PKA-reg type II (cAMP-dependent), cPKC (conventional), ATP6V1B2, NDUFB1, AP3S1, Serotonin receptor, CHMP5, GABA-A receptor alpha-4 subunit, ADSS, Rab-27B, PPID, TRPC, HTR5A, VDAC 1, C17orf76, COX VIa, CLCN4, Osteopontin, ZNF238, SMRT, Big ET-1, NHE6, Rab-3C, PKA-reg (cAMP-dependent), Lingo1, PP1-cat, HMDH, Neurokinin A, UQCR10, NR3A, Cables1, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, StARD4, GRM6, Histone H2, LIPA, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, NPR3, C9orf5, GP-IB alpha, Galpha(i)-specific amine GPCRs, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, CAP1, HSP90 beta, Vinexin, COL25A1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, Guanylate cyclase (alpha-1/beta-1), SYT16, Guanylate cyclase beta, Glycine receptor, Fatty acid-binding protein, HINT, Synaptoporin, SgK223, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, SPSY, COX Va, eIF4A2, ATP5A, Glycine receptor beta chain, CAPZA, RTL1, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, sRAGE, Glyoxalase I, DDX51, Galpha(q)-specific peptide GPCRs, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), TBC1D10C, B-FABP, Patched, TNK1, CHKB-AS1, MEF2, NAPB, HNMT, APRIO, BTBD10, ACSL4, ATF/CREB, RAI1, Hdj-2, LAMP2-C, G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, MRLC, eIF4A, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, ATP6V1B, Kv4.2 channel, PRNP, TMS-1, MPTP complex, STAG3, RHEB2, NKCC1, Neurocalcin delta, HIST2H2BE, PKC-beta1, PDE4A, Calmodulin, LPL, DIRAS2, Apo-2L(TNFSF10), SET1B,</p> |
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|----|---------------------------|------|-----------|-----------|-----|---|
|    |                           |      |           |           |     | PDE11A, FLJ45455, Endophilin A1, STAC2, Activin, Aquaporin 1, C6orf27, Calcyclin, SCOT, Octanoyl-holo-acp, ADHX, ERK1/2, AATC, UGCG, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, HTR2A, MPP7, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, CCK8-GlyArgArg, IMPA1, UFC1, DKK1, SOD1, KIAA1024, PPP4R2, SAP102, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, DBH-AS1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, ATP6AP2, CALB1, Tubulin alpha-4A, Pcdh19, CD166, GAD2, NF-I, NPNT, MRPL3, HXK3, Neuroserpin, COX VIIa-2, 14-3-3, RAGE, 14-3-3 eta, ZCCHC12, SNX10   |
| 11 | Psychiatry and Psychology | 7410 | 6.351E-21 | 1.260E-18 | 357 | PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, ILDR2, MAL2, GLSK, Rab-3B, COX VIc, GAD1, MEGF10, PTCH2, N-chimaerin, APJ, Smooth muscle myosin, ELOVL5, Peroxiredoxin, UBL5, Endothelin-1, Neuropeptide K, AP-1 gamma subunits, Nkpd1, REV-ERBalpha, BRSK2, UQCRQPC, P2Y11, G-protein beta, LAS1L, UQCRH, Rab-6A, PSMA5, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, NDUFA1, DCMC, PRKAR2B, PLD5, NPFF receptor 2, NDUFB4, MC4R, NDUFA8, C12orf62, Synaptotagmin I, Guanylate cyclase, KCNK2, HSP70, Substance P extracellular region, DDX3Y, CNR1, Glycogen phosphorylase, Synaptotagmin IV, HDBP1, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, PDE, Cystatin C, PPT1, SDHB, DKK3, LUZP2, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, CCK8, GPR124, TPH2, Neuropeptide gamma, RAB39B, Aha1, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, GUCY1B1, ORP-family, Tenascin-C, CEACAM, TRPC5, PKC-beta, KIS, PAFAH gamma, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, FLJ35776, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, FAM69A, Rab-6, TXNRD1, ORP8, AMIGO2, PIMT, TRPV1, PRR12, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, TM2D3, Ephrin-A receptor 5, CRH receptor 2, Semaphorin 5A, NSF, CaMK IV, CHCHD2, GLRA, GABA-A receptor beta-2 subunit, CECR2, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, G-protein gamma, UBE2D1, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, A830006F12Rik, Secretogranin V, EGF, Pro-CCK, SYTC, Dynein, |

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|--|--|--|--|--|---|
|  |  |  |  |  | <p>axonemal, heavy chains, BMPR1A, PKA-reg type II (cAMP-dependent), cPKC (conventional), ATP6V1B2, NDUFB1, DLL4, AP3S1, Serotonin receptor, CHMP5, GABA-A receptor alpha-4 subunit, ADSS, Rab-27B, PPID, TRPC, HTR5A, VDAC 1, C17orf76, COX VIa, CLCN4, Osteopontin, ZNF238, SMRT, Big ET-1, NHE6, Rab-3C, PKA-reg (cAMP-dependent), Lingo1, PP1-cat, HMDH, Neurokinin A, UQCR10, NR3A, Cables1, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, StARD4, GRM6, Histone H2, LIPA, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, NPR3, C9orf5, GP-IB alpha, Galpha(i)-specific amine GPCRs, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, CAP1, HSP90 beta, Vinexin, COL25A1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, Guanylate cyclase (alpha-1/beta-1), SYT16, Guanylate cyclase beta, Glycine receptor, Fatty acid-binding protein, HINT, Synaptoporin, SgK223, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, SPSY, COX Va, eIF4A2, ATP5A, Glycine receptor beta chain, CAPZA, RTL1, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, sRAGE, Glyoxalase I, DDX51, Galpha(q)-specific peptide GPCRs, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), TBC1D10C, B-FABP, Patched, TNK1, CHKB-AS1, MEF2, NAPB, HNMT, APRIO, BTBD10, ACSL4, ATF/CREB, RAI1, Hdj-2, LAMP2-C, G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, MRLC, eIF4A, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, ATP6V1B, Kv4.2 channel, PRNP, TMS-1, MPTP complex, STAG3, RHEB2, NKCC1, Neurocalcin delta, HIST2H2BE, PKC-beta1, PDE4A, Calmodulin, LPL, DIRAS2, Apo-2L(TNFSF10), SET1B, PDE11A, FLJ45455, Endophilin A1, STAC2, Activin, Aquaporin 1, C6orf27, Calcyclin, SCOT, Octanoyl-holo-acp, ADHX, ERK1/2, AATC, UGCG, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, HTR2A, MPP7, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, CCK8-GlyArgArg, IMPA1, UFC1, DKK1, SOD1, KIAA1024, PPP4R2, SAP102, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, DBH-AS1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, ATP6AP2, CALB1, Tubulin alpha-4A, Pcdh19, CD166, GAD2, NF-1, NPNT, MRPL3, HXK3, Neuroserpin, COX VIIa-2, 14-3-3, RAGE, 14-3-3 eta, ZCCHC12, SNX10</p> |
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|----|---------------------------------|------|-----------|-----------|-----|---|
| 12 | Central Nervous System Diseases | 9151 | 1.693E-20 | 3.079E-18 | 416 | <p>PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAM, HMGCLL1, Cadherin 8, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, IRF1, ILDR2, MAL2, GLSK, Rab-3B, COX Vic, GAD1, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, HPCA, APJ, ELOVL5, Peroxiredoxin, Activin A, UBL5, Esterase D, Endothelin-1, Trehalase, Neuropeptide K, T-plastin, Nkpd1, BRSK2, UQCRQPC, G-protein beta, KLHL4, LAS1L, ALDR, UQCRH, Rab-6A, Mucin 5B, PSMA5, NDUFAB1, CCK8-Gly, BTBD12, NDUFA1, DNAH1, MRPL1, Lgi4, Pannexin-1, FAM90A1, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, MELC, NPFF receptor 2, NDUFB4, MC4R, NDUFA8, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, Substance P extracellular region, DDX3Y, CNR1, Glycogen phosphorylase, Synaptotagmin IV, PPM1E, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, SCF, SDHB, SLC39A10, DKK3, LUZP2, ANKRD36B, HCN2, Guanylate cyclase alpha, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, LINC00342, D330028D13Rik, Kv3.3, ORP-family, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, LASS6, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, ATG9B, TM2D3, Ephrin-A receptor 5, LAPTM4B, IDUA, CRH receptor 2, SLC2A13, Semaphorin 5A, RPL9, NSF, CaMK IV, CHCHD2, GLRA, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, G-protein gamma, UBE2D1, ZNF70, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, A830006F12Rik, EGF, Pro-CCK, Dynein, axonemal, heavy chains, MMADHC, HIST1H2BN, PKA-reg type II (cAMP-dependent), NELL1, cPKC (conventional), NDUFB1, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, GABA-A receptor alpha-4 subunit, PPID, TRPC, SLC7A5, HTR5A, VDAC 1, C17orf76, WIF1, COX VIa, CLCN4, Osteopontin, SMRT, Big ET-1, NHE6, Rab-3C, M-Ras, PKA-reg (cAMP-dependent), RNF152, Lingo1, PP1-cat, HMDH, Neurokinin A, PDLIM2, UQCR10, GUCY1A3, Clathrin heavy chain, Substance P, AP-3 sigma subunits, StARD4, GRM6, Histone H2, LIPA, MCT1 (SLC16A1),</p> |
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|    |          |      |           |           |     | <p>ARHGAP18, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, LINGO1-AS1, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, CAP1, HSP90 beta, TXNIP (VDUP1), Vinexin, COL25A1, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PANX2, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Glycine receptor, Fatty acid-binding protein, HINT, Synaptoporin, MAML1, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, Glycine receptor beta chain, CAPZA, RTL1, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, sRAGE, SLC25A46, Glyoxalase I, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, MAFbx, SNAP190, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, B-FABP, C17orf72, Patched, TNK1, CHKB-AS1, XK, MEF2, NAPB, ADAR3, HNMT, APRIO, BTBD10, MEK4/7, Peg10, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, LAMP2-C, G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, IDI1, AP-4, MRLC, BMI-1, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, HSPC138, MPTP complex, ENC1, STAG3, RHEB2, NKCC1, Neurocalcin delta, Malin, HIST2H2BE, PKC-beta1, Calmodulin, LPL, DIRAS2, NELL2, Apo-2L(TNFSF10), SET1B, LOXL2, HSPC125, USMG5, Endophilin A1, Activin, Aquaporin 1, NDFIP1, Calcyclin, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ERK1/2, AATC, UGCG, Anks4b, NFIC, CaMK II delta, HSC70, PKC, SSTR2, SUR1, HTR2A, PMM2, MPP7, GS1-124K5.11, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, Protein kinase G, ERK2 (MAPK1), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), TMEM70, PRKAR1A, IGFALS, CCK8-GlyArgArg, UFC1, Nephrocystin-4, DKK1, sKITLG, SSTR1, Guanine deaminase, SOD1, PPP4R2, GSE1, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, DBH-AS1, Galpha(s)-specific peptide GPCRs, ATP5L, ACTR3, OXR1, CALB1, Tubulin alpha-4A, RhoE, Pcdh19, CD166, GAD2, NF-I, MRPL3, Neuroserpin, COX VIIa-2, Midkine, SAMD10, ARP3, PXDN, 14-3-3, RAGE, 14-3-3 eta, SNX10</p> |
| 13 | Dementia | 4320 | 8.626E-20 | 1.449E-17 | 238 | <p>PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, MAL2, Rab-3B, COX VIc, GAD1, PTCH2, N-chimaerin, Peroxiredoxin, UBL5, Endothelin-1, Neuropeptide K, Nkpd1, UQCRQPC, G-protein beta, UQCRH, Rab-6A, PSMA5, NDUFAB1, CCK8-Gly, NDUFA1, PRKAR2B, NPFF receptor 2,</p>   |

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|--|--|--|--|--|---|
|  |  |  |  |  | <p> NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, DDX3Y, CNR1, Synaptotagmin IV, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, Septin 1, PDE, Cystatin C, PPT1, SDHB, DKK3, LUZP2, CCK8, Neuropeptide gamma, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, ORP-family, Tenascin-C, CEACAM, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, Rab-6, TXNRD1, ORP8, AMIGO2, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, TM2D3, Ephrin-A receptor 5, NSF, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein gamma, UBE2D1, Galpha(i)-specific metabotropic glutamate GPCRs, A830006F12Rik, EGF, Pro-CCK, Dynein, axonemal, heavy chains, PKA-reg type II (cAMP-dependent), cPKC (conventional), NDUFB1, Serotonin receptor, CHMP5, GABA-A receptor alpha-4 subunit, PPID, TRPC, HTR5A, VDAC 1, C17orf76, COX VIa, Osteopontin, SMRT, Big ET-1, NHE6, Rab-3C, PKA-reg (cAMP-dependent), PP1-cat, HMDH, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, StARD4, Histone H2, LIPA, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, NCX1, DNAJC12, HCN, Protein kinase G1, CAP1, HSP90 beta, Vinexin, COL25A1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, SYT16, Fatty acid-binding protein, Synaptoporin, MDH1, ASAH, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, sRAGE, Galpha(q)-specific peptide GPCRs, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), B-FABP, Patched, TNK1, MEF2, NAPB, HNMT, APRIO, ACSL4, ATF/CREB, LAMP2-C, Acyl-CoA synthetase, PP2A catalytic, MRLC, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, MPTP complex, STAG3, RHEB2, NKCC1, Neurocalcin delta, HIST2H2BE, PKC-beta1, LPL, DIRAS2, Apo-2L(TNFSF10), Aquaporin 1, Calcyclin, SCOT, Octanoyl-holo-acp, ERK1/2, AATC, UGCG, CaMK II delta, HSC70, PKC, SSTR2, HTR2A, MPP7, ARPP-19, K-cadherin (CDH6), MEF2C, Protein kinase G, ERK2 (MAPK1), DREV1, LISCH7, Ran, OAT, CCK8-GlyArgArg, UFC1, DKK1, SOD1, FSTL5, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, ATP5L, CALB1, Tubulin alpha-4A, CD166, GAD2, Neuroserpin, COX VIIa-2, 14-3-3, RAGE, 14-3-3 eta, SNX10 </p> |
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| 14 | Genetic Diseases, Inborn | 7327 | 1.796E-19 | 2.776E-17 | 349 | <p>PLP1, NPY, PP2A cat (alpha), PRPS1, HSP90, PAK3, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, IRF1, ILDR2, MAL2, COX VIc, GAD1, SMVT, MEGF10, THAP11, PTCH2, N-chimaerin, SUCLG1, Smooth muscle myosin, ELOVL5, Peroxiredoxin, Activin A, Esterase D, Endothelin-1, Neuropeptide K, PSMB5, ARG2, T-plastin, REV-ERBalpha, BRSK2, UQCRQPC, DYNLT3, G-protein beta, UQCRH, Mucin 5B, PSMA5, NDUFAB1, CCK8-Gly, NckAP1, BTBD12, NDUFA1, LSMD1, DNAH1, MCM6, OGFRL1, DCMC, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, MELC, NDUFB4, NDUFA8, Synaptotagmin I, Guanylate cyclase, ARL6, HSP70, Substance P extracellular region, CNR1, Glycogen phosphorylase, Synaptotagmin IV, Synaptotagmin, PRDX3, Thioredoxin, NDUFA4, ATP6V1A (70kD), HSPA4, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, SCF, SDHB, IGSF9B, ANKRD36B, NCKP1 subunit, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, UGT8, Exostosin-like 2, Kv3.3, ORP-family, B3GN6, Tenascin-C, CEACAM, TRPC5, PKC-beta, TCP1-theta, PRDX1, G-protein beta/gamma, NDUFB6, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, FUT2, UQCRB, CPT-1A, S100, TXNRD1, CC188, ORP8, PIMT, TRPV1, PDK3, ZFHX4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, IDUA, V-ATPase E subunit, GRAIL, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, DOK7, SYP, Carbohydrate sulfotransferases, MOCS2(small), Rho GTPase, PDE4, G-protein gamma, UBE2D1, PRPS2, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, EGF, Pro-CCK, SYTC, Dynein, axonemal, heavy chains, BMPR1A, MMADHC, LOC283174, PKA-reg type II (cAMP-dependent), cPKC (conventional), NDUFB1, DLL4, ELOVL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, PYGM, Sp8, ACTR10, MOC2B, WIF1, COX VIa, CLCN4, Osteopontin, SMRT, Big ET-1, CysLT2 receptor, NHE6, PKA-reg (cAMP-dependent), ANT, HMDH, Neurokinin A, PDLIM2, UQCR10, Clathrin heavy chain, Substance P, StARD4, GRM6, Histone H2, LIPA, MCT1 (SLC16A1), CCK5, COPS4, Galpha(q)-specific amine GPCRs, UQCRFS1, Histone H2A, NPR3, C9orf5, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, DNAJC12, HCN, RTEL1-TNFRSF6B, HLF, CAP1, TXNIP (VDUP1), COL25A1, MEGF6, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, SYT16, Fatty acid-binding protein, HINT, MAML1, IZUMO1,</p> |
|----|--------------------------|------|-----------|-----------|-----|--|

|    |                          |      |           |           |     |   |
|----|--------------------------|------|-----------|-----------|-----|---|
|    |                          |      |           |           |     | MDH1, ASAH, GABA-A receptor alpha-3 subunit, DYNL1, SPOCK3, SPSY, COX Va, Tetraspanin-3, ATP5A, Nek8, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCRs, sRAGE, SLC25A46, Glyoxalase I, Galpha(q)-specific peptide GPCRs, ATP6V1C, MAFbx, NDUFA5, Tubulin alpha, Creatine kinase, DSCAML1, MRAP2, B-FABP, Azi1, Patched, TNK1, XK, MEF2, NAPB, HNMT, Sec23, APRIO, SCS-A, MEK4/7, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, CQ107, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, IDI1, MRLC, BMI-1, SNAPs, RNF175, LAMP2, COX VIa-1, YPEL5, ATP6V1B, Kv4.2 channel, PRNP, HSPC138, MPTP complex, RHEB2, NKCC1, Malin, PKC-beta1, PDE4A, LPL, NELL2, SUMO-3, ATP6V1E, Apo-2L(TNFRSF10), LOXL2, NOLA3 (NOP10), HSPC125, USMG5, Activin, Aquaporin 1, NME5, Calcyclin, SCOT, Octanoyl-holo-acp, ERK1/2, AATC, UGCG, NFIC, CaMK II delta, HSC70, PKC, HTR2A, PMM2, SLC25A4, GS1-124K5.11, K-cadherin (CDH6), MEF2C, ERK2 (MAPK1), OAT, MEK4(MAP2K4), TMEM70, IGFALS, CCK8-GlyArgArg, CLCN5, IMPA1, Nephrocystin-4, sKITLG, PRPS, SOD1, TFIIB, SAP102, SPDYE5, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, CLDND1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, ATP6AP2, CALB1, SRm300, Pcdh19, CD166, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, ACOXL, Midkine, SAMD10, ARP3, 14-3-3, RAGE, ATP1beta subunit, CHST6 |
| 15 | Neurocognitive Disorders | 4347 | 1.907E-19 | 2.776E-17 | 238 | PLP1, NPY, FAM3C, PP2A cat (alpha), HSP90, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiotensin 1, Alpha crystallin B, ET-1, MAL2, Rab-3B, COX VIc, GAD1, PTCH2, N-chimaerin, Peroxiredoxin, UBL5, Endothelin-1, Neuropeptide K, Nkpd1, UQCRQPC, G-protein beta, UQCRH, Rab-6A, PSMA5, NDUFAB1, CCK8-Gly, NDUFA1, PRKAR2B, NPFF receptor 2, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, DDX3Y, CNR1, Synaptotagmin IV, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, Septin 1, PDE, Cystatin C, PPT1, SDHB, DKK3, LUZP2, CCK8, Neuropeptide gamma, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, ORP-family, Tenascin-C, CEACAM, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, NDUFB6, SDFR1, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, UQCRB, S100, Rab-6, TXNRD1, ORP8, AMIGO2, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, Rab-3, TM2D3, Ephrin-A receptor 5, NSF, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, G-protein   |

|    |                         |       |           |           |     |  |
|----|-------------------------|-------|-----------|-----------|-----|--|
|    |                         |       |           |           |     | <p>gamma, UBE2D1, Galpha(i)-specific metabotropic glutamate GPCRs, A830006F12Rik, EGF, Pro-CCK, Dynein, axonemal, heavy chains, PKA-reg type II (cAMP-dependent), cPKC (conventional), NDUFB1, Serotonin receptor, CHMP5, GABA-A receptor alpha-4 subunit, PPID, TRPC, HTR5A, VDAC 1, C17orf76, COX VIa, Osteopontin, SMRT, Big ET-1, NHE6, Rab-3C, PKA-reg (cAMP-dependent), PP1-cat, HMDH, Neurokinin A, UQCR10, Clathrin heavy chain, Substance P, StARD4, Histone H2, LIPA, CCK5, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, NCX1, DNAJC12, HCN, Protein kinase G1, CAP1, HSP90 beta, Vinexin, COL25A1, NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, SYT16, Fatty acid-binding protein, Synaptopodin, MDH1, ASAH, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, CAPZA, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, sRAGE, Galpha(q)-specific peptide GPCRs, Histone H2B, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), B-FABP, Patched, TNK1, MEF2, NAPB, HNMT, APRI0, ACSL4, ATF/CREB, LAMP2-C, Acyl-CoA synthetase, PP2A catalytic, MRLC, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, PRNP, MPTP complex, STAG3, RHEB2, NKCC1, Neurocalcin delta, HIST2H2BE, PKC-beta1, LPL, DIRAS2, Apo-2L(TNFSF10), Aquaporin 1, Calcyclin, SCOT, Octanoyl-holo-acp, ERK1/2, AATC, UGCG, CaMK II delta, HSC70, PKC, SSTR2, HTR2A, MPP7, ARPP-19, K-cadherin (CDH6), MEF2C, Protein kinase G, ERK2 (MAPK1), DREV1, LISCH7, Ran, OAT, CCK8-GlyArgArg, UFC1, DKK1, SOD1, FSTL5, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, ATP5L, CALB1, Tubulin alpha-4A, CD166, GAD2, Neuroserpin, COX VIIa-2, 14-3-3, RAGE, 14-3-3 eta, SNX10</p> |
| 16 | Nervous System Diseases | 13323 | 1.685E-17 | 2.300E-15 | 540 | <p>PLP1, Cyclin G, NPY, FAM3C, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, HMGCLL1, Cadherin 8, CPSF1, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, G3BP2, IRF1, ILDR2, MAL2, GLSK, Rab-3B, COX VIc, GAD1, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, SUCLG1, HPCA, APJ, Smooth muscle myosin, ELOVL5, Peroxiredoxin, Activin A, UBL5, Esterase D, Endothelin-1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, T-plastin, Nkpd1, REV-ERBalpha, BRSK2, UQCRQPC, DYNLT3, P2Y11, G-protein beta, KLHL4, LAS1L, ALDR, CRTL1, UQCRH, Rab-6A, Mucin 5B, PSMA5, NDUFAB1, CCK8-Gly, NckAP1, KIAA1276, BTBD12, NDUFA1, DNAH1, MRPL1, Lgi4, Pannexin-1, DCMC, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-</p>   |



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|  |  |  |  |  | <p>lipoyllysine, PRKAR2B, MELC, PLD5, NPFF receptor 2, NDUFB4, MC4R, NDUFA8, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, Substance P extracellular region, DDX3Y, CNR1, Glycogen phosphorylase, Synaptotagmin IV, CITED2, PPM1E, HDBP1, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, LUZP2, ANKRD36B, NCKP1 subunit, HCN2, Guanylate cyclase alpha, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, LINC00342, D330028D13Rik, Kv3.3, ORP-family, B3GN6, LY6G5B, Tenascin-C, HSDL1, CEACAM, TRPC5, PKC-beta, KIS, PAFAH gamma, TCP1-theta, PRDX1, G-protein beta/gamma, NET6(TSPAN13), NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, FUT2, UQCRB, CPT-1A, S100, FAM69A, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, LASS6, PIMT, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, FAM38B, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, SLC2A13, Semaphorin 5A, GRAIL, RPL9, NSF, Tomt, ADAM-TS10, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, MYO15B, DOK7, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, GTPBP3, Lba1, G-protein gamma, UBE2D1, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, A830006F12Rik, Secretogranin V, EGF, ATP5B, Pro-CCK, SYTC, XKR4, Dynein, axonemal, heavy chains, Semaphorin 3E, MMADHC, LOC283174, HIST1H2BN, PKA-reg type II (cAMP-dependent), NELL1, cPKC (conventional), ATP6V1B2, NDUFB1, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, GABA-A receptor alpha-4 subunit, Rab-27B, PPID, TRPC, SLC7A5, HTR5A, Sp8, PDK4, VDAC 1, C17orf76, WIF1, COX VIa, CLCN4, Osteopontin, ZNF238, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, M-Ras, PKA-reg (cAMP-dependent), RNFL152, Lingo1, ANT, PP1-cat, HMDH, Neurokinin A, PDLIM2, UQCR10, GUCY1A3, Clathrin heavy chain, Substance P, AP-3 sigma subunits, PSM10 (Gankyrin), StARD4, GRM6, Histone H2, LIPA, MCT1 (SLC16A1), ARHGAP18, CCK5, COPS4, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors,</p> |
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|  |  |  |  |  | <p>Histone H2A, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, LINGO1-AS1, SLC26A4-AS1, NCX1, DNAJC12, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, CAP1, HSP90 beta, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PANX2, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Glycine receptor, Fatty acid-binding protein, FOXP4, HINT, Synaptoporin, MAML1, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, DYNLT, SPSY, COX Va, ATP5A, Glycine receptor beta chain, CAPZA, RTL1, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPSRs, Cyclin G1, sRAGE, SLC25A46, Glyoxalase I, PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, MAFbx, SNAP190, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, MRAP2, PAP-II, B-FABP, Azi1, C17orf72, Patched, TNK1, CHKB-AS1, XK, MEF2, SLC2A1-AS1, NAPB, ADAR3, PGAM1, HNMT, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, CQ107, DelGIP1, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, GAS41, IDI1, AP-4, MRLC, BMI-1, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, ATP6V1B, Kv4.2 channel, PRNP, HSPC138, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, NKCC1, Neurocalcin delta, Malin, HIST2H2BE, ATP6V0B, PKC-beta1, WDT2, Calmodulin, CENPP, LPL, DIRAS2, NELL2, SUMO-3, Apo-2L(TNFSF10), SET1B, LOXL2, FLJ45455, HSPC125, USMG5, Endophilin A1, Activin, Aquaporin 1, NDFIP1, C6orf27, NME5, Calcyclin, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ERK1/2, CDw52, AATC, UGCG, Anks4b, NFIC, CaMK II delta, HSC70, SLC35A5, PKC, SSTR2, SUR1, HTR2A, PMM2, SLC25A4, MPP7, GS1-124K5.11, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, Protein kinase G, ERK2 (MAPK1), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), TMEM70, PRKAR1A, IGFALS, CCK8-GlyArgArg, CLCN5, IMPA1, UFC1, Nephrocystin-4, DKK1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, KIAA1024, PPP4R2, GSE1, MMP-28, SAP102, FSTL5, SPDYE5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, DBH-AS1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, SRm300, RhoE, Pcdh19, CD166, GAD2, TCP1-epsilon, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, Midkine,</p> |
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|    |                   |       |           |           |     |  |
|----|-------------------|-------|-----------|-----------|-----|--|
|    |                   |       |           |           |     | SAMD10, ARP3, PXDN, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, ZCCHC12, SNX10, CMAS   |
| 17 | Neoplasms by Site | 25424 | 1.093E-15 | 1.404E-13 | 861 | SCAP2, Cyclin G, FBXO45, NPY, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, Alpha crystallin B, TMEM87B, AEBP1, ET-1, G3BP2, RhoN, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, Rab-3B, MAGEH-1, SLC35E2B, COX VIc, SMVT, C1D, MEGF10, THAP11, TINP1, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, LOC284837, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, T-plastin, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, IL-17D, BRSK2, UQCRQPC, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, JWA, ALDR, CRTL1, UQCRH, TMC4, Rab-6A, RGS8, Mucin 5B, SC4MOL, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, KIAA1276, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, OGFRL1, NKIRAS1, DCMC, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, SCRT2, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, CITED2, PPM1E, SLIRP, HDBP1, NUDT4P1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf15, PPT1, SCF, SDHB, MGAT4A, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, VIPR1-AS1, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, Guanylate cyclase alpha, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, Aha1, PTPN18, RGS4, VSIG2, VDAC 3, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SEL1, C13orf37, ORP-family, B3GN6, LY6G5B, Tenascin-C, Myopodin, HSDL1, PP1-cat gamma, |

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|  |  |  |  |  | <p>CEACAM, ODF3, TRPC5, PKC-beta, KIS, PAFAH gamma, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, NET6(TSPAN13), SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, ATP5E, SCRT1, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, LINC02043, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, TMEM45A, ZFH2, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, H41, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, TMEM86B, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALT1, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, Neurexophilin 1, AP complex 2 small (sigma) chain, TMEM39B, ADSS, Rab-27B, mADAMTS5, PPID, TRPC, SLC7A5, HTR5A, PYGM, NOP14-AS1, ACTR10, PDK4, VDAC 1, C17orf76, WIF1, NDRG3, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SLC6A1-AS1, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, M-Ras, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TRP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, HMDH, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, C9orf5, GP-IB alpha,</p> |
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|  |  |  |  |  | <p>DOC1, Galpha(i)-specific amine GPCRs, CCNI2, Stch, DAT1, TRPC4, PMCA1, LINGO1-AS1, Rab-23, NCX1, DNAJC12, SLBP, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, PMS2L3, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GTL3, USP2-AS1, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, BEX2, SPSY, COX Va, Tetraspanin-3, Copine-4, Destrin, eIF4A2, BRK, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), MAFbx, SNAP190, WDR47, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, VIP32, Azi1, NUDT4, DYNLL, Patched, TNK1, XK, MEF2, INCA1, SLC2A1-AS1, NAPB, ADAR3, BICRA, PGAM1, HNMT, TAPBPL, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, F262, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, GAS41, IDI1, SNX7, ARRC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, OAZIN, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, C1orf115, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Quinone oxidoreductase, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, Osrf, SLC16A1-AS1, FAM22A, TM2D2, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Neurocalcin delta, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, SUMO-3, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, NOLA3 (NOP10), HSPC125, USMG5, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, NME5, CLIC4, Calcyclin, FAM186B,</p> |
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|----|---|------|-----------|-----------|-----|---|
|    |   |      |           |           |     | <p>Syntenin 1, SCOT, Octanoyl-holo-acc, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, CDW52, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), ARL5, SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, SULT4A1, MRPL33, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, SLC25A25-AS1, LISCH7, Ran, OAT, MEK4(MAP2K4), CBR3-AS1, DACH2, C14orf2, TMEM70, Mindin, PRKAR1A, IGFALS, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, CLDND1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, Pcdh19, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-1, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, C8orf83, AATBC, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, SNX10, CMAS, TCTE3, CHST6</p> |
| 18 | Congenital, Hereditary, and Neonatal Diseases and Abnormalities | 9068 | 2.913E-15 | 3.533E-13 | 393 | <p>PLP1, Cyclin G, NPY, PP2A cat (alpha), PRPS1, HSP90, PAK3, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, AEBP1, ET-1, G3BP2, IRF1, ILDR2, MAL2, COX VIc, GAD1, SMVT, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, SUCLG1, Smooth muscle myosin, ELOVL5, RNF207, Peroxiredoxin, Activin A, Esterase D, Endothelin-1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, T-plastin, REV-ERBalpha, BRSK2, UQCRQPC, DYNLT3, G-protein beta, ALDR, UQCRH, Mucin 5B, PSMA5, NFKBIL2, NDUFAB1, CCK8-Gly, NckAP1, BTBD12, NDUFA1, LSMD1, DNAH1, Lgi4, MCM6, OGFRL1, DCMC, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, MELC, NDUFB4, MC4R, NDUFA8, Synaptotagmin I, Guanylate cyclase, ARL6, HSP70, Substance P extracellular region, CNR1, Glycogen phosphorylase, Synaptotagmin IV, CITED2, HDBP1, Synaptotagmin, PRDX3, Thioredoxin, NDUFA4, ATP6V1A (70kD), HSPA4, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, SCF, SDHB, IGSF9B, ANKRD36B, NCKP1 subunit, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, 14-3-3</p>   |

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|  |  |  |  |  | <p>beta/alpha, GABA-A receptor alpha-1 subunit, UGT8, Exostosin-like 2, Kv3.3, ORP-family, B3GN6, Tenascin-C, CEACAM, TRPC5, PKC-beta, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, NDUFB6, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, FUT2, UQCRB, CPT-1A, S100, TXNRD1, CC188, ORP8, PIMT, TRPV1, PDK3, ZFHx4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, Rab-3, FAM38B, ZFHx2, IDUA, V-ATPase E subunit, GRAIL, GPR176, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, DOK7, SYP, Carbohydrate sulfotransferases, MOCS2(small), Rho GTPase, PDE4, G-protein gamma, UBE2D1, PRPS2, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, EGF, Pro-CCK, SYTC, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, MMADHC, LOC283174, PKA-reg type II (cAMP-dependent), NELL1, cPKC (conventional), NDUFB1, DLL4, ELOVL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, PYGM, Sp8, ACTR10, MOC2B, WIF1, COX VIa, CLCN4, Osteopontin, SMRT, Big ET-1, CysLT2 receptor, NHE6, M-Ras, PKA-reg (cAMP-dependent), ANT, HMDH, Neurokinin A, PDLIM2, UQCR10, Clathrin heavy chain, Substance P, StARD4, GRM6, Histone H2, LIPA, MCT1 (SLC16A1), CCK5, COPS4, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, Histone H2A, NPR3, C9orf5, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, DNAJC12, HCN, RTEL1-TNFRSF6B, HLF, CAP1, TXNIP (VDUP1), COL25A1, C14orf142, MEGF6, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, FLJ32001, SYT16, Fatty acid-binding protein, PSG3, HINT, MAML1, IZUMO1, MDH1, ASAH, GABA-A receptor alpha-3 subunit, DYNLT, SPOCK3, SPSY, COX Va, Tetraspanin-3, ATP5A, Nek8, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCR, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, Galpha(q)-specific peptide GPCRs, ATP6V1C, Histone H2B, MAFbx, NDUFA5, Tubulin alpha, Creatine kinase, DSCAML1, MRAP2, B-FABP, Azi1, Patched, TNK1, XK, MEF2, SLC2A1-AS1, NAPB, HNMT, Sec23, APRI0, SCS-A, MEK4/7, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, CQ107, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, IDI1, MRLC, BMI-1, SNAPs, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, YPEL5, ATP6V1B, Kv4.2 channel, PRNP, HSPC138, SLC16A1-AS1, MPTP complex, RHEB2, NKCC1, Malin, PKC-beta1, PDE4A, LPL, NELL2, SUMO-3, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10),</p> |
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|----|--|------|-----------|-----------|-----|---|
|    |  |      |           |           |     | HSPC125, USMG5, Activin, Aquaporin 1, NME5, Calcyclin, SCOT, Octanoyl-holo-acp, ZNF517, ERK1/2, AATC, UGCG, NFIC, CaMK II delta, HSC70, PKC, SUR1, HTR2A, PMM2, SLC25A4, GS1-124K5.11, K-cadherin (CDH6), MEF2C, ERK2 (MAPK1), OAT, MEK4(MAP2K4), DACH2, TMEM70, PRKAR1A, IGFALS, CCK8-GlyArgArg, CLCN5, IMPA1, UFC1, Nephrocystin-4, DKK1, sKITLG, PRPS, SOD1, TFIIB, SAP102, SPDYE5, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, PTCHD1, CLDND1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, ATP6AP2, CALB1, SRm300, Pcdh19, CD166, TIP27, DRIL2, TCP1-epsilon, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, Midkine, SAMD10, ARP3, PXDN, 14-3-3, RAGE, ATP1beta subunit, CHST6  |
| 19 | Schizophrenia  | 1615 | 3.534E-15 | 4.060E-13 | 111 | PLP1, NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, MEGF10, Peroxiredoxin, Neuropeptide K, G-protein beta, Importin (karyopherin)-alpha, CCK8-Gly, HSP70, Substance P extracellular region, CNR1, Synaptotagmin, MRLC2, ATP6V1A (70kD), PDE, PPT1, Galpha(q)-specific Class A Orphan/other GPCRs, CCK8, TPH2, Neuropeptide gamma, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, KIS, G-protein beta/gamma, SDFR1, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, FAM69A, PIMT, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, CRH receptor 2, GABA-A receptor beta-2 subunit, SYP, Carbohydrate sulfotransferases, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, GABA-A receptor alpha-4 subunit, ADSS, HTR5A, Neurokinin A, IL3RA, Substance P, CCK5, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Protein kinase G1, NDUFS6, GABA-A receptor alpha-5 subunit, PANX2, Fatty acid-binding protein, MDH1, eIF4A2, ATP5A, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Glyoxalase I, Galpha(q)-specific peptide GPCRs, Tubulin alpha, Creatine kinase, B-FABP, HNMT, APRIO, ACSL4, ATF/CREB, Acyl-CoA synthetase, MRLC, eIF4A, Galpha(s)-specific CRF GPCRs, PRNP, PDE4A, Calmodulin, PDE11A, Endophilin A1, Aquaporin 1, ADHX, ERK1/2, HSC70, PI3K reg class IA (p55-gamma), PKC, HTR2A, SULT4A1, Protein kinase G, ERK2 (MAPK1), OAT, CCK8-GlyArgArg, SOD1, SAP102, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, CALB1, GAD2, COX VIIa-2, 14-3-3, 14-3-3 eta |
| 20 | Schizophrenia Spectrum and Other Psychotic Disorders | 1675 | 6.978E-15 | 7.616E-13 | 113 | PLP1, NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, MEGF10, Smooth muscle myosin, Peroxiredoxin, Neuropeptide K, G-protein beta, Importin (karyopherin)-alpha,  |



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|----|--------------------|-------|-----------|-----------|-----|---|
|    |                    |       |           |           |     | CCK8-Gly, HSP70, Substance P extracellular region, CNR1, Synaptotagmin, MRLC2, ATP6V1A (70kD), PDE, PPT1, Galpha(q)-specific Class A Orphan/other GPCRs, CCK8, TPH2, Neuropeptide gamma, RGS4, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, KIS, G-protein beta/gamma, SDFR1, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, FAM69A, PIMT, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, CRH receptor 2, GABA-A receptor beta-2 subunit, SYP, Carbohydrate sulfotransferases, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, GABA-A receptor alpha-4 subunit, ADSS, HTR5A, Neurokinin A, IL3RA, Substance P, CCK5, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Protein kinase G1, NDUFS6, GABA-A receptor alpha-5 subunit, PANX2, Fatty acid-binding protein, MDH1, GABA-A receptor alpha-3 subunit, eIF4A2, ATP5A, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Glyoxalase I, Galpha(q)-specific peptide GPCRs, Tubulin alpha, Creatine kinase, B-FABP, HNMT, APRIO, ACSL4, ATF/CREB, Acyl-CoA synthetase, MRLC, eIF4A, Galpha(s)-specific CRF GPCRs, PRNP, PDE4A, Calmodulin, PDE11A, Endophilin A1, Aquaporin 1, ADHX, ERK1/2, HSC70, PI3K reg class IA (p55-gamma), PKC, HTR2A, SULT4A1, Protein kinase G, ERK2 (MAPK1), OAT, CCK8-GlyArgArg, SOD1, SAP102, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, CALB1, GAD2, COX VIIa-2, 14-3-3, 14-3-3 eta |
| 21 | Thoracic Neoplasms | 20326 | 9.992E-15 | 1.039E-12 | 733 | SCAP2, Cyclin G, FBXO45, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, TMEM87B, AEBP1, ET-1, G3BP2, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, Rab-3B, MAGEH-1, COX VIc, SMVT, C1D, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, BRSK2, UQCRQPC, DYNLT3, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, ALDR, CRTL1, UQCRH, Rab-6A, RGS8, Mucin 5B, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1,  |

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|  |  |  |  |  | <p>MCM6, NKIRAS1, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, Substance P extracellular region, DDX3Y, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, PPM1E, HDBP1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, CNIH2, Tcf15, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, VSIG2, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SEL1, ORP-family, B3GN6, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, KIS, PRDX1, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFHx4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, CECR2, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4,</p> |
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|--|--|--|--|--|---|
|  |  |  |  |  | <p>Serotonin receptor, CHMP5, Neurexophilin 1, TMEM39B, ADSS, Rab-27B, mADAMTS5, TRPC, SLC7A5, HTR5A, ACTR10, PDK4, VDAC 1, WIF1, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, Tetraspanin-3, Copine-4, Destrin, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, NAPB, ADAR3, BICRA, HNMT, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, eIF2S1, Glutaredoxin, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, C1orf115, KAD6, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, Osrf, FAM22A, DNAJA2, TMS-1, MPTP complex, ENC1,</p> |
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|    |                             |       |           |           |     |  |
|----|-----------------------------|-------|-----------|-----------|-----|--|
|    |                             |       |           |           |     | STAG3, RHEB2, CENPL, NKCC1, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10), HSPC125, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, SLC25A4, MPP7, CCDC57, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, PRKAR1A, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CMAS, CHST6 |
| 22 | Respiratory Tract Neoplasms | 20404 | 1.071E-14 | 1.062E-12 | 735 | SCAP2, Cyclin G, FBXO45, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, TMEM87B, AEBP1, ET-1, G3BP2, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, Rab-3B, MAGEH-1, COX VIc, SMVT, C1D, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, BRSK2, UQCRCPC, DYNLT3, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, ALDR, CRTL1, UQCRH, Rab-6A, RGS8, Mucin 5B, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C,   |

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|  |  |  |  |  | <p>TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, OGFRL1, NKIRAS1, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, Substance P extracellular region, DDX3Y, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, PPM1E, HDBP1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, CNIH2, Tcf15, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, VSIG2, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SELI, ORP-family, B3GN6, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, KIS, PRDX1, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC</p> |
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|  |  |  |  |  | <p>(conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, Serotonin receptor, CHMP5, Neurexophilin 1, TMEM39B, ADSS, Rab-27B, mADAMTS5, TRPC, SLC7A5, HTR5A, ACTR10, PDK4, VDAC 1, WIF1, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, Tetraspanin-3, Copine-4, Destrin, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPSRs, STARD7, B3GT2, Cyclin G1, sRAGE, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, INCA1, NAPB, ADAR3, BICRA, HNMT, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, eIF2S1, Glutaredoxin, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, C1orf115, KAD6, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2,</p> |
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|    |                |       |           |           |     | <p>PRNP, Osr1, FAM22A, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10), HSPC125, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, SLC25A4, MPP7, CCDC57, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-1, MRPL3, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CMAS, CHST6</p> |
| 23 | Lung Neoplasms | 20304 | 1.289E-14 | 1.224E-12 | 732 | <p>SCAP2, Cyclin G, FBXO45, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, TMEM87B, AEBP1, ET-1, G3BP2, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, Rab-3B, MAGEH-1, COX VIc, SMVT, C1D, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, BRSK2, UQCRQPC, DYNLT3, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, ALDR, CRTL1, UQCRH, Rab-6A, RGS8, Mucin 5B, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L</p>  |

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|  |  |  |  |  | <p>(CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, NKIRAS1, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, Substance P extracellular region, DDX3Y, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, PPM1E, HDBP1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, CNIH2, Tcf5, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, VSI2, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SEL1, ORP-family, B3GN6, LY6G5B, Tenascin-C, CEACAM, TRPC5, PKC-beta, KIS, PRDX1, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, CECR2, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-</p> |
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|  |  |  |  |  | <p>dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, Serotonin receptor, CHMP5, Neurexophilin 1, TMEM39B, ADSS, Rab-27B, mADAMTS5, TRPC, SLC7A5, HTR5A, ACTR10, PDK4, VDAC 1, WIF1, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, Tetraspanin-3, Copine-4, Destrin, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCR, STARD7, B3GT2, Cyclin G1, sRAGE, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, NAPB, ADAR3, BICRA, HNMT, Sec23, APRI0, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, eIF2S1, Glutaredoxin, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, C1orf115, KAD6, TMEM87A, YPEL5, TSNARE1,</p> |
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|----|------------------------|------|-----------|-----------|-----|--|
|    |                        |      |           |           |     | ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, Osr, FAM22A, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10), HSPC125, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, SLC25A4, MPP7, CCDC57, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CMAS, CHST6 |
| 24 | Panic Disorder         | 127  | 1.912E-14 | 1.739E-12 | 26  | NPY, Galpha(s)-specific nucleotide-like GPCRs, GAD1, G-protein beta, CCK8-Gly, PDE, CCK8, TPH2, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, CRH receptor 2, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, Pro-CCK, Serotonin receptor, CCK5, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Glyoxalase I, Galpha(q)-specific peptide GPCRs, ATF/CREB, Galpha(s)-specific CRF GPCRs, HTR2A, CCK8-GlyArgArg   |
| 25 | Neuromuscular Diseases | 4369 | 4.173E-14 | 3.644E-12 | 221 | PLP1, NPY, PP2A cat (alpha), PRPS1, HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, IRF1, ILDR2, COX VIc, GAD1, MEGF10, PTCH2, Tubulin alpha 1A, SUCLG1, ELOVL5, Peroxiredoxin, Activin A, Endothelin-1, Neuropeptide K, T-plastin, DYNLT3, G-protein beta, LAS1L, ALDR, PSMA5, NDUFAB1, NckAP1, NDUFA1, MGF, MELC, NDUFB4,  |

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|    |                      |       |           |           |     | <p>NDUFA8, Synaptotagmin I, COCH, HSP70, Substance P extracellular region, DnaJB9, Synaptotagmin, CNTN1 (F3), Thioredoxin, NDUFA4, HSPA4, PDE, Cystatin C, SCF, SDHB, IGSF9B, DKK3, NCKP1 subunit, GPR124, TPH2, Neuropeptide gamma, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, ORP-family, Tenascin-C, PKC-beta, KIS, TCP1-theta, PRDX1, G-protein beta/gamma, NDUFB6, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, TXNRD1, TRPV1, PDK3, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, FAM38B, IDUA, RPL9, CHCHD2, GLRA, DKK2, GABA-A receptor beta-2 subunit, DOK7, Rho GTPase, PDE4, G-protein gamma, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, ATP5B, SYTC, Dynein, axonemal, heavy chains, LOC283174, NELL1, cPKC (conventional), NDUFB1, PSMA1, Serotonin receptor, PDK4, WIF1, COX VIa, Osteopontin, SMRT, Big ET-1, PKA-reg (cAMP-dependent), ANT, Neurokinin A, Substance P, Histone H2, MCT1 (SLC16A1), ARHGAP18, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, NCX1, HSP90 beta, MEGF6, NDUFS6, Activin beta A, CDK5, Glycine receptor, Fatty acid-binding protein, HINT, MDH1, ASAH, DYNLT, COX Va, Glycine receptor beta chain, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, MAFbx, NDUFA5, Tubulin alpha, Creatine kinase, DSCAML1, B-FABP, Azi1, Patched, MEF2, ADAR3, HNMT, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, ATF/CREB, GLGB, RAI1, G-protein gamma 3, Hdj-2, CQ107, LAMP2-C, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, MRLC, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, PRNP, MPTP complex, PKC-beta1, Calmodulin, Apo-2L(TNFSF10), HSPC125, Activin, Aquaporin 1, NME5, Calcyclin, Octanoyl-holo-acp, KCRS, ERK1/2, AATC, UGCG, HSC70, PKC, SUR1, HTR2A, SLC25A4, MEF2C, ERK2 (MAPK1), MEK4(MAP2K4), TMEM70, PRKAR1A, IGFALS, IMPA1, DKK1, sKITLG, PRPS, SOD1, TFIIB, CALM2, PI3K reg class IA, CALB1, Tubulin alpha-4A, GAD2, TCP1-epsilon, NF-I, HXK3, COX VIIa-2, Midkine, SAMD10, PXDN, 14-3-3, RAGE, ATP1beta subunit, SNX10</p> |
| 26 | Urogenital Neoplasms | 20725 | 1.062E-13 | 8.914E-12 | 740 | <p>Cyclin G, FBXO45, NPY, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, AEBP1, ET-1, G3BP2, RhoN, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, Rab-3B, MAGEH-1, SLC35E2B, COX VIc, SMVT, C1D, MEGF10, THAP11, TINP1, PTCH2, N-</p>   |

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|  |  |  |  |  | <p>chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, LOC284837, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, IL-17D, BRSK2, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, JWA, ALDR, CRTL1, TMC4, Mucin 5B, SC4MOL, PSMA5, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, NckAP1, KIAA1276, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, DNAH1, MRPL1, Lgi4, GPR137C, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, OGFRL1, NKIRAS1, DCMC, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, UNRIP, NDUFA8, Synaptotagmin I, COCH, Guanylate cyclase, KCNK2, HSP70, CCDC4, SCRT2, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, PPM1E, SLIRP, HDBP1, NUDT4P1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf15, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, Aha1, PTPN18, RGS4, VSIG2, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, SEL1, C13orf37, ORP-family, B3GN6, Tenascin-C, Myopodin, HSDL1, CEACAM, ODF3, TRPC5, PKC-beta, KIS, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, NET6(TSPAN13), SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, Aldose reductase, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, H41, ZNF433,</p> |
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|  |  |  |  |  | <p>CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, cPKC (conventional), ATP6V1B2, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, Apelin, Neurexophilin 1, TMEM39B, ADSS, mADAMTS5, TRPC, SLC7A5, HTR5A, NOP14-AS1, ACTR10, PDK4, VDAC 1, C17orf76, WIF1, NDRG3, SUCB1, ATP6V1H, Osteopontin, Slp5, SLC6A1-AS1, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, CHAMP, PKA-reg (cAMP-dependent), TRP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, KLHL35, MCT1 (SLC16A1), ARHGAP18, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, CCNI2, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, PSG3, HINT, ENPP4, MAML1, KIAA0143, SOHLH1, IZUMO1, FLJ37078, GTL3, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, TMEM74, TM6SF1, SPSY, COX Va, Tetraspanin-3, Copine-4, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCR, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), SNAP190, WDR47, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, PAP-II, B-FABP, VIP32, Azi1, NUDT4, DYNLL, Patched,</p> |
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|    |           |       |           |           |     | <p>TNK1, XK, MEF2, SLC2A1-AS1, NAPB, ADAR3, BICRA, PGAM1, TAPBPL, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, GAS41, IDI1, ARRDC2, AP-4, MRLC, eIF4A, BMI-1, SNAPs, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, Osrif, FAM22A, TM2D2, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Neurocalcin delta, Malin, C1orf59, PKC-beta1, PDE4A, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, SUMO-3, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, NOLA3 (NOP10), Endophilin A1, STAC2, Activin, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, NME5, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, SULT4A1, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, SLC25A25-AS1, LISCH7, Ran, OAT, MEK4(MAP2K4), CBR3-AS1, DACH2, C14orf2, TMEM70, PRKAR1A, IGFALS, CLCN5, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, AggreCANase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, Galpha(s)-specific peptide GPCRs, TSPAN19, TCP1-alpha, ACTR3, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, Pcdh19, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, Midkine, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), C8orf83, AATBC, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, TCTE3, CHST6</p> |
| 27 | Neoplasms | 26016 | 1.234E-13 | 9.978E-12 | 869 | <p>SCAP2, PLP1, Cyclin G, FBXO45, NPY, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, LINC01410, Semaphorin 3C,</p>  |

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|  |  |  |  |  | <p>Alpha crystallin B, TMEM87B, AEBP1, ET-1, G3BP2, RhoN, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, Rab-3B, MAGEH-1, SLC35E2B, COX VIc, GAD1, SMVT, C1D, MEGF10, THAP11, TINP1, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, LOC284837, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, T-plastin, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, IL-17D, BRSK2, UQCRQPC, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, JWA, ALDR, CRTL1, UQCRH, TMC4, Rab-6A, RGS8, Mucin 5B, SC4MOL, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, KIAA1276, GLIPR, BTBD12, NDUFA1, CDC18L (CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, OGFRL1, NKIRAS1, DCMC, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, SCRT2, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, CITED2, PPM1E, SLIRP, HDBP1, NUDT4P1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf15, PPT1, SCF, SDHB, MGAT4A, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, VIPR1-AS1, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, Guanylate cyclase alpha, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, Aha1, PTPN18, RGS4, VSIG2, VDAC 3, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SEL1, C13orf37, ORP-family, B3GN6, LY6G5B, Tenascin-C, Myopodin, HSDL1, PP1-cat gamma, CEACAM, ODF3, TRPC5, PKC-beta, KIS, PAFAH gamma, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, NET6(TSPAN13), SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, ATP5E, SCRT1, CPT-1A, S100, Rab-6,</p> |
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|  |  |  |  |  | <p>TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, LINC02043, FLJ38984, LASS6, PIMT, TRPV1, PRR12, PDK3, ZFHX4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, TMEM45A, ZFHX2, Ephrin-A receptor 5, LAPT4M4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, H41, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, TMEM86B, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALT1, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, Neurexophilin 1, AP complex 2 small (sigma) chain, TMEM39B, ADSS, Rab-27B, mADAMTS5, PPID, TRPC, SLC7A5, HTR5A, PYGM, NOP14-AS1, ACTR10, PDK4, VDAC 1, C17orf76, WIF1, NDRG3, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SLC6A1-AS1, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, M-Ras, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TRP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, HMDH, Neurokinin A, PDLIM2, NR3A, GUCY1A3, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCERS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, CCNI2, Stch, DAT1, TRPC4, PMCA1, LINGO1-AS1, Rab-23, NCX1, DNAJ12, SLBP, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, PMS2L3, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L,</p> |
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|  |  |  |  |  | <p>PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, Sgk223, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GTL3, USP2-AS1, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, BEX2, SPSY, COX Va, Tetraspanin-3, Copine-4, Dextrin, eIF4A2, BRK, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), MAFbx, SNAP190, WDR47, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, VIP32, Azi1, NUDT4, DYNLL, Patched, TNK1, XK, MEF2, INCA1, SLC2A1-AS1, NAPB, ADAR3, BICRA, PGAM1, HNMT, TAPBPL, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, F262, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, GAS41, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, OAZIN, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, C1orf115, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Quinone oxidoreductase, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, Osrf, SLC16A1-AS1, FAM22A, TM2D2, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Neurocalcin delta, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, SUMO-3, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, KLHL2, NOLA3 (NOP10), HSPC125, USMG5, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, NME5, CLIC4, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, CDW52, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), ARL5, SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate</p> |
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|    |               |       |           |           |     | Cyclase 1, soluble, APEL13, MEF2C, SULT4A1, MRPL33, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, SLC25A25-AS1, LISCH7, Ran, OAT, MEK4(MAP2K4), CBR3-AS1, DACH2, C14orf2, TMEM70, Mindin, PRKAR1A, IGFALS, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, CLDND1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, Pcdh19, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, C8orf83, AATBC, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, SNX10, CMAS, TCTE3, CHST6  |
| 28 | Lung Diseases | 20966 | 4.896E-13 | 3.817E-11 | 744 | SCAP2, Cyclin G, FBXO45, NPY, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, TMEM87B, AEBP1, ET-1, G3BP2, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, Rab-3B, MAGEH-1, COX VIc, SMVT, C1D, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, IL-17D, BRSK2, UQCRQPC, DYNLT3, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, ALDR, CRTL1, UQCRH, Rab-6A, RGS8, Mucin 5B, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, LSMD1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, NKIRAS1, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, Substance P extracellular region, DDX3Y, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, |

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|  |  |  |  |  | <p>Tim17, PPM1E, HDBP1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf15, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, VSIG2, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SELI, ORP-family, B3GN6, LY6G5B, Tenascin-C, PP1-cat gamma, CEACAM, TRPC5, PKC-beta, KIS, PRDX1, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, CECR2, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, Serotonin receptor, CHMP5, Neurexophilin 1, TMEM39B, ADSS, Rab-27B, mADAMTS5, TRPC, SLC7A5, HTR5A, ACTR10, PDK4, VDAC 1, WIF1, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TReP-132,</p> |
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|  |  |  |  |  | <p>RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), STARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, COX Va, Tetraspanin-3, Copine-4, Dextrin, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCR, STARD7, B3GT2, Cyclin G1, sRAGE, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, MAFbx, SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, NAPB, ADAR3, BICRA, HNMT, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, OAZIN, eIF2S1, Glutaredoxin, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, C1orf115, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, Osrf, FAM22A, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10), HSPC125,</p> |
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|----|----------------------------|-------|-----------|-----------|-----|--|
|    |                            |       |           |           |     | Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, SLC25A4, MPP7, CCDC57, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, PRKAR1A, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CMAS, CHST6 |
| 29 | Respiratory Tract Diseases | 21141 | 7.524E-13 | 5.664E-11 | 748 | SCAP2, Cyclin G, FBXO45, NPY, C13orf36, FAM3C, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, ZNF34, Semaphorin 3C, TMEM87B, AEBP1, ET-1, G3BP2, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, Rab-3B, MAGEH-1, COX VIc, SMVT, C1D, MEGF10, THAP11, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, REV-ERBalpha, IL-17D, BRSK2, UQCRQPC, DYNLT3, UBXD3, G-protein beta, KLHL4, LAS1L, SC5D, ALDR, CRTLL1, UQCRH, Rab-6A, RGS8, Mucin 5B, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, LSM1, DNAH1, MRPL1, Lgi4, GPR137C, TTLL9, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, MCM6, OGFRL1, NKIRAS1, HPCAL4, RHBDL3, PSD2, FAM90A1, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1,   |

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|  |  |  |  |  | <p>NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Synaptotagmin I, COCH, Guanylate cyclase, ARL6, KCNK2, HSP70, CCDC4, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, PPM1E, HDBP1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf15, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, LOC441108, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, RGS4, VSIG2, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SELI, ORP-family, B3GN6, LY6G5B, Tenascin-C, PP1-cat gamma, CEACAM, TRPC5, PKC-beta, KIS, PRDX1, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, LASS6, TRPV1, PRR12, PDK3, ZFHX4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, CHCHD2, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, RBM18, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, HKR4, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, Serotonin receptor, CHMP5, Neurexophilin 1, TMEM39B, ADSS, Rab-27B, mADAMTS5, TRPC,</p> |
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|  |  |  |  |  | <p>SLC7A5, HTR5A, ACTR10, PDK4, VDAC 1, WIF1, COX VIa, SUCB1, ATP6V1H, Osteopontin, ATP5G3, Slp5, ABHD10, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, SMIM43_132332, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), STARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, TMEM14A, LRRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, RTEL1-TNFRSF6B, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, MEGF6, NDUFS6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, Tmem134, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, MORN1, SOHLH1, IZUMO1, FLJ37078, TOM22, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, SLC16A13, Atg101, TMEM74, TM6SF1, COX Va, Tetraspanin-3, Copine-4, Destrin, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, MAFbx, SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, INCA1, NAPB, ADAR3, BICRA, HNMT, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, LOC440248, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, LAMP2-C, FN14(TNFRSF12A), Trim45, RSL24D1, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, C9orf106, SNAPs, OAZIN, eIF2S1, Glutaredoxin, RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, C1orf115, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, Osrf, FAM22A, DNAJA2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2,</p> |
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|    |                            |       |           |           |     | <p>CENPL, NKCC1, Malin, C1orf59, HIST2H2BE, ATP6V0B, PKC-beta1, PDE4A, WDT2, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), LOXL2, PDE11A, NOLA3 (NOP10), HSPC125, Endophilin A1, STAC2, Activin, SIPAR, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, Carboxypeptidase M, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, PI3K reg class IA (p55-gamma), SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, SLC25A4, MPP7, CCDC57, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, PRKAR1A, CCK8-GlyArgArg, CLCN5, STX16-NPEPL1, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, GPR22, TSPAN19, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, CD166, TIP27, GAD2, DRIL2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, MRPL3, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, FLJ37464, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARM CX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CMAS, CHST6</p> |
| 30 | Female Urogenital Diseases | 19660 | 1.715E-12 | 1.248E-10 | 706 | <p>Cyclin G, FBXO45, NPY, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, LINC01410, Semaphorin 3C, Alpha crystallin B, AEBP1, ET-1, G3BP2, RhoN, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, MAGEH-1, SLC35E2B, SMVT, C1D, MEGF10, THAP11, TINP1, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, LOC284837, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, IL-17D, BRSK2, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, JWA, ALDR, CRTL1, TMC4, Mucin 5B, SC4MOL, PSMA5, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, DNAH1, MRPL1, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1,</p>   |



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|  |  |  |  |  | <p>OGFRL1, NKIRAS1, DCMC, PSD2, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, Synaptotagmin I, COCH, Guanylate cyclase, KCNK2, HSP70, CCDC4, SCRT2, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, Glycogen phosphorylase, Synaptotagmin IV, Tim17, CITED2, PPM1E, SLIRP, NUDT4P1, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, Tcf5, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, Aha1, PTPN18, RGS4, VSIG2, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, SEL1, C13orf37, ORP-family, B3GN6, Tenascin-C, Myopodin, HSDL1, CEACAM, TRPC5, PKC-beta, KIS, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, Aldose reductase, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, H41, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, Secretogranin V, EGF, GlyRA2, ATP5B, NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, LOC283174, HIST1H2BN, Neurexophilin 2, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, cPKC (conventional), ATP6V1B2, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, Neurexophilin 1, TMEM39B, ADSS,</p> |
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|  |  |  |  |  | <p>mADAMTS5, TRPC, SLC7A5, HTR5A, NOP14-AS1, ACTR10, PDK4, VDAC 1, WIF1, SUCB1, ATP6V1H, Osteopontin, Slp5, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, HMDH, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CalDAG-GEFII, Histone H2, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, LRR51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, CCNI2, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, MEGF6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, PSG3, HINT, MAML1, KIAA0143, SOHLH1, IZUMO1, FLJ37078, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNLT, TMEM74, TM6SF1, SPSY, COX Va, Tetraspanin-3, Copine-4, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), SNAP190, WDR47, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, PAP-II, B-FABP, VIP32, Azi1, NUDT4, Patched, TNK1, XK, MEF2, SLC2A1-AS1, NAPB, ADAR3, BICRA, PGAM1, TAPBPL, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, GAS41, IDI1, ARRDC2, MRLC, eIF4A, BMI-1, SNAPs, eIF2S1, Glutaredoxin, Galpha(s)-specific CRF GPCRs, LAMP2, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, Osrif, FAM22A, TM2D2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Neurocalcin delta, Malin, C1orf59, PKC-beta1, PDE4A, ZSCAN1, CAB39L, Calmodulin, GENPP, LPL, DIRAS2,</p> |
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|    |  |       |           |           |     | NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, NOLA3 (NOP10), Endophilin A1, STAC2, Activin, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, NME5, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, C14orf2, TMEM70, CCK8-GlyArgArg, CLCN5, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIIB, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, Galpha(s)-specific peptide GPCRs, TSPAN19, TCP1-alpha, ACTR3, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, Pcdh19, CD166, TIP27, GAD2, PGM2L1, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, ACOXL, Midkine, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARM CX3, ACCN3 (ASIC3), C8orf83, AATBC, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CHST6 |
| 31 | Female Urogenital Diseases and Pregnancy Complications | 19809 | 1.865E-12 | 1.314E-10 | 710 | Cyclin G, FBXO45, NPY, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, ZYG11B, CPSF1, ZNF575, ARP6, CXorf57, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, LINC01410, Semaphorin 3C, Alpha crystallin B, AEBP1, ET-1, G3BP2, RhoN, MBD6, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, MAGEH-1, SLC35E2B, SMVT, C1D, MEGF10, THAP11, TINP1, PTCH2, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, LOC284837, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, UBL5, D630023F18Rik, Esterase D, Endothelin-1, SULT1A1, Trehalase, Neuropeptide K, PSMB5, AP-1 gamma subunits, ARG2, DUOX1, Nkpd1, NETO2, GHITM, IL-17D, BRSK2, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, JWA, ALDR, CRTL1, TMC4, Mucin 5B, SC4MOL, PSMA5, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, DNAH1, MRPL1, MOBKL1A, AP1G2, ZNF707, LOC153328, Pannexin-1, OGFRL1, NKIRAS1, DCMC, PSD2, NIPSNAP3A, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, PLD5, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, Synaptotagmin I, COCH, Guanylate cyclase, KCNK2, HSP70,  |

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|  |  |  |  |  | <p>CCDC4, SCRT2, Substance P extracellular region, DDX3Y, CNR1, MAPBPIP, Glycogen phosphorylase, Synaptotagmin IV, Tim17, CITED2, PPM1E, SLIRP, NUDT4P1, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, ZMAT1, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, Tcf5, PPT1, SCF, SDHB, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, OAF, ATP5G, C6orf168, CCK8, GPR124, TPH2, Neuropeptide gamma, KAL1, RAB39B, Aha1, PTPN18, RGS4, VSIG2, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, D330028D13Rik, GUCY1B1, FLRT3, Exostosin-like 2, SEL1, C13orf37, ORP-family, B3GN6, Tenascin-C, Myopodin, HSDL1, CEACAM, TRPC5, PKC-beta, KIS, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, TORC1, KLHL13, UQCRB, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, FLJ38984, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, PRRG1, Aldose reductase, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, TMEM45A, Ephrin-A receptor 5, LAPT4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, NSF, Tomt, ADAM-TS10, GPR176, FAM102B, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, FBXO2, H41, ZNF433, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, Rho GTPase, PDE4, GTPBP3, Tensin 2, Lba1, G-protein gamma, UBE2D1, OSGIN2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, Secretogranin V, EGF, GlyRA2, ATP5B, NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, LOC283174, HIST1H2BN, Neurexophilin 2, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, cPKC (conventional), ATP6V1B2, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, Apelin, Neurexophilin 1, TMEM39B, ADSS, mADAMTS5, TRPC, SLC7A5, HTR5A, PYGM, NOP14-AS1, ACTR10, PDK4, VDAC 1, WIF1, SUCB1, ATP6V1H, Osteopontin, Slp5, SMRT, Big ET-1, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, CHAMP, PKA-reg (cAMP-dependent), TReP-132,</p> |
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|  |  |  |  |  | <p>RNF152, Lingo1, ANT, PP1-cat, CFA74, HMDH, Neurokinin A, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, PSMD10 (Gankyrin), StARD4, GRM6, CHTF18, CaIDAG-GEFII, Histone H2, KLHL35, MCT1 (SLC16A1), ARHGAP18, CCK5, LRRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, C9orf5, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, CCNI2, Stch, TRPC4, PMCA1, NCX1, DNAJC12, SLBP, HCN, Protein kinase G1, HLF, BDH, C1orf113, LENG8, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, MEGF6, Calponin-1, Activin beta A, BRMS1L, Zeta-sarcoglycan, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, PSG3, HINT, MAML1, KIAA0143, SOHLH1, IZUMO1, FLJ37078, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, ISOC1, DYNL1, TMEM74, TM6SF1, SPSY, COX Va, Tetraspanin-3, Copine-4, eIF4A2, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), SNAP190, WDR47, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, PAP-II, B-FABP, VIP32, Azi1, NUDT4, Patched, TNK1, XK, MEF2, SLC2A1-AS1, NAPB, ADAR3, BICRA, PGAM1, TAPBPL, Sec23, APRIO, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, RAI1, G-protein gamma 3, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, GAS41, IDI1, ARRDC2, MRLC, eIF4A, BMI-1, SNAPs, eIF2S1, Glutaredoxin, Galpha(s)-specific CRF GPCRs, LAMP2, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, Osrf, FAM22A, TM2D2, TMS-1, MPTP complex, ENC1, STAG3, RHEB2, CENPL, NKCC1, Neurocalcin delta, Malin, C1orf59, PKC-beta1, PDE4A, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, NOLA3 (NOP10), Endophilin A1, STAC2, Activin, C1orf43, Aquaporin 1, NDFIP1, KCTD16, C6orf27, NME5, Calcyclin, FAM186B, Syntenin 1, SCOT, Octanoyl-</p> |
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|    |                        |      |           |           |     | <p>holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, HSC70, SLC35A5, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, APEL13, MEF2C, SULT4A1, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, C14orf2, TMEM70, CCK8-GlyArgArg, CLCN5, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, Galpha(s)-specific peptide GPCRs, TSPAN19, TCP1-alpha, ACTR3, OXR1, CALB1, Tubulin alpha-4A, CALML6, SRm300, RhoE, Pcdh19, CD166, TIP27, GAD2, ACYL2, PGM2L1, NF-I, MRPL3, HXK3, Neuroserpin, COX VIIa-2, DROXL, Midkine, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), C8orf83, AATBC, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1, ZCCHC12, CHST6</p>   |
| 32 | Parkinsonian Disorders | 2001 | 6.878E-12 | 4.692E-10 | 119 | <p>NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, ET-1, GAD1, HPCA, Endothelin-1, Neuropeptide K, ALDR, PSMA5, NDUFAB1, CCK8-Gly, NDUFA1, MGF, NDUFB4, NDUFA8, HSP70, Substance P extracellular region, CNR1, PPM1E, DnaJB9, Synaptotagmin, CNTN1 (F3), NDUFA4, HSPA4, Cystatin C, SCF, SDHB, SLC39A10, DKK3, CCK8, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, LY6G5B, NDUFB6, SUR, NDUFS4, Galpha(i)-specific peptide GPCRs, S100, AMIGO2, LASS6, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, NDUFB3, IDUA, SLC2A13, Semaphorin 5A, CHCHD2, FBXO2, SYP, EGF, Pro-CCK, HIST1H2BN, NDUFB1, AP3S1, Serotonin receptor, TRPC, VDAC 1, Osteopontin, Big ET-1, Lingo1, Neurokinin A, Substance P, AP-3 sigma subunits, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, Histone H2A, Galpha(i)-specific amine GPCRs, DNAJC12, NDUFS6, CDK5, PAK, FLJ32001, Fatty acid-binding protein, CAPZA, Galpha(i)-specific cannabis GPCRs, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NDUFA5, B-FABP, MEF2, HNMT, APRIO, ATF/CREB, RAI1, LAMP2-C, Galpha(s)-specific CRF GPCRs, LAMP2, YPEL5, PRNP, MPTP complex, HIST2H2BE, Endophilin A1, Aquaporin 1, NDFIP1, Syntenin 1, Octanoyl-holo-acp, ADHX, HSC70, SUR1, HTR2A, CCK8-GlyArgArg, sKITLG, SOD1, FOXP1/2/4 proteins, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, ARP3, 14-3-3, RAGE, 14-3-3 eta</p> |

|    |                           |      |           |           |     |  |
|----|---------------------------|------|-----------|-----------|-----|--|
| 33 | Neurologic Manifestations | 4790 | 1.390E-11 | 9.196E-10 | 227 | <p>PLP1, NPY, PRPS1, PAK3, PAM, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, TMEM87B, ET-1, ILDR2, GAD1, THAP11, Tubulin alpha 1A, HPCA, APJ, Smooth muscle myosin, ELOVL5, Peroxiredoxin, Endothelin-1, Neuropeptide K, PSMB5, BRSK2, G-protein beta, KLHL4, LAS1L, PSMA5, CCK8-Gly, NDUFA1, DCMC, PSD2, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, NPFF receptor 2, Synaptotagmin I, COCH, Guanylate cyclase, HSP70, Substance P extracellular region, CNR1, Glycogen phosphorylase, HDBP1, Synaptotagmin, PRDX3, ATP6V1A (70kD), HSPA4, Dynein, axonemal, light chains, PDE, Cystatin C, SCF, SDHB, SLC39A10, ANKRD36B, HCN2, CCK8, TPH2, Neuropeptide gamma, RAB39B, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, ORP-family, Tenascin-C, CEACAM, TRPC5, PAFAH gamma, PRDX1, G-protein beta/gamma, SUR, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, TRPV1, PRR12, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, Rab-3, FAM38B, IP3KA, GRAIL, NSF, Tomt, GLRA, GABA-A receptor beta-2 subunit, DOK7, SYP, Rho GTPase, PDE4, GTPBP3, G-protein gamma, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, EGF, Pro-CCK, Dynein, axonemal, heavy chains, Semaphorin 3E, PKA-reg type II (cAMP-dependent), cPKC (conventional), ATP6V1B2, DLL4, ELOVL4, PSMA1, Serotonin receptor, Apelin, Rab-27B, TRPC, CLCN4, ZNF238, SMRT, Big ET-1, NHE6, PKA-reg (cAMP-dependent), Lingo1, ANT, Neurokinin A, PDLIM2, Clathrin heavy chain, Substance P, PSMD10 (Gankyrin), StARD4, Histone H2, CCK5, COPS4, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, SLC26A4-AS1, HCN, HLF, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PAK, Glycine receptor, Fatty acid-binding protein, HINT, MAML1, ASAH, SPSY, Glycine receptor beta chain, RTL1, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, SLC25A46, PDH beta, Galpha(q)-specific peptide GPCRs, MAFbx, Tubulin alpha, DSCAML1, TBC1D10C, MRAP2, B-FABP, Patched, MEF2, PGAM1, HNMT, APRI0, ACSL4, ATF/CREB, GLGB, ODP2, RAI1, Hdj-2, DelGIP1, LAMP2-C, Acyl-CoA synthetase, IDI1, BMI-1, eIF2S1, Galpha(s)-specific CRF GPCRs, LAMP2, ATP6V1B, PRNP, TMS-1, MPTP complex, RHEB2, NKCC1, SUMO-3, SET1B, FLJ45455, Aquaporin 1, C6orf27, ERK1/2, AATC, NFIC, SLC35A5, PKC, SUR1, HTR2A, PMM2, SLC25A4, APEL13, MEF2C, ERK2 (MAPK1), Ran, IGFALS, CCK8-GlyArgArg, CLCN5, sKITLG, PRPS, SOD1, KIAA1024, MMP-28, SAP102, SPDYE5, FOXP1/2/4 proteins, PTCHD1, DBH-AS1, TCP1-alpha, ATP6AP2, Tubulin</p> |
|----|---------------------------|------|-----------|-----------|-----|--|

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|----|-------------------|------|-----------|-----------|-----|---|
|    |                   |      |           |           |     | alpha-4A, SRm300, Pcdh19, GAD2, TCP1-epsilon, NF-I, Neuroserpin, ACOXL, 14-3-3, ACCN3 (ASIC3), ZCCHC12  |
| 34 | Anxiety Disorders | 254  | 2.261E-11 | 1.452E-09 | 32  | NPY, Galpha(s)-specific nucleotide-like GPCRs, GAD1, G-protein beta, CCK8-Gly, CNR1, PDE, CCK8, TPH2, G-protein beta/gamma, FLJ35776, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, CRH receptor 2, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, Pro-CCK, Serotonin receptor, CCK5, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Glycine receptor, GABA-A receptor alpha-3 subunit, Glycine receptor beta chain, Galpha(i)-specific cannabis GPSRs, Glyoxalase I, Galpha(q)-specific peptide GPCRs, ATF/CREB, Galpha(s)-specific CRF GPCRs, HTR2A, CCK8-GlyArgArg   |
| 35 | Synucleinopathies | 2054 | 3.643E-11 | 2.272E-09 | 119 | NPY, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, ET-1, GAD1, HPCA, Endothelin-1, Neuropeptide K, BRSK2, ALDR, PSMA5, NDUFAB1, CCK8-Gly, NDUFA1, MGF, NDUFB4, NDUFA8, HSP70, Substance P extracellular region, CNR1, DnaJB9, Synaptotagmin, CNTN1 (F3), NDUFA4, HSPA4, Cystatin C, SCF, SDHB, DKK3, CCK8, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, LY6G5B, NDUFB6, SUR, NDUFS4, Galpha(i)-specific peptide GPCRs, S100, AMIGO2, LASS6, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, NDUFB3, IDUA, SLC2A13, Semaphorin 5A, CHCHD2, FBXO2, SYP, EGF, Pro-CCK, HIST1H2BN, NDUFB1, AP3S1, Serotonin receptor, TRPC, VDAC 1, Osteopontin, Big ET-1, Lingo1, Neurokinin A, Substance P, AP-3 sigma subunits, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, DNAJC12, NDUFS6, CDK5, FLJ32001, Fatty acid-binding protein, CAPZA, Galpha(i)-specific cannabis GPSRs, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NDUFA5, B-FABP, MEF2, HNMT, APRIO, ATF/CREB, RAI1, LAMP2-C, Galpha(s)-specific CRF GPCRs, LAMP2, YPEL5, PRNP, MPTP complex, HIST2H2BE, Endophilin A1, Aquaporin 1, NDFIP1, Syntenin 1, Octanoyl-holo-acp, ADHX, HSC70, SUR1, HTR2A, GS1-124K5.11, CCK8-GlyArgArg, sKITLG, SOD1, FOXP1/2/4 proteins, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, ARP3, 14-3-3, RAGE, 14-3-3 eta |
| 36 | Mood Disorders    | 1270 | 1.750E-10 | 1.061E-08 | 83  | NPY, HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, ELOVL5, Neuropeptide K, REV-ERBalpha, G-protein beta, Importin (karyopherin)-alpha, CCK8-Gly, KCNK2, HSP70, Substance P extracellular region, CNR1, Synaptotagmin IV,  |



|    |          |      |           |           |     |   |
|----|----------|------|-----------|-----------|-----|---|
|    |          |      |           |           |     | Synaptotagmin, PDE, CCK8, TPH2, Neuropeptide gamma, RGS4, GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, S100, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, CRH receptor 2, SYP, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, Pro-CCK, Dynein, axonemal, heavy chains, cPKC (conventional), Serotonin receptor, Rab-27B, TRPC, Neurokinin A, NR3A, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, Histone H2A, NPR3, Galpha(i)-specific amine GPCRs, Protein kinase G1, GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, PKC-beta2, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Glyoxalase I, Galpha(q)-specific peptide GPCRs, BTBD10, ACSL4, ATF/CREB, G-protein beta-4, Acyl-CoA synthetase, Galpha(s)-specific CRF GPCRs, PKC-beta1, PDE4A, Apo-2L(TNFSF10), PDE11A, ERK1/2, CaMK II delta, PKC, HTR2A, Protein kinase G, ERK2 (MAPK1), CCK8-GlyArgArg, SOD1, SAP102, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, COX VIIa-2  |
| 37 | Epilepsy | 1751 | 1.849E-10 | 1.091E-08 | 104 | HSP90, Galpha(s)-specific nucleotide-like GPCRs, GAD1, Neuropeptide K, G-protein beta, Mucin 5B, NDUFA1, Lgi4, Pannexin-1, MC4R, Synaptotagmin I, HSP70, Substance P extracellular region, Synaptotagmin, ATP6V1A (70kD), HSPA4, Cystatin C, PPT1, SDHB, HCN2, Neuropeptide gamma, KAL1, GABA-A receptor alpha-1 subunit, ORP-family, Tenascin-C, PKC-beta, G-protein beta/gamma, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, TXNRD1, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, CRH receptor 2, NSF, GLRA, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, Galpha(i)-specific metabotropic glutamate GPCRs, cPKC (conventional), Serotonin receptor, Apelin, GABA-A receptor alpha-4 subunit, CLCN4, NHE6, Neurokinin A, Substance P, Histone H2, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Histone H2A, Galpha(i)-specific amine GPCRs, Stch, NCX1, HCN, GABA-A receptor alpha-5 subunit, PANX2, Glycine receptor, Fatty acid-binding protein, Glycine receptor beta chain, PKC-beta2, Calcineurin A (catalytic), sRAGE, Galpha(q)-specific peptide GPCRs, SNAP190, CHKB-AS1, MEF2, NAPP, APRI0, ATF/CREB, SNAPs, eIF2S1, Galpha(s)-specific CRF GPCRs, PRNP, RHEB2, NKCC1, Malin, PKC-beta1, SET1B, Aquaporin 1, ERK1/2, HSC70, PKC, SSTR2, HTR2A, APEL13, MEF2C, ERK2 (MAPK1), SSTR1, SOD1, PPP4R2, PI3K reg class IA, PTCHD1, Galpha(s)-specific peptide GPCRs, ACTR3, Pcdh19, GAD2, Neuroserpin, ARP3, 14-3-3, RAGE |

|    |                     |      |           |           |     |   |
|----|---------------------|------|-----------|-----------|-----|---|
| 38 | Parkinson Disease   | 1876 | 2.298E-10 | 1.320E-08 | 109 | Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, GAD1, HPCA, Neuropeptide K, ALDR, PSMA5, NDUFAB1, CCK8-Gly, NDUFA1, MGF, NDUFB4, NDUFA8, HSP70, Substance P extracellular region, CNR1, DnaJB9, Synaptotagmin, NDUFA4, HSPA4, Cystatin C, SCF, SDHB, CCK8, Neuropeptide gamma, RAB39B, 14-3-3 beta/alpha, LY6G5B, NDUFB6, SUR, NDUFS4, Galpha(i)-specific peptide GPCRs, S100, AMIGO2, LASS6, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, NDUFB3, IDUA, SLC2A13, Semaphorin 5A, CHCHD2, FBXO2, SYP, EGF, Pro-CCK, HIST1H2BN, NDUFB1, AP3S1, Serotonin receptor, TRPC, VDAC 1, Osteopontin, Lingo1, Neurokinin A, Substance P, AP-3 sigma subunits, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, Histone H2A, Galpha(i)-specific amine GPCRs, DNAJC12, NDUFS6, CDK5, FLJ32001, Fatty acid-binding protein, CAPZA, Galpha(i)-specific cannabis GPCR, sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NDUFA5, B-FABP, MEF2, HNMT, APRIO, ATF/CREB, RAI1, LAMP2-C, Galpha(s)-specific CRF GPCRs, LAMP2, YPEL5, PRNP, MPTP complex, HIST2H2BE, Endophilin A1, Aquaporin 1, NDFIP1, Syntenin 1, Octanoyl-holo-acyl-CoA synthetase, ADHX, HSC70, SUR1, HTR2A, CCK8-GlyArgArg, sKITLG, SOD1, FOXP1/2/4 proteins, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, ARP3, 14-3-3, RAGE, 14-3-3 eta |
| 39 | Depressive Disorder | 1214 | 2.595E-10 | 1.453E-08 | 80  | NPY, HSP90, PAM, GLSK, GAD1, ELOVL5, Neuropeptide K, REV-ERBalpha, G-protein beta, Importin (karyopherin)-alpha, CCK8-Gly, KCNK2, HSP70, Substance P extracellular region, CNR1, Synaptotagmin IV, Synaptotagmin, PDE, CCK8, TPH2, Neuropeptide gamma, RGS4, GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, S100, COX VIIa, CRH receptor 2, SYP, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, Pro-CCK, Dynein, axonemal, heavy chains, cPKC (conventional), Serotonin receptor, Rab-27B, TRPC, Neurokinin A, NR3A, Substance P, Histone H2, CCK5, Galpha(q)-specific amine GPCRs, Histone H2A, NPR3, Galpha(i)-specific amine GPCRs, Protein kinase G1, GABA-A receptor alpha-5 subunit, GABA-A receptor alpha-3 subunit, PKC-beta2, Galpha(i)-specific cannabis GPCR, Glyoxalase I, Galpha(q)-specific peptide GPCRs, BTBD10, ACSL4, ATF/CREB, G-protein beta-4, Acyl-CoA synthetase, Galpha(s)-specific CRF GPCRs, PKC-beta1, PDE4A, Apo-2L(TNFSF10), PDE11A, ERK1/2, CaMK II delta, PKC, HTR2A, Protein kinase G, ERK2 (MAPK1), CCK8-GlyArgArg, SOD1, SAP102, PI3K reg class IA, DBH-AS1, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, COX VIIa-2   |

|    |                      |      |           |           |     |   |
|----|----------------------|------|-----------|-----------|-----|---|
| 40 | Spinal Cord Diseases | 2384 | 8.295E-10 | 4.527E-08 | 128 | <p>PP2A cat (alpha), HSP90, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, IRF1, COX VIc, GAD1, THAP11, Tubulin alpha 1A, ELOVL5, Peroxiredoxin, T-plastin, BRSK2, G-protein beta, LAS1L, PSMA5, NDUFAB1, NDUFA1, MELC, NDUFB4, NDUFA8, Synaptotagmin I, HSP70, DnaJB9, Synaptotagmin, NDUFA4, HSPA4, Cystatin C, SDHB, ANKRD36B, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, Kv3.3, PKC-beta, G-protein beta/gamma, NDUFB6, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, TXNRD1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, NDUFB3, IDUA, RPL9, CHCHD2, GABA-A receptor beta-2 subunit, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, NELL1, cPKC (conventional), NDUFB1, ELOVL4, PSMA1, Serotonin receptor, TRPC, COX VIa, Osteopontin, SMRT, PKA-reg (cAMP-dependent), PDLIM2, Histone H2, ARHGAP18, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, NCX1, HLF, NDUFS6, CDK5, Glycine receptor, Fatty acid-binding protein, HINT, COX Va, Glycine receptor beta chain, CAPZA, PKC-beta2, Calcineurin A (catalytic), sRAGE, SLC25A46, Galpha(q)-specific peptide GPCRs, MAFbx, NDUFA5, Tubulin alpha, Creatine kinase, MEF2, ADAR3, HNMT, APRIO, BTBD10, Peg10, ATF/CREB, RAI1, LAMP2-C, G-protein beta-4, Acyl-CoA synthetase, PP2A catalytic, LAMP2, COX VIa-1, PRNP, PKC-beta1, Apo-2L(TNFSF10), Aquaporin 1, Calyculin, Octanoyl-holo-acp, KCRS, UGCG, NFIC, HSC70, PKC, GS1-124K5.11, MEF2C, PRKAR1A, DKK1, SOD1, Tubulin alpha-4A, GAD2, NF-I, COX VIIa-2, Midkine, SAMD10, 14-3-3, RAGE, SNX10</p> |
| 41 | Epileptic Syndromes  | 1187 | 1.163E-09 | 6.194E-08 | 77  | <p>HSP90, Galpha(s)-specific nucleotide-like GPCRs, GAD1, Neuropeptide K, G-protein beta, Mucin 5B, NDUFA1, Lgi4, Pannexin-1, MC4R, Synaptotagmin I, HSP70, Substance P extracellular region, Synaptotagmin, ATP6V1A (70kD), HSPA4, PPT1, SDHB, Neuropeptide gamma, GABA-A receptor alpha-1 subunit, ORP-family, Tenascin-C, PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, TXNRD1, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, CRH receptor 2, NSF, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, Galpha(i)-specific metabotropic glutamate GPCRs, cPKC (conventional), Serotonin receptor, Apelin, Neukinin A, Substance P, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, HCN, GABA-A receptor alpha-5 subunit, PANX2, PKC-beta2, Calcineurin A (catalytic), Galpha(q)-specific peptide GPCRs, SNAP190, CHKB-AS1, MEF2, NAPB, APRIO, ATF/CREB, SNAPs, eIF2S1, Galpha(s)-</p>  |

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|----|--------------------|------|-----------|-----------|-----|--|
|    |                    |      |           |           |     | specific CRF GPCRs, PRNP, NKCC1, Malin, PKC-beta1, Aquaporin 1, HSC70, PKC, SSTR2, HTR2A, APEL13, MEF2C, SOD1, PPP4R2, PI3K reg class IA, PTCHD1, Galpha(s)-specific peptide GPCRs, Pcdh19, Neuroserpin  |
| 42 | Metabolic Diseases | 6085 | 1.779E-09 | 8.899E-08 | 264 | SCAP2, PLP1, NPY, PP2A cat (alpha), PRPS1, HSP90, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, ET-1, IRF1, ILDR2, GLSK, COX VIc, GAD1, SMVT, Tubulin alpha 1A, ELOVL5, RNF207, Peroxiredoxin, UBL5, Esterase D, Endothelin-1, Neuropeptide K, T-plastin, G-protein beta, ALDR, PSMA5, NDUFAB1, NDUFA1, MCM6, DCMC, MGF, PDH E2 subunit N6-lipoyllysine, PRKAR2B, MELC, NDUFB4, MC4R, NDUFA8, Synaptotagmin I, HSP70, Substance P extracellular region, DDX3Y, CNR1, Glycogen phosphorylase, DnaJB9, Synaptotagmin, Thioredoxin, NDUFA4, HSPA4, PDE, Cystatin C, PPT1, SCF, SDHB, DKK3, Galpha(q)-specific Class A Orphan/other GPCRs, TPH2, Neuropeptide gamma, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, UGT8, ORP-family, CEACAM, PKC-beta, TCP1-theta, PRDX1, G-protein beta/gamma, NDUFB6, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, FUT2, UQCRB, CPT-1A, S100, TXNRD1, VWA2, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, Aldose reductase, NDUFB3, ATG9B, FAM38B, IDUA, CRH receptor 2, CaMK IV, CHCHD2, GABA-A receptor beta-2 subunit, SYP, MOCS2(small), Rho GTPase, PDE4, GTPBP3, G-protein gamma, UBE2D1, PRPS2, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, ChREBP, A830006F12Rik, EGF, Dynein, axonemal, heavy chains, BMPR1A, MMADHC, PKA-reg type II (cAMP-dependent), NELL1, cPKC (conventional), NDUFB1, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, Neurexophilin 1, AP complex 2 small (sigma) chain, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, PYGM, MOC2B, PDK4, COX VIa, CLCN4, ATP6V1H, Osteopontin, Big ET-1, PKA-reg (cAMP-dependent), ANT, HMDH, Neurokinin A, TCP1-delta, Substance P, AP-3 sigma subunits, CalDAG-GEFII, Histone H2, LIPA, MCT1 (SLC16A1), ARHGAP18, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, NCX1, DNAJC12, HLF, TXNIP (VDUP1), NDUFS6, GABA-A receptor alpha-5 subunit, CDK5, PAK, Fatty acid-binding protein, ASAH, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, Selenoprotein P, CAPZA, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCR, sRAGE, SLC25A46, Glyoxalase I, Galpha(q)-specific peptide GPCRs, ATP6V1C, MAFbx, |

|    |                                   |      |           |           |     |   |
|----|-----------------------------------|------|-----------|-----------|-----|---|
|    |                                   |      |           |           |     | NDUFA5, Tubulin alpha, Creatine kinase, Patched, MEF2, SLC2A1-AS1, ADAR3, HNMT, APRI0, BTBD10, Peg10, ACSL4, CEACAM1, ATF/CREB, GLGB, ODP2, RAI1, LAMP2-C, FEM1B, Acyl-CoA synthetase, PP2A catalytic, IDI1, MRLC, BMI-1, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, ATP6V1B, Protein kinase G 2, PRNP, HSPC138, SLC16A1-AS1, MPTP complex, RHEB2, PKC-beta1, LPL, SUMO-3, Apo-2L(TNFSF10), LOXL2, HSPC125, USMG5, Activin, Aquaporin 1, Calcyclin, SCOT, Octanoyl-holo-acp, KCRS, ERK1/2, AATC, UGCG, HSC70, PKC, SUR1, HTR2A, PMM2, SLC25A4, APEL13, MEF2C, Protein kinase G, ERK2 (MAPK1), SLC25A25-AS1, CBR3-AS1, TMEM70, PRKAR1A, CLCN5, DKK1, sKITLG, PRPS, SOD1, MAP1, RPESP, FOXP1/2/4 proteins, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, CALB1, Tubulin alpha-4A, TIP27, GAD2, COX VIIa-2, Midkine, SAMD10, IRS6(DOK5), PXDN, 14-3-3, RAGE, ATP1beta subunit, SNX10         |
| 43 | Craniomandibular Disorders        | 32   | 1.794E-09 | 8.899E-08 | 11  | Neuropeptide K, Substance P extracellular region, Neuropeptide gamma, Serotonin receptor, Neurokinin A, Substance P, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, ERK1/2, HTR2A, ERK2 (MAPK1)  |
| 44 | Temporomandibular Joint Disorders | 32   | 1.794E-09 | 8.899E-08 | 11  | Neuropeptide K, Substance P extracellular region, Neuropeptide gamma, Serotonin receptor, Neurokinin A, Substance P, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, ERK1/2, HTR2A, ERK2 (MAPK1)  |
| 45 | Borderline Personality Disorder   | 19   | 1.857E-09 | 9.009E-08 | 9   | PKC-beta, cPKC (conventional), Serotonin receptor, Galpha(q)-specific amine GPCRs, PKC-beta2, Galpha(q)-specific peptide GPCRs, PKC-beta1, PKC, HTR2A   |
| 46 | Behavior and Behavior Mechanisms  | 1741 | 2.526E-09 | 1.169E-07 | 100 | PAK3, NPEPL1, Galpha(s)-specific nucleotide-like GPCRs, ILDR2, GLSK, BRSK2, G-protein beta, LAS1L, CCK8-Gly, DCMC, PRKAR2B, Synaptotagmin I, HSP70, CNR1, Glycogen phosphorylase, Synaptotagmin IV, HDBP1, Synaptotagmin, ATP6V1A (70kD), PDE, HCN2, CCK8, TPH2, RAB39B, GABA-A receptor alpha-1 subunit, TUSC3, TRPC5, PAFAH gamma, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, PRR12, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, Pro-CCK, PKA-reg type II (cAMP-dependent), cPKC (conventional), ATP6V1B2, DLL4, Serotonin receptor, Rab-27B, TRPC, CLCN4, ZNF238, NHE6, PKA-reg (cAMP-dependent), Lingo1, Clathrin heavy chain, CCK5, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, GP-IB alpha, Galpha(i)- |

|    |                               |     |           |           |    |   |
|----|-------------------------------|-----|-----------|-----------|----|---|
|    |                               |     |           |           |    | specific amine GPCRs, HCN, GABA-A receptor alpha-5 subunit, CDK5, PAK, Glycine receptor, SPSY, Glycine receptor beta chain, RTL1, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, TBC1D10C, Patched, MEF2, HNMT, ACSL4, ATF/CREB, Hdj-2, Acyl-CoA synthetase, Galpha(s)-specific CRF GPCRs, ATP6V1B, TMS-1, RHEB2, SET1B, FLJ45455, C6orf27, AATC, SLC35A5, PKC, HTR2A, MEF2C, CCK8-GlyArgArg, KIAA1024, SAP102, FOXP1/2/4 proteins, ATP6AP2, Pcdh19, NF-I, 14-3-3, ZCCHC12  |
| 47 | Personality Disorders         | 33  | 2.615E-09 | 1.169E-07 | 11 | TPH2, PKC-beta, cPKC (conventional), Serotonin receptor, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, PKC-beta2, Galpha(q)-specific peptide GPCRs, PKC-beta1, PKC, HTR2A   |
| 48 | Bipolar and Related Disorders | 903 | 2.624E-09 | 1.169E-07 | 63 | NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, GAD1, REV-ERBalpha, G-protein beta, Synaptotagmin I, HSP70, CNR1, Synaptotagmin, PDE, TPH2, RGS4, GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, FAM69A, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, CRH receptor 2, GLRA, SYP, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, cPKC (conventional), Serotonin receptor, TRPC, SMRT, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Protein kinase G1, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, PKC-beta2, Galpha(i)-specific cannabis GPCR, Glyoxalase I, Galpha(q)-specific peptide GPCRs, APRIO, ATF/CREB, SNAPs, Galpha(s)-specific CRF GPCRs, PRNP, PKC-beta1, PDE4A, Apo-2L(TNFSF10), PDE11A, ERK1/2, PKC, HTR2A, Protein kinase G, ERK2 (MAPK1), IMPA1, SOD1, SAP102, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, COX VIIa-2 |
| 49 | Bipolar Disorder              | 903 | 2.624E-09 | 1.169E-07 | 63 | NPY, HSP90, Galpha(s)-specific nucleotide-like GPCRs, GAD1, REV-ERBalpha, G-protein beta, Synaptotagmin I, HSP70, CNR1, Synaptotagmin, PDE, TPH2, RGS4, GABA-A receptor alpha-1 subunit, PKC-beta, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, S100, FAM69A, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, CRH receptor 2, GLRA, SYP, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, cPKC (conventional), Serotonin receptor, TRPC, SMRT, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, Protein kinase G1, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, PKC-beta2, Galpha(i)-specific cannabis GPCR, Glyoxalase I, Galpha(q)-specific peptide GPCRs, APRIO, ATF/CREB, SNAPs, Galpha(s)-   |

|    |                          |       |           |           |     |  |
|----|--------------------------|-------|-----------|-----------|-----|--|
|    |                          |       |           |           |     | specific CRF GPCRs, PRNP, PKC-beta1, PDE4A, Apo-2L(TNFSF10), PDE11A, ERK1/2, PKC, HTR2A, Protein kinase G, ERK2 (MAPK1), IMPA1, SOD1, SAP102, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, CALB1, GAD2, COX VIIa-2   |
| 50 | Genital Diseases, Female | 15572 | 2.767E-09 | 1.208E-07 | 571 | Cyclin G, FBXO45, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, CPSF1, ARP6, CXorf57, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, LINC01410, Semaphorin 3C, Alpha crystallin B, AEBP1, G3BP2, RhoN, MBD6, IRF1, FILIP, ZnT-2, MAGEH-1, SMVT, MEGF10, THAP11, TINP1, PTCH2, Tubulin alpha 1A, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, GLB1B2, RNF207, Peroxiredoxin, Activin A, D630023F18Rik, Esterase D, SULT1A1, PSMB5, AP-1 gamma subunits, ARG2, DUOX1, NETO2, GHITM, IL-17D, BRSK2, DYNLT3, P2Y11, UBXD3, G-protein beta, KLHL4, LAS1L, JWA, CRTL1, Mucin 5B, SC4MOL, PSMA5, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, CCK8-Gly, NckAP1, GLIPR, BTBD12, CDC18L (CDC6), ANKRD50, DNAH1, MOBKL1A, AP1G2, ZNF707, Pannexin-1, OGFRL1, NKIRAS1, PSD2, NIPSNAP3A, MGF, TIP47, PRKAR2B, MELC, NPFF receptor 2, NDUFB4, UNRIP, NDUFA8, Synaptotagmin I, COCH, Guanylate cyclase, KCNK2, HSP70, CCDC4, DDX3Y, MAPBP1P, Glycogen phosphorylase, CITED2, PPM1E, NUDT4P1, DnaJB9, Synaptotagmin, CNTN1 (F3), Thioredoxin, ZMAT1, ATP6V1A (70kD), HSPA4, JMJ3D, Septin 1, PDE, Cystatin C, Tcf15, PPT1, SCF, SDHB, IGSF9B, DKK3, Karyopherin alpha 2, LUZP2, PNMAL1, NCKP1 subunit, TM9SF2, HCN2, D123, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, C6orf168, CCK8, GPR124, TPH2, KAL1, RAB39B, PTPN18, RGS4, VSIG2, TUSC3, UGT8, GUCY1B1, SELI, C13orf37, ORP-family, Tenascin-C, HSDL1, CEACAM, TRPC5, PKC-beta, KIS, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, VBP-1, TORC1, KLHL13, CPT-1A, S100, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, TRPV1, PRR12, PDK3, ZFH4, Galpha(q)-specific nucleotide-like GPCRs, ATP6V1C1, PRRG1, Aldose reductase, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, APOL3, Ephrin-A receptor 5, LAPTM4B, IDUA, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, NSF, Tomt, ADAM-TS10, GPR176, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, ZNF433, CECR2, SYP, Carbohydrate sulfotransferases, LACTB2, Rho GTPase, PDE4, Lba1, G-protein gamma, OSGIN2, PRPS2, ZNF70, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor |

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|  |  |  |  |  | <p>4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, Secretogranin V, EGF, GlyRA2, ATP5B, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, LOC283174, HIST1H2BN, Neurexophilin 2, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, cPKC (conventional), ATP6V1B2, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, Neurexophilin 1, TMEM39B, ADSS, mADAMTS5, TRPC, SLC7A5, HTR5A, NOP14-AS1, ACTR10, PDK4, VDAC 1, WIF1, SUCB1, ATP6V1H, Osteopontin, Slp5, SMRT, CysLT2 receptor, NHE6, Rab-3C, KCY, CREB4, PC4, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, ANT, CFA74, HMDH, PDLIM2, NR3A, KLHDC4, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, AP-3 sigma subunits, PSMD10 (Gankyrin), StARD4, GRM6, CalDAG-GEFII, Histone H2, MCT1 (SLC16A1), ARHGAP18, CCK5, LRRCS1, Galpha(q)-specific amine GPCRs, UQCRFS1, Maestro, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, DOC1, Galpha(i)-specific amine GPCRs, Stch, TRPC4, PMCA1, NCX1, SLBP, HCN, BDH, C1orf113, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, C14orf142, MEGF6, Calponin-1, Activin beta A, BRMS1L, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), FLJ32001, SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, PSG3, HINT, MAML1, KIAA0143, SOHLH1, IZUMO1, FLJ37078, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, DYNLT, TMEM74, TM6SF1, SPSY, COX Va, Copine-4, eIF4A2, Glycine receptor beta chain, Nek8, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, PKC-beta2, Calcineurin A (catalytic), TOP1MT, Galpha(i)-specific cannabis GPCRs, STARD7, B3GT2, Cyclin G1, sRAGE, SLC25A46, DDX51, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), SNAP190, WDR47, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, PAP-II, VIP32, Azi1, NUDT4, Patched, TNK1, XK, MEF2, NAPB, ADAR3, PGAM1, TAPBPL, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, CEACAM1, RANBP6, ATF/CREB, GLGB, RAI1, Hdj-2, LAMP2-C, FN14(TNFRSF12A), Trim45, C3orf59, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, SULT1A1 isoform 1, CAPZA2, IDI1, ARRDC2, MRLC, eIF4A, BMI-1, SNAPs, eIF2S1, Glutaredoxin, LAMP2, KAD6, TMEM87A, TSNARE1, ATP6V1B, Kv4.2 channel, PKD1L1, Protein kinase G 2, FAM22A, TM2D2, TMS-1, MPTP complex, STAG3, RHEB2, NKCC1, C1orf59, PKC-</p> |
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|--|--|--|--|--|---|
|  |  |  |  |  | <p>beta1, PDE4A, ZSCAN1, CAB39L, Calmodulin, CENPP, LPL, NELL2, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, NOLA3 (NOP10), Endophilin A1, STAC2, Activin, C1orf43, Aquaporin 1, NDFIP1, FAM186B, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ZNF517, ERK1/2, AATC, UGCG, SLC29A4, Anks4b, NFIC, HSC70, PKC, SSTR2, SUR1, ABTB1, C19orf55, HTR2A, PMM2, SLC25A4, MPP7, ATP1B3, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), DACH2, CCK8-GlyArgArg, CLCN5, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, sKITLG, SSTR1, PRPS, SOD1, TFIIB, KIAA1024, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, EVI2A, MAP1, RPESP, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, Galpha(s)-specific peptide GPCRs, TSPAN19, TCP1-alpha, ACTR3, OXR1, Tubulin alpha-4A, CALML6, SRm300, Pcdh19, CD166, TIP27, GAD2, PGM2L1, NF-I, MRPL3, HXK3, Neuroserpin, Midkine, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), C8orf83, RAGE, ATP1beta subunit, Myospryn, Glutaredoxin 1, CHST6</p> |
|--|--|--|--|--|---|

Table A14. Top 50 KCL BrainBank Diseases by Biomarkers enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| # | Term Name                | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names  |
|---|--------------------------|-----------|-----------|------------------------|-------------------|--|
| 1 | COVID-19                 | 882       | 1.599E-25 | 1.491E-22              | 65                | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |
| 2 | Pneumonia, Viral         | 882       | 1.599E-25 | 1.491E-22              | 65                | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |
| 3 | Coronaviridae Infections | 903       | 5.926E-25 | 2.209E-22              | 65                | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |

|   |                        |     |           |           |    |   |
|---|------------------------|-----|-----------|-----------|----|---|
| 4 | Coronavirus Infections | 903 | 5.926E-25 | 2.209E-22 | 65 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |
| 5 | Nidovirales Infections | 903 | 5.926E-25 | 2.209E-22 | 65 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |
| 6 | Pneumonia              | 950 | 9.705E-24 | 3.015E-21 | 65 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), HGF, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, C4b, WNT, beta-MSH, KVD16, HLAC |

|    |  |      |           |           |    |  |
|----|--|------|-----------|-----------|----|--|
| 7  | Respiratory Tract Infections                       | 1482 | 1.143E-22 | 3.043E-20 | 80 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), HGF, MxB, KV139, GSTs, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, PLA2, CD44, C4, ACTH, MHC Class I alpha chain, Ficolin, RSAD2, CD44 soluble, alpha-MSH, IGKC, DCPS, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), ALDOB, proACTH, SOD3 (EC-SOD), POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, NALP3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, RXR, IFI44, CD44 (EXT), Galpha(s)-specific peptide GPCRs, C4b, WNT, beta-MSH, KVD16, HLAC, LIRB |
| 8  | Alstrom Syndrome                                   | 40   | 2.427E-22 | 5.395E-20 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH   |
| 9  | Sensation  | 74   | 2.605E-22 | 5.395E-20 | 22 | CLIP, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, ACES, beta-MSH   |
| 10 | Musculoskeletal and Neural Physiological Phenomena | 177  | 3.215E-22 | 5.992E-20 | 30 | CLIP, ACTH, alpha-MSH, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, MC4R, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, gamma-LPH, ACTH 1-17, P2Y1, DA-alphaMSH, gamma2-MSH, gamma3-MSH, Galpha(s)-specific peptide GPCRs, ACES, beta-MSH, CART   |
| 11 | Nervous System Physiological Phenomena             | 77   | 6.956E-22 | 1.143E-19 | 22 | CLIP, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, ACES, beta-MSH   |
| 12 | Pediatric Obesity                                  | 42   | 7.357E-22 | 1.143E-19 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH   |

|    |                       |     |           |           |    |   |
|----|-----------------------|-----|-----------|-----------|----|---|
| 13 | Hepatitis, Autoimmune | 112 | 8.626E-22 | 1.237E-19 | 25 | GSTs, CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Fc gamma RII beta, Joining peptide (JP), Beta-MSH / Beta-Endorphin, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH, HLAC  |
| 14 | Vitiligo              | 102 | 1.497E-21 | 1.993E-19 | 24 | GSTs, CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, MLANA, Galpha(s)-specific peptide GPCRs, ACES, beta-MSH, HLAC  |
| 15 | Lupus Nephritis       | 550 | 4.096E-21 | 5.089E-19 | 47 | HMG1,2, Kappa chain (Ig light chain), A20, KV139, C4Ab, C4A protein, CLIP, VCAM1, C4, ACTH, MHC Class I alpha chain, Ficolin, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, proACTH, POMC, sVCAM1, Fc gamma RII beta, APOL1, Joining peptide (JP), Beta-MSH / Beta-Endorphin, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, Ficolin-1, gamma-LPH, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), gamma3-MSH, C4a, C4b, beta-MSH, KVD16, HLAC |
| 16 | Alopecia Areata       | 75  | 9.734E-21 | 1.134E-18 | 21 | CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, APRIL(TNFSF13), gamma3-MSH, beta-MSH, HLAC   |
| 17 | Spinal Fractures      | 49  | 2.172E-20 | 2.131E-18 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH  |
| 18 | Spinal Injuries       | 49  | 2.172E-20 | 2.131E-18 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH  |
| 19 | Back Injuries         | 49  | 2.172E-20 | 2.131E-18 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH  |

|    |                               |      |           |           |    |   |
|----|-------------------------------|------|-----------|-----------|----|---|
| 20 | Eclampsia                     | 80   | 4.349E-20 | 4.054E-18 | 21 | CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, HYEP, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH   |
| 21 | Mesothelioma                  | 265  | 5.198E-20 | 4.404E-18 | 33 | Calretinin, GSTs, CLIP, CD44, ACTH, CD44 soluble, alpha-MSH, HYEP, GSTM3, beta-Endorphin, CD44 (ICD), proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, gamma-LPH, CEACAM21, ACTH 1-17, DA-alphaMSH, gamma2-MSH, PR (membrane), gamma3-MSH, CD44 (EXT), WNT, beta-MSH, WIF1, PR (nuclear)   |
| 22 | Neoplasms, Mesothelial        | 265  | 5.198E-20 | 4.404E-18 | 33 | Calretinin, GSTs, CLIP, CD44, ACTH, CD44 soluble, alpha-MSH, HYEP, GSTM3, beta-Endorphin, CD44 (ICD), proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, gamma-LPH, CEACAM21, ACTH 1-17, DA-alphaMSH, gamma2-MSH, PR (membrane), gamma3-MSH, CD44 (EXT), WNT, beta-MSH, WIF1, PR (nuclear)   |
| 23 | Arthritis, Rheumatoid         | 2207 | 1.503E-19 | 1.218E-17 | 94 | HDC, HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), Histone H2, HGF, A20, Histone H2A, KV139, GSTs, C4Ab, C4A protein, CLIP, Annexin I, VCAM1, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, UHRF1, CD44 soluble, alpha-MSH, HYEP, IGKC, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, proACTH, SOD3 (EC-SOD), POMC, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Seprase, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, Galpha(i)-specific peptide GPCRs, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, gamma-LPH, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, CEACAM21, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, APRIL(TNFSF13), PR (membrane), gamma3-MSH, C4a, IFI44, MMP-28, CD44 (EXT), PLA2G5, C4b, ACES, WNT, beta-MSH, KVD16, PR (nuclear), Midkine, HLAC, LIRB |
| 24 | Pituitary ACTH Hypersecretion | 54   | 1.695E-19 | 1.317E-17 | 18 | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH,   |

|    |                              |      |           |           |     |  |
|----|------------------------------|------|-----------|-----------|-----|--|
|    |                              |      |           |           |     | N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH   |
| 25 | Eye Diseases                 | 2865 | 3.273E-19 | 2.440E-17 | 109 | HDC, HMG1,2, Angiopoietin 1, R-spondins, Kappa chain (Ig light chain), Histone H2, HGF, A20, KV139, GSTs, C4Ab, C4A protein, CLIP, KiSS-1, Tubulin beta, VCAM1, PLA2, CD44, C4, MFG8, SAMD11, SIX3, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, Beta dystroglycan, UHRF1, CD44 soluble, alpha-MSH, HYEP, IGKC, GSTM3, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, proACTH, SOD3 (EC-SOD), POMC, WFS1, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, ABCA13, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, Connexin 26, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, HKDC1, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, 2'-5'-oligoadenylate synthetase, SLC4A4, gamma-LPH, Aquaporin 1, H28, Tubulin beta 2B, MxA, ACTH 1-17, DA-alphaMSH, Carbohydrate sulfotransferases, Ig light chain, C4Aa, OAS3, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), GFAP, PR (membrane), gamma3-MSH, C4a, POU class III, IFI44, MLANA, Dystroglycan, CD44 (EXT), SOX3, Galpha(s)-specific peptide GPCRs, CYP4V2, C4b, WNT, beta-MSH, KVD16, PR (nuclear), HLAC, LIRB, Alpha dystroglycan, CHST6 |
| 26 | Adrenocortical Hyperfunction | 143  | 4.856E-19 | 3.481E-17 | 25  | CLIP, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, GIPR, Connexin 26, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, SLC12A1, gamma2-MSH, PR (membrane), gamma3-MSH, Galpha(s)-specific peptide GPCRs, beta-MSH, PR (nuclear)  |
| 27 | Hypopigmentation             | 147  | 9.746E-19 | 6.729E-17 | 25  | GSTs, CLIP, Tubulin beta, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, MLANA, Galpha(s)-specific peptide GPCRs, ACES, beta-MSH, HLAC   |
| 28 | Alopecia                     | 107  | 1.719E-18 | 1.145E-16 | 22  | MCR, CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, APRIL(TNFSF13), gamma3-MSH, beta-MSH, HLAC   |

|    |                       |      |           |           |     |   |
|----|-----------------------|------|-----------|-----------|-----|---|
| 29 | Carcinoma, Basal Cell | 283  | 3.598E-18 | 2.313E-16 | 32  | GSTs, CLIP, Tubulin beta, CD44, Fatty acid-binding protein, ACTH, Beta dystroglycan, CD44 soluble, alpha-MSH, beta-Endorphin, CD44 (ICD), proACTH, POMC, Seprase, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, Dystroglycan, CD44 (EXT), Galpha(s)-specific peptide GPCRs, WNT, beta-MSH, Alpha dystroglycan   |
| 30 | Rheumatic Diseases    | 2611 | 3.858E-18 | 2.322E-16 | 101 | HDC, HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), Histone H2, HGF, A20, Histone H2A, KV139, GSTs, C4Ab, C4A protein, APJ, MCR, CLIP, Annexin I, VCAM1, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, UHRF1, CD44 soluble, alpha-MSH, SULF1, HYEP, IGKC, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, proACTH, SOD3 (EC-SOD), POMC, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Seprase, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, Galpha(i)-specific peptide GPCRs, GLVR1, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, gamma-LPH, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, CEACAM21, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), PR (membrane), gamma3-MSH, C4a, RXR, IFI44, MMP-28, CD44 (EXT), PLA2G5, C4b, ACES, WNT, beta-MSH, KVD16, PR (nuclear), Midkine, HLAC, LIRB |
| 31 | Glomerulonephritis    | 766  | 3.861E-18 | 2.322E-16 | 51  | HMG1,2, Kappa chain (Ig light chain), A20, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, C4, ACTH, MHC Class I alpha chain, Ficolin, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, proACTH, POMC, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Beta-MSH / Beta-Endorphin, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, gamma-LPH, Aquaporin 1, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), gamma3-MSH, C4a, C4b, beta-MSH, KVD16, HLAC  |



|    |                       |      |           |           |     |   |
|----|-----------------------|------|-----------|-----------|-----|---|
| 32 | Neoplasms, Basal Cell | 286  | 4.929E-18 | 2.871E-16 | 32  | GSTs, CLIP, Tubulin beta, CD44, Fatty acid-binding protein, ACTH, Beta dystroglycan, CD44 soluble, alpha-MSH, beta-Endorphin, CD44 (ICD), proACTH, POMC, Seprase, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, Dystroglycan, CD44 (EXT), Galpha(s)-specific peptide GPCRs, WNT, beta-MSH, Alpha dystroglycan   |
| 33 | Arthritis             | 2622 | 5.184E-18 | 2.928E-16 | 101 | HDC, HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), Histone H2, HGF, A20, Histone H2A, KV139, GSTs, C4Ab, C4A protein, APJ, CLIP, Annexin I, VCAM1, IGHA1, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, UHRF1, CD44 soluble, alpha-MSH, SULF1, HYPE, IGKC, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, proACTH, SOD3 (EC-SOD), POMC, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Seprase, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, Galpha(i)-specific peptide GPCRs, GLVR1, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, gamma-LPH, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, CEACAM21, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), PR (membrane), gamma3-MSH, C4a, RXR, IFI44, MMP-28, CD44 (EXT), PLA2G5, C4b, ACES, WNT, beta-MSH, KVD16, PR (nuclear), Midkine, HLAC, LIRB |
| 34 | Cushing Syndrome      | 114  | 7.301E-18 | 4.003E-16 | 22  | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, GIPR, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, PR (membrane), gamma3-MSH, Galpha(s)-specific peptide GPCRs, beta-MSH, PR (nuclear)   |

|    |                        |      |           |           |     |  |
|----|------------------------|------|-----------|-----------|-----|--|
| 35 | Joint Diseases         | 2683 | 8.318E-18 | 4.430E-16 | 102 | HDC, HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), Histone H2, HGF, A20, Histone H2A, KV139, GSTs, C4Ab, C4A protein, APJ, CLIP, Annexin I, VCAM1, IGHA1, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, UHRF1, CD44 soluble, alpha-MSH, SULF1, HYPEP, IGKC, Carbonic anhydrase XII, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, proACTH, SOD3 (EC-SOD), POMC, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Sepsase, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, Galpha(i)-specific peptide GPCRs, GLVR1, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, gamma-LPH, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, CEACAM21, ACTH 1-17, DA-alphaMSH, Carbohydrate sulfotransferases, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), PR (membrane), gamma3-MSH, C4a, RXR, IFI44, MMP-28, CD44 (EXT), PLA2G5, C4b, ACES, WNT, beta-MSH, KVD16, PR (nuclear), Midkine, HLAC, LIRB |
| 36 | Hypotrichosis          | 116  | 1.082E-17 | 5.605E-16 | 22  | MCR, CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, APRIL(TNFSF13), gamma3-MSH, beta-MSH, HLAC   |
| 37 | Brain Infarction       | 385  | 1.338E-17 | 6.743E-16 | 36  | HGF, Biglycan proteoglycan, APJ, CLIP, VCAM1, PLA2, Fatty acid-binding protein, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Biglycan, Joining peptide (JP), Beta-MSH / Beta-Endorphin, CD147, N-POMC, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, L-FABP, Galpha(i)-specific peptide GPCRs, gamma-LPH, Galpha(i)-specific EDG GPCRs, ACTH 1-17, DA-alphaMSH, gamma2-MSH, GFAP, gamma3-MSH, beta-MSH, Midkine   |
| 38 | Pigmentation Disorders | 217  | 1.499E-17 | 7.353E-16 | 28  | GSTs, CLIP, Tubulin beta, ACTH, MHC Class I alpha chain, RSAD2, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, IFI27, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, H28, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, MLANA, Galpha(s)-specific peptide GPCRs, ACES, beta-MSH, HLAC  |

|    |                               |      |           |           |    |  |
|----|-------------------------------|------|-----------|-----------|----|--|
| 39 | Nephritis                     | 792  | 1.568E-17 | 7.496E-16 | 51 | HMG1,2, Kappa chain (Ig light chain), A20, KV139, C4Ab, C4A protein, CLIP, VCAM1, IGHA1, C4, ACTH, MHC Class I alpha chain, Ficolin, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, proACTH, POMC, sVCAM1, PLAT (TPA), Fc gamma RII beta, APOL1, Joining peptide (JP), Beta-MSH / Beta-Endorphin, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, gamma-LPH, Aquaporin 1, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), gamma3-MSH, C4a, C4b, beta-MSH, KVD16, HLAC   |
| 40 | RNA Virus Infections          | 1920 | 1.691E-17 | 7.878E-16 | 83 | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), Histone H2, HGF, OASL, MxB, Histone H2A, KV139, GZMH, GSTs, C4Ab, C4A protein, APJ, CLIP, VCAM1, IGHA1, PLA2, C4, ACTH, MHC Class I alpha chain, Ficolin, RSAD2, Beta dystroglycan, alpha-MSH, HYEP, IGKC, beta-Endorphin, GPNMB (Osteoactivin), IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Seprase, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, CPT-1A, I-TAC, Apo-2L(TNFSF10), Lactoferrin, 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, CEACAM21, ACTH 1-17, DA-alphaMSH, SLC12A1, Ig light chain, C4Aa, OAS3, EGF, gamma2-MSH, APRIL(TNFSF13), GFAP, gamma3-MSH, C4a, IFI44, Dystroglycan, C4b, WNT, beta-MSH, KVD16, Midkine, HLAC, LIRB, Alpha dystroglycan |
| 41 | Lupus Erythematosus, Systemic | 1768 | 1.933E-17 | 8.790E-16 | 79 | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), HGF, A20, OASL, MxB, KV139, GSTs, C4Ab, C4A protein, CLIP, EPST11, VCAM1, PLA2, CD44, C4, MFGE8, ACTH, MHC Class I alpha chain, Ficolin, RSAD2, CD44 soluble, alpha-MSH, IGKC, beta-Endorphin, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), proACTH, SOD3 (EC-SOD), POMC, XAF1, Cystatin C, sVCAM1, PLAT (TPA), Fc gamma RII beta, Seprase, APOL1, ILT4, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, CD147, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, S1P1 receptor, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, 2'-5'-oligoadenylate synthetase, gamma-LPH, H28, MxA, Galpha(i)-specific EDG GPCRs, ACTH 1-17, DA-alphaMSH, Ig light chain, C4Aa, OAS3, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), gamma3-MSH, C4a, IFI44, CD44 (EXT), C4b, beta-MSH, KVD16, HLAC, LIRB                                  |

|    |                       |     |           |           |    |   |
|----|-----------------------|-----|-----------|-----------|----|---|
| 42 | Osteoporosis          | 322 | 2.100E-17 | 9.321E-16 | 33 | HGF, GSTs, CLIP, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, I-TAC, Lactoferrin, Calcitonin receptor, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, NQO1, PR (membrane), gamma3-MSH, WNT, beta-MSH, PR (nuclear), HLAC  |
| 43 | Adrenal Insufficiency | 154 | 3.989E-17 | 1.699E-15 | 24 | HGF, MCR, CLIP, PLA2, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Seprase, Joining peptide (JP), Beta-MSH / Beta-Endorphin, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH   |
| 44 | Cerebral Infarction   | 307 | 4.010E-17 | 1.699E-15 | 32 | HGF, Biglycan proteoglycan, CLIP, PLA2, Fatty acid-binding protein, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, PLAT (TPA), Biglycan, Joining peptide (JP), Beta-MSH / Beta-Endorphin, CD147, N-POMC, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, L-FABP, gamma-LPH, Galpha(i)-specific EDG GPCRs, ACTH 1-17, DA-alphaMSH, gamma2-MSH, GFAP, gamma3-MSH, beta-MSH, Midkine  |
| 45 | Brain Ischemia        | 448 | 4.234E-17 | 1.754E-15 | 38 | HGF, Biglycan proteoglycan, APJ, CLIP, VCAM1, PLA2, HIF-prolyl hydroxylase, Fatty acid-binding protein, ACTH, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, sVCAM1, PLAT (TPA), Biglycan, Joining peptide (JP), Beta-MSH / Beta-Endorphin, CD147, N-POMC, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, L-FABP, Galpha(i)-specific peptide GPCRs, gamma-LPH, Galpha(i)-specific EDG GPCRs, ACTH 1-17, DA-alphaMSH, NALP3, gamma2-MSH, GFAP, gamma3-MSH, beta-MSH, Midkine |

|    |                             |      |           |           |    |   |
|----|-----------------------------|------|-----------|-----------|----|---|
| 46 | Wounds and Injuries         | 1314 | 5.280E-17 | 2.139E-15 | 66 | DCSH1, HMG1,2, HGF, GSTs, Connexin 30, Biglycan proteoglycan, CLIP, Annexin I, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, Ficolin, CD44 soluble, alpha-MSH, beta-Endorphin, GPNMB (Osteoactivin), Galpha(q)-specific peptide GPCRs, CD44 (ICD), MAFbx, proACTH, POMC, Neurocan, Cystatin C, Biglycan, Seprase, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Connexin 26, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, L-FABP, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, gamma-LPH, Galpha(i)-specific EDG GPCRs, ACTH 1-17, P2Y1, DA-alphaMSH, Carbohydrate sulfotransferases, EGF, gamma2-MSH, NQO1, GFAP, PR (membrane), gamma3-MSH, C4a, MMP-28, CD44 (EXT), ECEL1, C4b, WNT, beta-MSH, PR (nuclear), DPH2   |
| 47 | Hepatitis, Chronic          | 848  | 5.733E-17 | 2.274E-15 | 52 | Kappa chain (Ig light chain), Histone H2, HGF, Histone H2A, KV139, GSTs, CLIP, PLA2, ACTH, MHC Class I alpha chain, Ficolin, alpha-MSH, HYPE, IGKC, beta-Endorphin, GPNMB (Osteoactivin), EAT-2, Galpha(q)-specific peptide GPCRs, Histone H2B, proACTH, POMC, Fc gamma RII beta, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, Fc gamma RII, IFI27, N-POMC, CEACAM, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, CPT-1A, I-TAC, Apo-2L(TNFSF10), 2'-5'-oligoadenylate synthetase, gamma-LPH, MxA, ACTH 1-17, DA-alphaMSH, Ig light chain, OAS3, gamma2-MSH, gamma3-MSH, IFI44, ACES, WNT, beta-MSH, KVD16, Midkine, HLAC   |
| 48 | Hypersensitivity, Immediate | 1858 | 9.752E-17 | 3.787E-15 | 80 | HDC, HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), A20, Nk3R, KV139, GSTs, CAT-2, Biglycan proteoglycan, C4Ab, C4A protein, CLIP, SMG6, Tubulin beta, SULT1A1, VCAM1, PLA2, CD44, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, CD44 soluble, alpha-MSH, HYPE, IGKC, ASCT1 (SLC1A4), GSTM3, beta-Endorphin, Galpha(q)-specific peptide GPCRs, CD44 (ICD), proACTH, SOD3 (EC-SOD), POMC, Cystatin C, sVCAM1, Biglycan, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, SULT1A1 isoform 1, Fc gamma RII, N-POMC, gamma-MSH, N-POC, beta-LPH, L-FABP, Galpha(i)-specific peptide GPCRs, CPT-1A, S1P1 receptor, I-TAC, Apo-2L(TNFSF10), Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, gamma-LPH, Galpha(i)-specific EDG GPCRs, ACTH 1-17, DA-alphaMSH, Carbohydrate sulfotransferases, Ig light chain, C4Aa, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), gamma3-MSH, C4a, RXR, MMP- |

|    |                         |      |           |           |     |   |
|----|-------------------------|------|-----------|-----------|-----|---|
|    |                         |      |           |           |     | 28, CD44 (EXT), PLA2G5, Galpha(s)-specific peptide GPCRs, C4b, beta-MSH, KVD16, HLAC, LIRB  |
| 49 | Cardiovascular Diseases | 4762 | 1.469E-16 | 5.504E-15 | 143 | HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), Histone H2, HGF, A20, Histone H2A, KV139, KCNE4, GSTs, Biglycan proteoglycan, C4Ab, C4A protein, APJ, MCR, CLIP, Caspase-10, Tubulin beta, APH-1, SLC4A1, Annexin I, VCAM1, PLA2, HIF-prolyl hydroxylase, CD44, C4, SIX3, Fatty acid-binding protein, ARHI, ACTH, MHC Class I alpha chain, Ficolin, RSAD2, Claudin-14, Beta dystroglycan, CD44 soluble, alpha-MSH, HYPE, IGKC, GSTM3, Nek8, beta-Endorphin, Galpha(s)-specific calcitonin GPCRs, MC4R, IGHG1, Galpha(q)-specific peptide GPCRs, CD44 (ICD), Histone H2B, MAFbx, proACTH, SOD3 (EC-SOD), POMC, Neurocan, Cystatin C, sVCAM1, PLAT (TPA), Biglycan, GBP6, Fc gamma RII beta, ABCA13, SOX17, APOL1, Joining peptide (JP), Perforin, Beta-MSH / Beta-Endorphin, BC028528, Fc gamma RII, GIPR, CD147, N-POMC, CEACAM, gamma-MSH, N-POC, PRSS11 (HtrA1), beta-LPH, L-FABP, NQO3A2, Galpha(i)-specific peptide GPCRs, GLVR1, CPT-1A, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Calcitonin receptor, STARD13, Galpha(q)-specific nucleotide-like GPCRs, AGS8, gamma-LPH, Aquaporin 1, C6orf27, MxA, Galpha(i)-specific EDG GPCRs, ACTH 1-17, P2Y1, RAB3IP, PKHD1, DA-alphaMSH, Carbohydrate sulfotransferases, MYEOV2, SLC12A1, Syntrophin gamma 2, Ig light chain, C4Aa, PLC-delta, NALP3, EGF, gamma2-MSH, NQO1, APRIL(TNFSF13), GFAP, PR (membrane), gamma3-MSH, C4a, RXR, FAM149A, Dystroglycan, CD44 (EXT), PLA2G5, LRRC55, GALNT2, SOX3, Galpha(s)-specific peptide GPCRs, Oct-2, CYP4V2, C4b, ACES, HMGCL, WNT, SPE2B, beta-MSH, Proline oxidase 1, WIF1, RXRG, CART, KVD16, PR (nuclear), Midkine, GREB1, HLAC, Myospryn, RNF152, Alpha dystroglycan |
| 50 | Pain                    | 321  | 1.476E-16 | 5.504E-15 | 32  | HMG1,2, C4Ab, C4A protein, CLIP, C4, Fatty acid-binding protein, ACTH, MHC Class I alpha chain, alpha-MSH, beta-Endorphin, Galpha(q)-specific peptide GPCRs, proACTH, POMC, Cystatin C, Joining peptide (JP), Beta-MSH / Beta-Endorphin, N-POMC, gamma-MSH, N-POC, beta-LPH, Galpha(i)-specific peptide GPCRs, gamma-LPH, ACTH 1-17, DA-alphaMSH, C4Aa, NALP3, gamma2-MSH, gamma3-MSH, C4a, C4b, ACES, beta-MSH   |

Table A15. Top 50 TargetALS Diseases by Biomarkers enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| # | Term Name               | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|---|-------------------------|-----------|-----------|------------------------|-------------------|---|
| 1 | regulation of transport | 2767      | 2.288E-23 | 1.198E-19              | 185               | PLP1, NPY, PP2A cat (alpha), HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, Rab-3B, HPCA, APJ, RNF207, Activin A, UBL5, Endothelin-1, AP-1 gamma subunits, ARG2, T-plastin, NETO2, REV-ERBalpha, BRSK2, G-protein beta, JWA, Synaptotagmin I, Guanylate cyclase, HSP70, CNR1, Synaptotagmin IV, Synaptotagmin, CNTN1 (F3), Thioredoxin, NDUFA4, Septin 1, PDE, CNIH2, PPT1, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, SHISA7, RGS4, Kv3.3, ORP-family, PP1-cat gamma, CEACAM, PKC-beta, KIS, G-protein beta/gamma, NET6(TSPAN13), SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, S100, ORP8, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, Ephrin-A receptor 5, IDUA, CRH receptor 2, NSF, Tomt, CaMK IV, GLRA, SYP, LPL1, Rho GTPase, PDE4, Dysferlin, Rap1GDS1, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, Apelin, AP complex 2 small (sigma) chain, Rab-27B, PPID, TRPC, VDAC 1, Osteopontin, Rab-3C, PKA-reg (cAMP-dependent), ANT, PP1-cat, HMDH, NDFIP2, NR3A, ECT2, Substance P, GRM6, MCT1 (SLC16A1), TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, HSP90 beta, Activin beta A, CDK5, PAK, FLJ32001, Glycine receptor, Fatty acid-binding protein, Kv9.3, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, Azi1, DYNLL, Patched, MEF2, NAPB, APRIO, ACSL4, F262, CEACAM1, ATF/CREB, Hdj-2, DelGIP1, Acyl-CoA synthetase, PP2A catalytic, SNAPs, OAZIN, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, Kv4.2 channel, Protein kinase G 2, PRNP, MPTP complex, NKCC1, Calmodulin, NELL2, FLJ45455, Endophilin A1, STAC2, Activin, Aquaporin 1, NDFIP1, CLIC4, Syntenin 1, SCOT, ERK1/2, CaMK II delta, HSC70, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, ARPP-19, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), Ran, DKK1, MPC2, SOD1, YIPF5, CALM2, Cyclophilin A, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, ACTR3, SIAH3, ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1 |

|   |                            |      |           |           |     |  |
|---|----------------------------|------|-----------|-----------|-----|--|
| 2 | nervous system development | 3420 | 3.074E-23 | 1.198E-19 | 213 | <p>PLP1, Cyclin G, FBXO45, NPY, PRPS1, HSP90, PAK3, PAM, Galpha(s)-specific nucleotide-like GPCRs, Semaphorin 3C, RhoN, MAL2, MEGF10, N-chimaerin, HPCA, Activin A, Endothelin-1, T-plastin, REV-ERBalpha, BRSK2, UQCRQPC, G-protein beta, CRTL1, RGS8, NckAP1, Lgi4, HPCAL4, PSD2, UNRIP, Synaptotagmin I, ARL6, HSP70, CNR1, Synaptotagmin IV, CITED2, Synaptotagmin, CNTN1 (F3), JMJD3, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, IGSF9B, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, ATP5G, GPR124, KAL1, RGS4, GABA-A receptor alpha-1 subunit, UGT8, FLRT3, B3GN6, Tenascin-C, PP1-cat gamma, TRPC5, KIS, PAFAH gamma, G-protein beta/gamma, B3GN1, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, AMIGO2, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, DNER, ZFH2, Ephrin-A receptor 5, IP3KA, CRH receptor 2, Semaphorin 5A, Tomt, GLRA, ZNF499, GABA-A receptor beta-2 subunit, CECR2, Carbohydrate sulfotransferases, Rho GTPase, G-protein gamma, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, Pro-CCK, Dynein, axonemal, heavy chains, BMPR1A, Semaphorin 3E, LOC283174, Myotrophin, NELL1, cPKC (conventional), DLL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, Osteopontin, ZNF238, SMRT, NHE6, Lingo1, PP1-cat, NR3A, Cables1, ECT2, Histone H2, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, BDH, HSP90 beta, COL25A1, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, BEX1, Glycine receptor, Fatty acid-binding protein, LPPR4, DYNLT, Glycine receptor beta chain, Selenoprotein P, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Cyclin G1, SLC25A46, SMIT, Galpha(q)-specific peptide GPCRs, Histone H2B, Creatine kinase, DSCAML1, B-FABP, DYNLL, Patched, XK, MEF2, HNMT, ACSL4, ATF/CREB, FN14(TNFRSF12A), G-protein beta-4, Acyl-CoA synthetase, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, ENC1, RHEB2, Calmodulin, PGRMC1, Endophilin A1, BTBD1, Activin, Aquaporin 1, NME5, Calcyclin, Syntenin 1, SCOT, ERK1/2, UGCG, HSC70, PKC, SSTR2, SUR1, MEF2C, SULT4A1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, IGALS, UFC1, Nephrocystin-4, DKK1, SSTR1, Guanine deaminase, PRPS, SOD1, SLC38A2, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PTCHD1, Galpha(s)-specific peptide GPCRs,</p> |
|---|----------------------------|------|-----------|-----------|-----|--|



|   |                                    |       |           |           |     |  |
|---|------------------------------------|-------|-----------|-----------|-----|--|
|   |                                    |       |           |           |     | ACTR3, ATP6AP2, Pcdh19, CD166, NF-I, Neuroserpin, Midkine, IRS6(DOK5), ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit  |
| 3 | central nervous system development | 1772  | 1.251E-22 | 3.251E-19 | 137 | PLP1, Cyclin G, FBXO45, NPY, HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, HPCA, Activin A, UQCRQPC, G-protein beta, CRTL1, RGS8, NckAP1, HPCAL4, Synaptotagmin I, ARL6, HSP70, Synaptotagmin IV, CITED2, Synaptotagmin, CNTN1 (F3), JMJD3, Cystatin C, PPT1, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, GPR124, RGS4, UGT8, PAFAH gamma, G-protein beta/gamma, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, AMIGO2, Galpha(q)-specific nucleotide-like GPCRs, DNER, ZFH2, Ephrin-A receptor 5, CRH receptor 2, Semaphorin 5A, GLRA, Carbohydrate sulfotransferases, Rho GTPase, G-protein gamma, Ephrin-A receptor 4, GYRA2, Dynein, axonemal, heavy chains, BMPR1A, Myotrophin, cPKC (conventional), DLL4, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, ZNF238, SMRT, Lingo1, Histone H2, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, BDH, HSP90 beta, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, Glycine receptor, Fatty acid-binding protein, Selenoprotein P, Calcineurin A (catalytic), Cyclin G1, SLC25A46, Galpha(q)-specific peptide GPCRs, Histone H2B, Creatine kinase, DSCAML1, B-FABP, DYNLL, Patched, MEF2, HNMT, ATF/CREB, G-protein beta-4, Acyl-CoA synthetase, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, Calmodulin, Endophilin A1, Activin, Aquaporin 1, NME5, SCOT, ERK1/2, HSC70, PKC, SSTR2, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, UFC1, DKK1, SSTR1, SLC38A2, CALM2, FOXP1/2/4 proteins, PTCHD1, Galpha(s)-specific peptide GPCRs, ACTR3, ATP6AP2, Pcdh19, NF-I, Neuroserpin, Midkine, ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit |
| 4 | cellular process                   | 20764 | 5.944E-22 | 1.158E-18 | 758 | SCAP2, PLP1, Cyclin G, FBXO45, NPY, FAM3C, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, HMGCLL1, Cadherin 8, ZYG11B, CPSF1, ARP6, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, TMEM87B, AEBP1, G3BP2, RhoN, IRF1, ILDR2, FILIP, ZnT-2, MAL2, GLSK, Rab-3B, MAGEH-1, SLC35E2B, COX VIc, GAD1, SMVT, C1D, MEGF10, TINP1, PTCH2, ZH11B, N-chimaerin, Tubulin alpha 1A, ATP5C, SUCLG1, HPCA, APJ, Smooth muscle myosin, EDIL3, FLJ12671, ELOVL5, RNF207, Peroxiredoxin, Activin A, UBL5,   |

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|  |  |  |  |  | <p>Esterase D, Endothelin-1, SULT1A1, Trehalase, PSMB5, AP-1 gamma subunits, ARG2, T-plastin, DUOX1, GSKIP, GHITM, REVERBalpha, IL-17D, BRSK2, UQCRQPC, DYNLT3, P2Y11, UBXD3, G-protein beta, LAS1L, SC5D, JWA, ALDR, CRTL1, UQCRH, TMC4, Rab-6A, RGS8, SC4MOL, MRPS6, PSMA5, CNOT7, MDS028, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, NckAP1, BTBD12, NDUFA1, CDC18L (CDC6), ANKRD50, DNAH1, MRPL1, Lgi4, TTLL9, MOBKL1A, AP1G2, DTX2, LOC153328, Pannexin-1, MCM6, NKIRAS1, DCMC, HPCAL4, PSD2, MGF, PDH E2 subunit N6-lipoyllysine, TIP47, PRKAR2B, MELC, DPY19L1, NPFF receptor 2, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, C12orf62, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, DDX3Y, CNR1, MAPBPIP, MYL6, Glycogen phosphorylase, Synaptotagmin IV, Tim17, CITED2, PPM1E, SLIRP, NUDT4P1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), Thioredoxin, MRLC2, NDUFA4, ATP6V1A (70kD), HSPA4, JMJD3, Septin 1, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, Tcf5, PPT1, SDHB, MGAT4A, SLC39A10, IGSF9B, DKK3, Karyopherin alpha 2, NCKP1 subunit, TM9SF2, HCN2, D123, Guanylate cyclase alpha, FLJ20674, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, ATP5G, GPR124, TPH2, SHISA7, KAL1, RAB39B, Aha1, PTPN18, RGS4, VDAC 3, 14-3-3 beta/alpha, BTBD18, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, GUCY1B1, FLRT3, Exostosin-like 2, Kv3.3, SELI, C13orf37, ORP-family, B3GN6, Tenascin-C, Myopodin, PP1-cat gamma, CEACAM, ODF3, TRPC5, PKC-beta, KIS, TCP1-theta, PRDX1, ELMO3, G-protein beta/gamma, B3GN1, SLC25A45, NDUFB6, SDFR1, SUR, ABO system transferase, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, VBP-1, FUT2, TORC1, KLHL13, UQCRB, ATP5E, CPT-1A, S100, Rab-6, TXNRD1, ORP8, KCNH5, AMIGO2, VWA2, LASS6, PIMT, TRPV1, PDK3, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, TIP41, ATP6V1C1, ZDH13, Aldose reductase, ATP6M, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, FAM38B, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, AMDHD2, CacyBP(SIP), InsP6 kinase 3, SLC2A13, Semaphorin 5A, Adropin, V-ATPase E subunit, GRAIL, UBA1L, RPL9, NSF, Tomt, ADAM-TS10, GPR176, CaMK IV, CHCHD2, GLRA, DKK2, GABA-A receptor beta-2 subunit, FBXO2, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, LACTB2, LPL1, MOCS2(small), Rho GTPase, PDE4, GTPBP3, Tensin 2, G-protein gamma, UBE2D1, OSGIN2, PLCXD2, PRPS2, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, TMEM86B,</p> |
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|  |  |  |  |  | <p>Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, Secretogranin V, EGF, GlyRA2, ATP5B, PPase (inorganic), NAP1L2, Pro-CCK, CED-6, SYTC, XKR4, Dynein, axonemal, heavy chains, B3GALTL, BMPR1A, Semaphorin 3E, MMADHC, MMD, LOC283174, HIST1H2BN, Neurexophilin 2, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, NELL1, CAP2, cPKC (conventional), SF3A2, ATP6V1B2, NDUFB1, DLL4, ELOVL4, AP3S1, PSMA1, Serotonin receptor, CHMP5, Apelin, AP complex 2 small (sigma) chain, GABA-A receptor alpha-4 subunit, ADSS, Rab-27B, PPID, TRPC, SLC7A5, HTR5A, PYGM, ACTR10, MOC2B, PDK4, VDAC 1, WIF1, NDRG3, COX VIa, SUCB1, CLCN4, ATP6V1H, Osteopontin, ATP5G3, ZNF238, Slp5, ABHD10, SMRT, CysLT2 receptor, NHE6, Rab-3C, RGS11, M-Ras, KCY, CREB4, PC4, CHAMP, PKA-reg (cAMP-dependent), TReP-132, RNF152, Lingo1, ANT, PP1-cat, CFA74, HMDH, PDLIM2, TCP1-delta, UQCR10, NDFIP2, NR3A, GUCY1A3, HSBP1, VTA1, Cables1, KIAA1110, ECT2, Clathrin heavy chain, IL3RA, Substance P, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), StARD4, MID1IP1, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, KLHL35, MCT1 (SLC16A1), ARHGAP18, COPS4, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, MRPL47, Histone H2A, HMP19, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, CCN2, Stch, TRPC4, PMCA1, Rab-23, NCX1, SLBP, HCN, Protein kinase G1, HLF, C1orf113, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), Vinexin, COL25A1, PMS2L3, NDUFS6, Calponin-1, Activin beta A, GABA-A receptor alpha-5 subunit, BRMS1L, Zeta-sarcoglycan, CDK5, PANX2, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), SYT16, Guanylate cyclase beta, BEX1, TCP1-eta, Glycine receptor, Fatty acid-binding protein, PSG3, FOXP4, HINT, ENPP4, MAML1, KIAA0143, Sgk223, SOHLH1, IZUMO1, TOM22, MDH1, GTL3, ASAH, GABA-A receptor alpha-3 subunit, GNT-IV, LPPR4, DYNLT, SLC16A13, Atg101, TMEM74, SPOCK3, BEX2, SPSY, COX Va, Copine-4, Dextrin, eIF4A2, BRK, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, Carbonic anhydrase XII, Kv9.3, RTL1, Calcineurin A (catalytic), LSM2, TOP1MT, Galpha(i)-specific cannabis GPCR, STARD7, 4833424O15Rik, B3GT2, Cyclin G1, SLC25A46, SEC23A, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, H2AFZ, ATP6V1C, Histone H2B, NCOA4 (ARA70), MAFbx, SNAP190, NDUFA5, Tubulin alpha, Creatine kinase, ACAP1(CENTB1), DSCAML1, TBC1D10C, DCK, MRAP2, PAP-II, B-FABP, VIP32, Azi1, NUDT4, DYNLL, Patched, TNK1, XK, MEF2, INCA1, NAPB, ADAR3, PGAM1, HNMT, TAPBPL,</p> |
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|---|----------------------------------|------|-----------|-----------|-----|--|
|   |                                  |      |           |           |     | <p>Sec23, APRI0, SCS-A, BTBD10, MEK4/7, Peg10, ACSL4, RENBP, F262, CEACAM1, RANBP6, ATF/CREB, GLGB, ODP2, G-protein gamma 3, Hdj-2, DelGIP1, FN14(TNFRSF12A), Trim45, RSL24D1, G-protein beta-4, Ccdc56, FEM1B, Acyl-CoA synthetase, PP2A catalytic, CAPZA2, GAS41, IDI1, SNX7, ARRDC2, ZFAND2A, AP-4, MRLC, eIF4A, BMI-1, SNAPs, OAZIN, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), RNF175, Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, KAD6, ALAS1, TMEM87A, YPEL5, TSNARE1, ATP6V1B, Quinone oxidoreductase, Kv4.2 channel, JKAMP, PKD1L1, Protein kinase G 2, PRNP, HSPC138, SNX16, DNAJA2, TMS-1, GKP3, MPTP complex, ENC1, STAG3, RHEB2, NKCC1, Neurocalcin delta, Malin, C1orf59, HIST2H2BE, ATP6V0B, PDE4A, WDT2, CAB39L, Calmodulin, CENPP, LPL, DIRAS2, NELL2, SUMO-3, FLJ31818, PGRMC1, ATP6V1E, Apo-2L(TNFSF10), SET1B, LOXL2, PDE11A, FLJ45455, KLHL2, NOLA3 (NOP10), HSPC125, Endophilin A1, BTBD1, STAC2, Activin, SIPAR, Aquaporin 1, NDFIP1, KCTD16, NME5, CLIC4, Calcyclin, Syntenin 1, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ERK1/2, Carboxypeptidase M, snRNP-G, CDw52, AATC, UGCG, SLC29A4, Anks4b, TRUB1, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), ARL5, SLC35A5, PKC, SSTR2, SUR1, ABTB1, HTR2A, PMM2, SLC25A4, MPP7, CCDC57, ATP1B3, ARPP-19, K-cadherin (CDH6), Guanylate Cyclase 1, soluble, MEF2C, SULT4A1, MRPL33, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, LISCH7, Ran, OAT, MEK4(MAP2K4), TMEM70, Mindin, PRKAR1A, IGFALS, CLCN5, IMPA1, TRIM23, UFC1, Nephrocystin-4, DKK1, PARM-1, MPC2, SSTR1, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, dJ222E13.2, PPP4R2, GDE1, SLC38A2, MMP-28, SAP102, FSTL5, MAP1, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, KIAA1614, PTCHD1, DCoHM, Galpha(s)-specific peptide GPCRs, GPR22, TCP1-alpha, ATP5L, ACTR3, ATP6AP2, OXR1, CALB1, Tubulin alpha-4A, SRm300, RhoE, Pcdh19, CD166, GAD2, SIAH3, PGM2L1, TCP1-epsilon, NF-I, NPNT, MRPL3, B930041F14Rik, HXK3, COX VIIa-2, ACOXL, NRBF2, Midkine, SAMD10, IRS6(DOK5), ARP3, PXDN, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1, ZCCHC12, SNX10, CMAS, TCTE3, CHST6</p> |
| 5 | regulation of biological quality | 5537 | 5.166E-21 | 7.309E-18 | 291 | <p>NPY, PP2A cat (alpha), HSP90, PAK3, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, RhoN, ILDR2, ZnT-2, GLSK, Rab-3B, GAD1, Tubulin alpha 1A, HPCA, APJ, Smooth muscle myosin, RNF207, Peroxiredoxin, Activin A, Endothelin-1, SULT1A1, DUOX1, NETO2,</p>   |

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|  |  |  |  |  | <p>REV-ERBalpha, BRSK2, G-protein beta, JWA, ALDR, CNOT7, NckAP1, NKIRAS1, MELC, MC4R, UNRIP, Synaptotagmin I, COCH, Guanylate cyclase, KCNK2, HSP70, DDX3Y, CNR1, Glycogen phosphorylase, Synaptotagmin IV, CITED2, Synaptotagmin, PRDX3, Thioredoxin, MRLC2, ATP6V1A (70kD), JMJD3, Dynein, axonemal, light chains, PDE, CNIH2, PPT1, SLC39A10, IGSF9B, DKK3, NCKP1 subunit, HCN2, Guanylate cyclase alpha, Galpha(q)-specific Class A Orphan/other GPCRs, ATP5G, SHISA7, RGS4, GABA-A receptor alpha-1 subunit, TUSC3, FLRT3, Kv3.3, ORP-family, CEACAM, TRPC5, PKC-beta, TCP1-theta, PRDX1, G-protein beta/gamma, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, TORC1, CPT-1A, S100, TXNRD1, KCNH5, AMIGO2, TRPV1, PDK3, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, Rab-3, ATG9B, FAM38B, Ephrin-A receptor 5, LAPTM4B, IDUA, IP3KA, CRH receptor 2, Semaphorin 5A, GRAIL, Tomt, GLRA, GABA-A receptor beta-2 subunit, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, Tensin 2, G-protein gamma, SOCS6, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, Secretogranin V, GlyRA2, ATP5B, Pro-CCK, XKR4, Semaphorin 3E, LOC283174, Myotrophin, cPKC (conventional), ATP6V1B2, Serotonin receptor, Apelin, GABA-A receptor alpha-4 subunit, PPID, TRPC, SLC7A5, PYGM, PDK4, ATP6V1H, Osteopontin, ZNF238, SMRT, NHE6, PKA-reg (cAMP-dependent), ANT, PP1-cat, HMDH, TCP1-delta, NR3A, GUCY1A3, Substance P, HBXIP, LIPA, MCT1 (SLC16A1), ARHGAP18, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, Protein kinase G1, HSP90 beta, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PAK, Guanylate cyclase (alpha-1/beta-1), TCP1-eta, Glycine receptor, Fatty acid-binding protein, ENPP4, SgK223, IZUMO1, GTL3, GABA-A receptor alpha-3 subunit, DYNLT, Destrin, Glycine receptor beta chain, CAPZA, Carbonic anhydrase XII, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, STARD7, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, NCOA4 (ARA70), Tubulin alpha, Creatine kinase, MRAP2, PAP-II, DYNLL, Patched, XK, MEF2, HNMT, APRIO, ACSL4, RENBP, F262, CEACAM1, ATF/CREB, G-protein gamma 3, FN14(TNFRSF12A), Acyl-CoA synthetase, PP2A catalytic, CAPZA2, MRLC, BMI-1, SNAPs, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, LAMP2, ALAS1, ATP6V1B, Kv4.2 channel, Protein kinase G 2, PRNP, MPTP complex, RHEB2, NKCC1, Neurocalcin delta,</p> |
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|   |                            |      |           |           |     |  |
|---|----------------------------|------|-----------|-----------|-----|--|
|   |                            |      |           |           |     | Calmodulin, LPL, NELL2, PGRMC1, FLJ45455, Endophilin A1, Activin, Aquaporin 1, NDFIP1, SCOCO, CLIC4, SCOT, ADHX, ERK1/2, CDw52, AATC, UGCG, SLC29A4, CaMK II delta, HSC70, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, Guanylate Cyclase 1, soluble, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Nephrocystin-4, DKK1, MPC2, SOD1, YIPF5, SAP102, MAP1, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, ATP6AP2, CALB1, RhoE, GAD2, SIAH3, TCP1-epsilon, HXK3, ACOXL, ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1, SNX10   |
| 6 | regulation of localization | 4055 | 5.626E-21 | 7.309E-18 | 233 | PLP1, NPY, PP2A cat (alpha), HSP90, PAK3, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, ZnT-2, Rab-3B, HPCA, APJ, RNF207, Activin A, UBL5, Endothelin-1, AP-1 gamma subunits, ARG2, T-plastin, DUOX1, NETO2, REV-ERBalpha, BRSK2, G-protein beta, JWA, NckAP1, MGF, TIP47, Synaptotagmin I, Guanylate cyclase, HSP70, SCRT2, CNR1, Synaptotagmin IV, CITED2, Synaptotagmin, CNTN1 (F3), Thioredoxin, NDUFA4, Septin 1, PDE, CNIH2, PPT1, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, GPR124, SHISA7, RGS4, Kv3.3, ORP-family, Myopodin, PP1-cat gamma, CEACAM, PKC-beta, KIS, TCP1-theta, G-protein beta/gamma, NET6(TSPAN13), SDFR1, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, SCRT1, CPT-1A, S100, ORP8, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, Ephrin-A receptor 5, IDUA, CRH receptor 2, Semaphorin 5A, NSF, Tomt, CaMK IV, GLRA, SYP, Carbohydrate sulfotransferases, LPL1, Rho GTPase, PDE4, G-protein gamma, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, EGF, ATP5B, Pro-CCK, Dynein, axonemal, heavy chains, BMPR1A, Semaphorin 3E, MMD, cPKC (conventional), DLL4, Serotonin receptor, Apelin, AP complex 2 small (sigma) chain, Rab-27B, PPID, TRPC, VDAC 1, Osteopontin, Rab-3C, PKA-reg (cAMP-dependent), ANT, PP1-cat, HMDH, TCP1-delta, NDFIP2, NR3A, ECT2, Clathrin heavy chain, Substance P, HBXIP, GRM6, MCT1 (SLC16A1), ARHGAP18, TMEM14A, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, HSP90 beta, Activin beta A, CDK5, PAK, FLJ32001, TCP1-eta, Glycine receptor, Fatty acid-binding protein, SgK223, GTL3, SPOCK3, ATP5A, Kv9.3, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, SMIT, Galpha(q)-specific peptide GPCRs, |

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|---|---------------------------------------|------|-----------|-----------|-----|---|
|   |                                       |      |           |           |     | MRAP2, Azi1, DYNLL, Patched, MEF2, NAPB, APRI0, ACSL4, F262, CEACAM1, ATF/CREB, Hdj-2, DelGIP1, Acyl-CoA synthetase, PP2A catalytic, SNAPs, OAZIN, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, Kv4.2 channel, Protein kinase G 2, PRNP, MPTP complex, NKCC1, Malin, Calmodulin, LPL, NELL2, SUMO-3, PGRMC1, FLJ45455, NOLA3 (NOP10), Endophilin A1, STAC2, Activin, Aquaporin 1, NDFIP1, CLIC4, Syntenin 1, SCOT, ERK1/2, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, SUR1, HTR2A, SLC25A4, ATP1B3, ARPP-19, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), Ran, DKK1, MPC2, SOD1, YIPF5, MMP-28, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, KIAA1614, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, SIAH3, TCP1-epsilon, Midkine, ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1  |
| 7 | inorganic ion transmembrane transport | 904  | 9.046E-20 | 1.007E-16 | 86  | ZnT-2, SMVT, ATP5C, Endothelin-1, UQCRQPC, UQCRH, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, ATP5G, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, TRPC5, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, KCNH5, TRPV1, COX VIIa, ATP6V1C1, ZDH13, ATP6M, V-ATPase E subunit, GLRA, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, ATP5B, Dynein, axonemal, heavy chains, ATP6V1B2, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NR3A, Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, Glycine receptor beta chain, Kv9.3, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, CALM2, ATP5L, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit |
| 8 | localization                          | 6993 | 1.333E-19 | 1.299E-16 | 340 | FBXO45, HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, TMEM87B, G3BP2, RhoN, ILDR2, ZnT-2, MAL2, Rab-3B, SLC35E2B, SMVT, MEGF10, ZH11B, Tubulin alpha 1A, ATP5C, Activin A, Endothelin-1, AP-1 gamma subunits, C18orf42, BRSK2, UQCRQPC, JWA, UQCRH, TMC4, Rab-6A, Importin (karyopherin)-alpha, NckAP1, ANKRD50, DNAH1, TTLL9, AP1G2, LOC153328, Pannexin-1, PSD2, MGF, TIP47, MC4R, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6,   |

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|  |  |  |  |  | <p>KCNK2, HSP70, DDX3Y, MAPBPIP, Synaptotagmin IV, Tim17, SLIRP, Synaptotagmin, Thioredoxin, MRLC2, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, Dynein, axonemal, light chains, PDE, CNIH2, PPT1, SLC39A10, Karyopherin alpha 2, NCKP1 subunit, TM9SF2, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, LMF1, ATP5G, GPR124, SHISA7, RAB39B, VDAC 3, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, UGT8, FLRT3, Kv3.3, C13orf37, ORP-family, CEACAM, TRPC5, PKC-beta, TCP1-theta, ELMO3, G-protein beta/gamma, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, CPT-1A, S100, Rab-6, ORP8, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, ZDH13, ATP6M, Rab-3, ATG9B, DNER, FAM38B, APOL3, LAPTM4B, SLC2A13, Semaphorin 5A, V-ATPase E subunit, GRAIL, NSF, CaMK IV, GLRA, GABA-A receptor beta-2 subunit, CECR2, DOK7, SYP, Carbohydrate sulfotransferases, TIMM17, Rho GTPase, PDE4, G-protein gamma, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, GlyRA2, ATP5B, Pro-CCK, CED-6, XKR4, Dynein, axonemal, heavy chains, Semaphorin 3E, cPKC (conventional), ATP6V1B2, AP3S1, Serotonin receptor, CHMP5, Apelin, AP complex 2 small (sigma) chain, GABA-A receptor alpha-4 subunit, Rab-27B, PPID, TRPC, SLC7A5, ACTR10, VDAC 1, COX VIa, CLCN4, ATP6V1H, Osteopontin, ATP5G3, Slp5, SMRT, NHE6, Rab-3C, ANT, TCP1-delta, UQCR10, NDFIP2, NR3A, HSBP1, VTA1, ECT2, Clathrin heavy chain, AP-3 sigma subunits, HBXIP, PSMD10 (Gankyrin), STARD4, CalDAG-GEFII, MCT1 (SLC16A1), TMEM14A, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, HMP19, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, SLBP, HCN, Protein kinase G1, C1orf113, CAP1, Anillin, TXNIP (VDUP1), Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, SYT16, TCP1-eta, Glycine receptor, Fatty acid-binding protein, HINT, KIAA0143, Sgk223, TOM22, GABA-A receptor alpha-3 subunit, LPPR4, DYNLT, SLC16A13, COX Va, Destrin, BRK, ATP5A, Glycine receptor beta chain, Carbonic anhydrase XII, Kv9.3, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, STARD7, SLC25A46, SEC23A, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, ATP6V1C, NCOA4 (ARA70), Tubulin alpha, ACAP1(CENTB1), TBC1D10C, MRAP2, B-FABP, Azi1, DYNLL, Patched, XK, MEF2, NAPB, Sec23, Peg10, ACSL4, CEACAM1, RANBP6, ATF/CREB, Hdj-2, FN14(TNFRSF12A), Acyl-CoA synthetase, SNX7, ARRDC2, ZFAND2A, MRLC, SNAPs, DLC1</p> |
|--|--|--|--|--|--|



|    |   |      |           |           |     |  |
|----|---|------|-----------|-----------|-----|--|
|    |   |      |           |           |     | (Dynein LC8a), Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, TMEM87A, TSNARE1, ATP6V1B, Kv4.2 channel, PKD1L1, Protein kinase G 2, HSPC138, SNX16, TMS-1, MPTP complex, STAG3, NKCC1, Neurocalcin delta, ATP6V0B, WDT2, Calmodulin, SUMO-3, ATP6V1E, LOXL2, FLJ45455, Endophilin A1, Activin, C1orf43, Aquaporin 1, NDFIP1, NME5, CLIC4, Calcyclin, Syntenin 1, ERK1/2, UGCG, SLC29A4, Anks4b, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), ARL5, SLC35A5, PKC, SUR1, HTR2A, SLC25A4, MPP7, ATP1B3, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, CLCN5, TRIM23, Nephrocystin-4, MPC2, SOD1, YIPF5, SLC38A2, SAP102, MAP1, CALM2, Cyclophilin A, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, ACTR3, RhoE, TCP1-epsilon, NPNT, Midkine, ARP3, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, SNX10   |
| 9  | regulation of establishment of protein localization | 913  | 1.698E-19 | 1.448E-16 | 86  | PP2A cat (alpha), HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, HPCA, UBL5, REV-ERBalpha, BRSK2, HSP70, CNR1, Synaptotagmin IV, Synaptotagmin, Thioredoxin, PDE, Galpha(q)-specific Class A Orphan/other GPCRs, ORP-family, KIS, TCP1-theta, SUR, Galpha(i)-specific peptide GPCRs, CPT-1A, Galpha(q)-specific nucleotide-like GPCRs, Ephrin-A receptor 5, IDUA, CRH receptor 2, Tomt, CaMK IV, LPL1, Rho GTPase, PDE4, Rap1GDS1, EGF, PPID, HMDH, TCP1-delta, NDFIP2, ECT2, MCT1 (SLC16A1), LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, Rab-23, HSP90 beta, CDK5, PAK, FLJ32001, TCP1-eta, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, Azi1, DYNLL, APRIO, ACSL4, F262, Hdj-2, DelGIP1, Acyl-CoA synthetase, PP2A catalytic, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, PRNP, NKCC1, Activin, NDFIP1, SCOT, ERK1/2, HSC70, PKC, SUR1, ERK2 (MAPK1), Calcineurin A (beta), Ran, MPC2, Cyclophilin A, PI3K reg class IA, TCP1-alpha, ACTR3, SIAH3, TCP1-epsilon, ARP3, 14-3-3, Glutaredoxin 1 |
| 10 | ion transmembrane transport                         | 1192 | 1.858E-19 | 1.448E-16 | 101 | ZnT-2, SMVT, ATP5C, Endothelin-1, UQCRQPC, JWA, UQCRH, TMC4, LOC153328, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, ATP5G, VDAC 3, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, TRPC5, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, S100, KCNH5, TRPV1, COX VIIa, ATP6V1C1, ZDH13, ATP6M, FAM38B, V-ATPase E subunit, GLRA, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, ATP5B, Dynein, axonemal, heavy chains, ATP6V1B2, Serotonin receptor, GABA-A  |

|    |           |      |           |           |     |  |
|----|-----------|------|-----------|-----------|-----|--|
|    |           |      |           |           |     | receptor alpha-4 subunit, TRPC, SLC7A5, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NR3A, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, COX Va, ATP5A, Glycine receptor beta chain, Kv9.3, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, CLIC4, Calcyclin, SLC29A4, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, MPC2, CALM2, ATP5L, 14-3-3, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit  |
| 11 | transport | 5211 | 6.052E-19 | 4.257E-16 | 272 | HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, TMEM87B, G3BP2, ILDR2, ZnT-2, MAL2, Rab-3B, SLC35E2B, SMVT, MEGF10, ZH11B, Tubulin alpha 1A, ATP5C, Activin A, Endothelin-1, AP-1 gamma subunits, BRSK2, UQCRQP, JWA, UQCRH, TMC4, Rab-6A, Importin (karyopherin)-alpha, ANKRD50, DNAH1, AP1G2, LOC153328, Pannexin-1, PSD2, TIP47, MC4R, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, Synaptotagmin IV, Tim17, Synaptotagmin, NDUFA4, ATP6V1A (70kD), HSPA4, Dynein, axonemal, light chains, CNIH2, PPT1, SLC39A10, Karyopherin alpha 2, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, LMF1, ATP5G, RAB39B, VDAC 3, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, ORP-family, CEACAM, TRPC5, PKC-beta, TCP1-theta, ELMO3, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, CPT-1A, S100, Rab-6, ORP8, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, ZDH13, ATP6M, Rab-3, ATG9B, DNER, FAM38B, APOL3, LAPTM4B, SLC2A13, V-ATPase E subunit, NSF, CaMK IV, GLRA, GABA-A receptor beta-2 subunit, CECR2, SYP, TIMM17, Rho GTPase, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, GlyRA2, ATP5B, CED-6, XKR4, Dynein, axonemal, heavy chains, cPKC (conventional), ATP6V1B2, AP3S1, Serotonin receptor, CHMP5, Apelin, AP complex 2 small (sigma) chain, GABA-A receptor alpha-4 subunit, Rab-27B, PPID, TRPC, SLC7A5, ACTR10, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, Slp5, SMRT, NHE6, Rab-3C, ANT, TCP1-delta, UQCR10, NDFIP2, NR3A, HSBP1, VTA1, ECT2, Clathrin heavy chain, AP-3 sigma subunits, STARD4, CalDAG-GEFII, MCT1 (SLC16A1), TMEM14A, Galpha(q)-specific amine GPCRs, UQCRFS1, HMP19, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, SLBP, HCN, |

|    |  |      |           |           |    |   |
|----|--|------|-----------|-----------|----|---|
|    |  |      |           |           |    | CAP1, TXNIP (VDUP1), Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, SYT16, TCP1-eta, Glycine receptor, Fatty acid-binding protein, HINT, TOM22, GABA-A receptor alpha-3 subunit, LPPR4, DYNLT, SLC16A13, COX Va, ATP5A, Glycine receptor beta chain, Carbonic anhydrase XII, Kv9.3, Calcineurin A (catalytic), STARD7, SLC25A46, SEC23A, SMIT, Galpha(q)-specific peptide GPCRs, ATP6V1C, NCOA4 (ARA70), Tubulin alpha, ACAP1(CENTB1), TBC1D10C, B-FABP, Azi1, DYNLL, XK, NAPB, Sec23, Peg10, ACSL4, CEACAM1, RANBP6, ATF/CREB, Hdj-2, Acyl-CoA synthetase, SNX7, ARRD2, ZFAND2A, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, TMEM87A, TSNARE1, ATP6V1B, Kv4.2 channel, PKD1L1, HSPC138, SNX16, TMS-1, MPTP complex, NKCC1, Neurocalcin delta, ATP6V0B, WDT2, Calmodulin, ATP6V1E, LOXL2, Endophilin A1, Activin, C1orf43, Aquaporin 1, NDFIP1, NME5, CLIC4, Calcyclin, Syntenin 1, ERK1/2, UGCG, SLC29A4, CaMK II delta, HSC70, ARL5, SLC35A5, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, CLCN5, TRIM23, MPC2, SOD1, YIPF5, SLC38A2, MAP1, CALM2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, TCP1-epsilon, 14-3-3, ARM CX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, SNX10 |
| 12 | generation of precursor metabolites and energy | 559  | 6.553E-19 | 4.257E-16 | 64 | HMGCLL1, COX VIc, ATP5C, SUCLG1, REV-ERBalpha, UQCRQPC, ALDR, UQCRH, NDUFAB1, NDUFA1, PDH E2 subunit N6-lipoyllysine, NDUFB4, MC4R, NDUFA8, Glycogen phosphorylase, NDUFA4, SDHB, Galpha(q)-specific Class A Orphan/other GPCRs, PP1-cat gamma, NDUFB6, NDUFS4, UQCRB, ATP5E, S100, COX VIIa, Aldose reductase, NDUFB3, ATP5B, NDUFB1, PYGM, COX VIa, SUCB1, ANT, PP1-cat, UQCR10, UQCRFS1, Galpha(i)-specific amine GPCRs, NDUFS6, MDH1, COX Va, ATP5A, PDH beta, Galpha(q)-specific peptide GPCRs, NDUFA5, MRAP2, PGAM1, SCS-A, F262, GLGB, ODP2, Glutaredoxin, COX VIa-1, MPTP complex, Malin, LOXL2, SCOT, Octanoyl-holo-acp, ADHX, SLC25A4, Galpha(s)-specific peptide GPCRs, ATP5L, HXK3, COX VIIa-2, COX VIIa-2L   |
| 13 | cation transport                               | 1181 | 9.256E-19 | 5.551E-16 | 99 | ZnT-2, SMVT, ATP5C, Endothelin-1, UQCRQPC, UQCRH, LOC153328, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, ATP5G, TUSC3, Kv3.3, TRPC5, PKC-beta, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, ZDH13, ATP6M, FAM38B, V-ATPase E subunit, NSF, Galpha(i)-   |

|    |                                     |      |           |           |    |  |
|----|-------------------------------------|------|-----------|-----------|----|--|
|    |                                     |      |           |           |    | specific metabotropic glutamate GPCRs, ATP5B, Dynein, axonemal, heavy chains, cPKC (conventional), ATP6V1B2, Serotonin receptor, TRPC, SLC7A5, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NDFIP2, NR3A, Clathrin heavy chain, Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, CDK5, PANX2, COX Va, ATP5A, Kv9.3, Calcineurin A (catalytic), SMIT, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, TMS-1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, NDFIP1, SLC29A4, CaMK II delta, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, SLC38A2, CALM2, ATP5L, 14-3-3, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit   |
| 14 | behavior                            | 1125 | 1.001E-18 | 5.572E-16 | 96 | NPY, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, JWA, Lgi4, PRKAR2B, MC4R, KCNK2, CNR1, Synaptotagmin IV, Synaptotagmin, CNTN1 (F3), PDE, Cystatin C, PPT1, Galpha(q)-specific Class A Orphan/other GPCRs, SHISA7, VDAC 3, G-protein beta/gamma, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, TORC1, CPT-1A, S100, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, ZFH2, IDUA, CRH receptor 2, GPR176, CaMK IV, GLRA, PDE4, G-protein gamma, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Pro-CCK, Dynein, axonemal, heavy chains, PKA-reg type II (cAMP-dependent), cPKC (conventional), Serotonin receptor, Apelin, TRPC, VDAC 1, PKA-reg (cAMP-dependent), HMDH, Substance P, GRM6, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, HCN, GABA-A receptor alpha-5 subunit, CDK5, PAK, Glycine receptor, Glycine receptor beta chain, Selenoprotein P, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, SLC25A46, Galpha(q)-specific peptide GPCRs, MRAP2, MEF2, APRIO, ATF/CREB, Galpha(s)-specific CRF GPCRs, ATP6V1B, Kv4.2 channel, PRNP, MPTP complex, PGRMC1, ERK1/2, PKC, SUR1, HTR2A, MEF2C, ERK2 (MAPK1), Calcineurin A (beta), Nephrocystin-4, DKK1, SOD1, FOXP1/2/4 proteins, PTCHD1, Galpha(s)-specific peptide GPCRs, OXR1, CALB1, Midkine, RAGE, ATP1beta subunit |
| 15 | regulation of muscle system process | 434  | 2.192E-18 | 1.139E-15 | 55 | HSP90, Galpha(s)-specific nucleotide-like GPCRs, Smooth muscle myosin, RNF207, Endothelin-1, ARG2, MELC, Guanylate cyclase, PDE, Guanylate cyclase alpha, RGS4, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, Galpha(q)-specific nucleotide-like GPCRs, Rho GTPase, PDE4, Myotrophin, cPKC (conventional), Serotonin receptor, TRPC, ANT, GUCY1A3,  |

|    |                    |      |           |           |     |   |
|----|--------------------|------|-----------|-----------|-----|---|
|    |                    |      |           |           |     | Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, PMCA1, NCX1, HCN, Protein kinase G1, Calponin-1, PAK, Guanylate cyclase (alpha-1/beta-1), Calcineurin A (catalytic), Galpha(q)-specific peptide GPCRs, MAFbx, MEF2, MRLC, MPTP complex, Calmodulin, CaMK II delta, PKC, SSTR2, SUR1, SLC25A4, Guanylate Cyclase 1, soluble, MEF2C, Protein kinase G, SOD1, CALM2, FOXP1/2/4 proteins, NPNT, ATP1beta subunit, Myospryn  |
| 16 | system development | 6559 | 2.400E-18 | 1.169E-15 | 320 | PLP1, Cyclin G, FBXO45, NPY, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, RhoN, IRF1, ILDR2, MAL2, MEGF10, PTCH2, N-chimaerin, HPCA, APJ, Smooth muscle myosin, Peroxiredoxin, Activin A, Endothelin-1, Trehalase, ARG2, T-plastin, REV-ERBalpha, BRSK2, UQCRQPC, G-protein beta, ALDR, CRTL1, RGS8, MDS028, NckAP1, Lgi4, NKIRAS1, HPCAL4, PSD2, MGF, MEPE, MELC, UNRIP, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, CNR1, MYL6, Synaptotagmin IV, CITED2, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), HSPA4, JMJD3, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, IGSF9B, DKK3, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, ATP5G, GPR124, KAL1, RGS4, GABA-A receptor alpha-1 subunit, UGT8, FLRT3, B3GN6, Tenascin-C, PP1-cat gamma, CEACAM, TRPC5, KIS, PAFAH gamma, PRDX1, G-protein beta/gamma, B3GN1, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, S100, TXNRD1, AMIGO2, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, Rab-3, MTG16 (CBFA2T3), ATG9B, DNER, ZFH2, Ephrin-A receptor 5, IDUA, IP3KA, CRH receptor 2, CacyBP(SIP), Semaphorin 5A, Tomt, CaMK IV, GLRA, ZNF499, GABA-A receptor beta-2 subunit, CECR2, Carbohydrate sulfotransferases, Rho GTPase, PDE4, Tensin 2, G-protein gamma, PRPS2, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, EGF, GlyRA2, ATP5B, Pro-CCK, Dynein, axonemal, heavy chains, BMPR1A, Semaphorin 3E, LOC283174, Myotrophin, NELL1, cPKC (conventional), DLL4, Serotonin receptor, Apelin, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, Osteopontin, ZNF238, SMRT, NHE6, M-Ras, CHAMP, PKA-reg (cAMP-dependent), Lingo1, ANT, PP1-cat, PDLIM2, NR3A, Cables1, ECT2, IL3RA, GRM6, Histone H2, LIPA, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, HLF, BDH, |

|    |                                 |     |           |           |    |  |
|----|---------------------------------|-----|-----------|-----------|----|--|
|    |                                 |     |           |           |    | HSP90 beta, Anillin, TXNIP (VDUP1), COL25A1, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PAK, BEX1, Glycine receptor, Fatty acid-binding protein, FOXP4, MAML1, SOHLH1, IZUMO1, ASAH, LPPR4, DYNLT, BRK, Glycine receptor beta chain, Nek8, Selenoprotein P, RTL1, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, STARD7, Cyclin G1, SLC25A46, Glyoxalase I, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, Histone H2B, NCOA4 (ARA70), Creatine kinase, DSCAML1, B-FABP, DYNLL, Patched, XK, MEF2, HNMT, MEK4/7, Peg10, ACSL4, CEACAM1, ATF/CREB, RAI1, FN14(TNFRSF12A), Trim45, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, MRLC, eIF4A, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, ALAS1, ATP6V1B, PKD1L1, HSPC138, MPTP complex, ENC1, RHEB2, NKCC1, WDT2, Calmodulin, PGRMC1, Apo-2L(TNFSF10), LOXL2, Endophilin A1, BTBD1, Activin, Aquaporin 1, NME5, CLIC4, Calcyclin, Syntenin 1, SCOT, KCRS, ERK1/2, UGCG, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, SSTR2, SUR1, SLC25A4, K-cadherin (CDH6), MEF2C, SULT4A1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, MEK4(MAP2K4), PRKAR1A, IGFALS, UFC1, Nephrocystin-4, DKK1, SSTR1, Guanine deaminase, PRPS, SOD1, KIAA1024, PPP4R2, SLC38A2, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, PTCHD1, Galpha(s)-specific peptide GPCRs, ACTR3, ATP6AP2, CALB1, Pcdh19, CD166, NF-I, NPNT, Neuroserpin, Midkine, IRS6(DOK5), ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, SNX10 |
| 17 | regulation of protein transport | 873 | 5.115E-18 | 2.346E-15 | 81 | PP2A cat (alpha), HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, HPCA, UBL5, REV-ERBalpha, BRSK2, HSP70, CNR1, Synaptotagmin IV, Synaptotagmin, Thioredoxin, PDE, Galpha(q)-specific Class A Orphan/other GPCRs, ORP-family, KIS, SUR, Galpha(i)-specific peptide GPCRs, CPT-1A, Galpha(q)-specific nucleotide-like GPCRs, Ephrin-A receptor 5, IDUA, CRH receptor 2, Tomt, CaMK IV, LPL1, Rho GTPase, PDE4, Rap1GDS1, EGF, PPID, HMDH, NDFIP2, ECT2, MCT1 (SLC16A1), LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, Rab-23, HSP90 beta, CDK5, PAK, FLJ32001, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, Galpha(q)-specific peptide GPCRs, Azi1, DYNLL, APRIO, ACSL4, F262, Hdj-2, DelGIP1, Acyl-CoA synthetase, PP2A catalytic, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, PRNP, NKCC1, Activin, NDFIP1, SCOT, ERK1/2, HSC70, PKC, SUR1, ERK2 (MAPK1), Calcineurin A (beta), Ran, MPC2,   |

|    |                               |      |           |           |     |   |
|----|-------------------------------|------|-----------|-----------|-----|---|
|    |                               |      |           |           |     | Cyclophilin A, PI3K reg class IA, ACTR3, SIAH3, ARP3, 14-3-3, Glutaredoxin 1  |
| 18 | synaptic signaling            | 769  | 6.011E-18 | 2.512E-15 | 75  | PLP1, NPY, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, G-protein beta, RGS8, Importin (karyopherin)-alpha, Synaptotagmin I, Guanylate cyclase, CNR1, Synaptotagmin IV, Synaptotagmin, PDE, CNIH2, PPT1, Karyopherin alpha 2, Guanylate cyclase alpha, VDAC 3, GABA-A receptor alpha-1 subunit, GUCY1B1, G-protein beta/gamma, SDFR1, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, TORC1, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, GPR176, CaMK IV, GLRA, GABA-A receptor beta-2 subunit, SYP, Rho GTPase, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, cPKC (conventional), Serotonin receptor, GABA-A receptor alpha-4 subunit, HTR5A, VDAC 1, GUCY1A3, Substance P, GRM6, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, GABA-A receptor alpha-5 subunit, CDK5, PAK, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, Glycine receptor, GABA-A receptor alpha-3 subunit, Glycine receptor beta chain, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, MEF2, NAPP, SNAPS, Kv4.2 channel, MPTP complex, FLJ45455, Syntenin 1, ERK1/2, PKC, HTR2A, Guanylate Cyclase 1, soluble, MEF2C, ERK2 (MAPK1), PTCHD1, Galpha(s)-specific peptide GPCRs, GAD2 |
| 19 | establishment of localization | 5405 | 6.123E-18 | 2.512E-15 | 276 | HSP90, PAM, Galpha(s)-specific nucleotide-like GPCRs, TMEM87B, G3BP2, ILDR2, ZnT-2, MAL2, Rab-3B, SLC35E2B, SMVT, MEGF10, ZH11B, Tubulin alpha 1A, ATP5C, Activin A, Endothelin-1, AP-1 gamma subunits, BRSK2, UQCRQPC, JWA, UQCRH, TMC4, Rab-6A, Importin (karyopherin)-alpha, ANKRD50, DNAH1, AP1G2, LOC153328, Pannexin-1, PSD2, TIP47, MC4R, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, Synaptotagmin IV, Tim17, Synaptotagmin, NDUFA4, ATP6V1A (70kD), HSPA4, Septin 1, Dynein, axonemal, light chains, CNIH2, PPT1, SLC39A10, Karyopherin alpha 2, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, LMF1, ATP5G, RAB39B, VDAC 3, 14-3-3 beta/alpha, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, ORP-family, CEACAM, TRPC5, PKC-beta, TCP1-theta, ELMO3, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, CPT-1A, S100, Rab-6, ORP8, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, ZDH13, ATP6M, Rab-3, ATG9B, DNER, FAM38B, APOL3, LAPTM4B,   |

|    |  |     |           |           |    |  |
|----|--|-----|-----------|-----------|----|--|
|    |  |     |           |           |    | SLC2A13, V-ATPase E subunit, NSF, CaMK IV, GLRA, GABA-A receptor beta-2 subunit, CECR2, SYP, TIMM17, Rho GTPase, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, GlyRA2, ATP5B, CED-6, XKR4, Dynein, axonemal, heavy chains, cPKC (conventional), ATP6V1B2, AP3S1, Serotonin receptor, CHMP5, Apelin, AP complex 2 small (sigma) chain, GABA-A receptor alpha-4 subunit, Rab-27B, PPID, TRPC, SLC7A5, ACTR10, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, Slp5, SMRT, NHE6, Rab-3C, ANT, TCP1-delta, UQCR10, NDFIP2, NR3A, HSBP1, VTA1, ECT2, Clathrin heavy chain, AP-3 sigma subunits, StARD4, CalDAG-GEFII, MCT1 (SLC16A1), TMEM14A, Galpha(q)-specific amine GPCRs, UQCRFS1, HMP19, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, SLBP, HCN, CAP1, TXNIP (VDUP1), Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, SYT16, TCP1-eta, Glycine receptor, Fatty acid-binding protein, HINT, TOM22, GABA-A receptor alpha-3 subunit, LPPR4, DYNLT, SLC16A13, COX Va, ATP5A, Glycine receptor beta chain, Carbonic anhydrase XII, Kv9.3, Calcineurin A (catalytic), STARD7, SLC25A46, SEC23A, SMIT, Galpha(q)-specific peptide GPCRs, ATP6V1C, NCOA4 (ARA70), Tubulin alpha, ACAP1(CENTB1), TBC1D10C, B-FABP, Azi1, DYNLL, XK, NAPB, Sec23, Peg10, ACSL4, CEACAM1, RANBP6, ATF/CREB, Hdj-2, Acyl-CoA synthetase, SNX7, ARRDC2, ZFAND2A, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, LAMP2, COX VIa-1, TMEM87A, TSNARE1, ATP6V1B, Kv4.2 channel, PKD1L1, HSPC138, SNX16, TMS-1, MPTP complex, NKCC1, Neurocalcin delta, ATP6V0B, WDT2, Calmodulin, ATP6V1E, LOXL2, Endophilin A1, Activin, C1orf43, Aquaporin 1, NDFIP1, NME5, CLIC4, Calcyclin, Syntenin 1, ERK1/2, UGCG, SLC29A4, CaMK II delta, HSC70, ARL5, SLC35A5, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, CLCN5, TRIM23, MPC2, SOD1, YIPF5, SLC38A2, MAP1, CALM2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ATP5L, ACTR3, TCP1-epsilon, NPNT, ARP3, 14-3-3, ARMCX3, ACCN3 (ASIC3), COX VIIa-2L, RAGE, 14-3-3 eta, ATP1beta subunit, SNX10 |
| 20 | inorganic cation transmembrane transport | 791 | 8.307E-18 | 3.238E-15 | 76 | ZnT-2, ATP5C, Endothelin-1, UQCRQPC, UQCRH, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, ATP5G, TUSC3, Kv3.3, TRPC5, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, KCNH5, TRPV1, COX VIIa, ATP6V1C1, ZDH13, ATP6M, V-ATPase E subunit, Galpha(i)-specific metabotropic glutamate GPCRs, ATP5B, Dynein, axonemal, heavy chains, ATP6V1B2,  |



|    |                                  |      |           |           |     |   |
|----|----------------------------------|------|-----------|-----------|-----|---|
|    |                                  |      |           |           |     | Serotonin receptor, TRPC, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NR3A, Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, COX Va, ATP5A, Kv9.3, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, CALM2, ATP5L, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit  |
| 21 | small molecule metabolic process | 2145 | 9.364E-18 | 3.319E-15 | 143 | PLP1, PRPS1, PAM, HMGCLL1, GLSK, GAD1, ATP5C, SUCLG1, ELOVL5, Esterase D, Endothelin-1, SULT1A1, ARG2, SC5D, ALDR, SC4MOL, NDUFAB1, DCMC, PDH E2 subunit N6-lipoyllysine, PRKAR2B, Guanylate cyclase, NUDT4P1, GIMAP7, Thioredoxin, ATP6V1A (70kD), PDE, PPT1, SDHB, Guanylate cyclase alpha, ATP5G, TPH2, GUCY1B1, Exostosin-like 2, ORP-family, PKC-beta, Galpha(i)-specific peptide GPCRs, FUT2, ATP5E, CPT-1A, TXNRD1, PIMT, PDK3, Aldose reductase, IP3KA, AMDHD2, InsP6 kinase 3, Carbohydrate sulfotransferases, LPL1, Rho GTPase, PDE4, PRPS2, Dysferlin, TME86B, ATP5B, SYTC, B3GALTL, MMADHC, PKA-reg type II (cAMP-dependent), cPKC (conventional), ELOVL4, Serotonin receptor, ADSS, PDK4, VDAC 1, SUCB1, Osteopontin, ATP5G3, ABHD10, KCY, PKA-reg (cAMP-dependent), HMDH, GUCY1A3, LIPA, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Rab-23, NDUFS6, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, Fatty acid-binding protein, HINT, ENPP4, MDH1, ASAH, SPSY, ATP5A, Carbonic anhydrase XII, Glyoxalase I, SMIT, PDH beta, Galpha(q)-specific peptide GPCRs, Tubulin alpha, DCK, NUDT4, PGAM1, HNMT, SCS-A, ACSL4, RENBP, F262, ATF/CREB, ODP2, Acyl-CoA synthetase, IDI1, OAZIN, Glutaredoxin, KAD6, ATP6V1B, Protein kinase G 2, TMS-1, GKP3, MPTP complex, PDE4A, LPL, NME5, SCOT, Octanoyl-holo-acp, ADHX, ERK1/2, AATC, PKC, PMM2, Guanylate Cyclase 1, soluble, Protein kinase G, RIFK, ERK2 (MAPK1), Ran, OAT, IMPA1, MPC2, Guanine deaminase, PRPS, GDE1, PI3K reg class IA, DCoHM, ATP5L, CALB1, GAD2, PGM2L1, HXK3, ACOXL, Glutaredoxin 1, CMAS |
| 22 | cation transmembrane transport   | 882  | 9.367E-18 | 3.319E-15 | 81  | ZnT-2, ATP5C, Endothelin-1, UQCRQPC, UQCRH, LOC153328, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, ATP5G, TUSC3, Kv3.3, TRPC5, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, KCNH5, TRPV1, COX VIIa, ATP6V1C1, ZDH13, ATP6M, FAM38B, V-ATPase E subunit, Galpha(i)-specific metabotropic glutamate GPCRs, ATP5B, Dynein,  |

|    |   |      |           |           |     |  |
|----|---|------|-----------|-----------|-----|--|
|    |   |      |           |           |     | axonemal, heavy chains, ATP6V1B2, Serotonin receptor, TRPC, SLC7A5, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NR3A, Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, COX Va, ATP5A, Kv9.3, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, SLC29A4, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, CALM2, ATP5L, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit  |
| 23 | regulation of ion transport                         | 1107 | 1.016E-17 | 3.442E-15 | 93  | PLP1, PP2A cat (alpha), Galpha(s)-specific nucleotide-like GPCRs, Rab-3B, HPCA, APJ, RNF207, Endothelin-1, ARG2, NETO2, G-protein beta, JWA, Synaptotagmin I, HSP70, CNR1, Synaptotagmin IV, Synaptotagmin, CNTN1 (F3), NDUFA4, PDE, CNIH2, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, SHISA7, RGS4, Kv3.3, PKC-beta, G-protein beta/gamma, NET6(TSPAN13), SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, KCNH5, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, CRH receptor 2, Rho GTPase, PDE4, Dysferlin, Galpha(i)-specific metabotropic glutamate GPCRs, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, TRPC, VDAC 1, ANT, GRM6, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, Protein kinase G1, CDK5, Kv9.3, Galpha(i)-specific cannabis GPCRs, Galpha(q)-specific peptide GPCRs, MEF2, APRIO, ACSL4, ATF/CREB, Acyl-CoA synthetase, PP2A catalytic, Glutaredoxin, Galpha(s)-specific CRF GPCRs, Kv4.2 channel, Protein kinase G 2, PRNP, MPTP complex, NKCC1, Calmodulin, FLJ45455, STAC2, CLIC4, CaMK II delta, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, MEF2C, Protein kinase G, CALM2, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1 |
| 24 | energy derivation by oxidation of organic compounds | 363  | 1.221E-17 | 3.966E-15 | 49  | COX VIc, ATP5C, SUCLG1, REV-ERBalpha, UQCRQPC, UQCRH, NDUFAB1, NDUFA1, PDH E2 subunit N6-lipoyllysine, NDUFB4, MC4R, NDUFA8, Glycogen phosphorylase, NDUFA4, SDHB, PP1-cat gamma, NDUFB6, NDUFS4, UQCRB, ATP5E, S100, COX VIIa, NDUFB3, ATP5B, NDUFB1, PYGM, COX VIa, SUCB1, PP1-cat, UQCR10, UQCRFS1, Galpha(i)-specific amine GPCRs, NDUFS6, MDH1, COX Va, ATP5A, PDH beta, NDUFA5, MRAP2, SCS-A, GLGB, ODP2, COX VIa-1, Malin, Octanoyl-holo-acp, Galpha(s)-specific peptide GPCRs, ATP5L, COX VIIa-2, COX VIIa-2L  |
| 25 | ion transport                                       | 1658 | 1.468E-17 | 4.578E-15 | 120 | ZnT-2, SMVT, ATP5C, Endothelin-1, UQCRQPC, JWA, UQCRH, TMC4, LOC153328, Pannexin-1, KCNK2, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, Galpha(q)-specific Class A Orphan/other   |

|    |                                     |      |           |           |     |  |
|----|-------------------------------------|------|-----------|-----------|-----|--|
|    |                                     |      |           |           |     | GPCRs, ATP5G, VDAC 3, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, CEACAM, TRPC5, PKC-beta, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, S100, KCNH5, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, COX VIIa, ATP6V1C1, ZDH13, ATP6M, FAM38B, V-ATPase E subunit, NSF, GLRA, GABA-A receptor beta-2 subunit, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, ATP5B, Dynein, axonemal, heavy chains, cPKC (conventional), ATP6V1B2, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, SLC7A5, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NDFIP2, NR3A, Clathrin heavy chain, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, GABA-A receptor alpha-5 subunit, CDK5, PANX2, PAK, Glycine receptor, GABA-A receptor alpha-3 subunit, SLC16A13, COX Va, ATP5A, Glycine receptor beta chain, Kv9.3, Calcineurin A (catalytic), SMIT, Galpha(q)-specific peptide GPCRs, ATP6V1C, CEACAM1, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, TMS-1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, NDFIP1, CLIC4, Calcyclin, SLC29A4, CaMK II delta, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, MPC2, SLC38A2, CALM2, ATP5L, 14-3-3, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit |
| 26 | response to organic cyclic compound | 1988 | 2.065E-17 | 6.110E-15 | 135 | PP2A cat (alpha), HSP90, PAK3, PAM, Galpha(s)-specific nucleotide-like GPCRs, Alpha crystallin B, IRF1, HPCA, Activin A, Endothelin-1, SULT1A1, ARG2, DUOX1, REV-ERBalpha, P2Y11, G-protein beta, JWA, Pannexin-1, TIP47, PRKAR2B, Guanylate cyclase, HSP70, CNR1, Glycogen phosphorylase, Thioredoxin, PDE, Cystatin C, HCN2, Guanylate cyclase alpha, Galpha(q)-specific Class A Orphan/other GPCRs, ATP5G, TPH2, RGS4, GABA-A receptor alpha-1 subunit, ORP-family, Tenascin-C, PKC-beta, G-protein beta/gamma, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, CPT-1A, S100, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Ephrin-A receptor 5, CRH receptor 2, GABA-A receptor beta-2 subunit, Rho GTPase, PDE4, G-protein gamma, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ATP5B, PKA-reg type II (cAMP-dependent), cPKC (conventional), Serotonin receptor, ADSS, TRPC, HTR5A, PYGM, Osteopontin, SMRT, PKA-reg (cAMP-dependent), TReP-132, HMDH, GUCY1A3, Substance P, Histone H2, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, HMP19, Galpha(i)-specific amine GPCRs, PMCA1, NCX1, HCN, BDH, HSP90 beta, TXNIP (VDUP1), Activin beta A, CDK5, PAK,  |

|    |                                    |      |           |           |     |   |
|----|------------------------------------|------|-----------|-----------|-----|---|
|    |                                    |      |           |           |     | Guanylate cyclase (alpha-1/beta-1), Fatty acid-binding protein, ATP5A, Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, H2AFZ, NCOA4 (ARA70), MAFbx, Patched, MEF2, HNMT, ATF/CREB, Hdj-2, Acyl-CoA synthetase, PP2A catalytic, IDI1, AP-4, BMI-1, Glutaredoxin, Galpha(s)-specific CRF GPCRs, ALAS1, Calmodulin, Activin, Aquaporin 1, ERK1/2, AATC, HSC70, PKC, SSTR2, HTR2A, ARPP-19, Guanylate Cyclase 1, soluble, MEF2C, ERK2 (MAPK1), Ran, IGFALS, SSTR1, SOD1, CALM2, FOXP1/2/4 proteins, PI3K reg class IA, ACTR3, NF-I, Midkine, ARP3, 14-3-3, RAGE, 14-3-3 eta, Glutaredoxin 1   |
| 27 | multicellular organism development | 7381 | 2.138E-17 | 6.110E-15 | 346 | PLP1, Cyclin G, FBXO45, NPY, FAM3C, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, RhoN, IRF1, ILDR2, MAL2, SLC35E2B, MEGF10, PTCH2, N-chimaerin, HPCA, APJ, Smooth muscle myosin, EDIL3, Peroxiredoxin, Activin A, Endothelin-1, Trehalase, ARG2, T-plastin, DUOX1, REV-ERBalpha, BRSK2, UQCRQPC, G-protein beta, ALDR, CRTL1, RGS8, MDS028, NckAP1, Lgi4, NKIRAS1, HPCAL4, PSD2, MGF, MEPE, MELC, UNRIP, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, DDX3Y, CNR1, MYL6, Synaptotagmin IV, CITED2, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), HSPA4, JMJD3, Dynein, axonemal, light chains, PDE, Cystatin C, PPT1, IGSF9B, DKK3, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, ATP5G, GPR124, KAL1, PTPN18, RGS4, GABA-A receptor alpha-1 subunit, UGT8, FLRT3, B3GN6, Tenascin-C, PP1-cat gamma, CEACAM, ODF3, TRPC5, KIS, PAFAH gamma, PRDX1, G-protein beta/gamma, B3GN1, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, S100, TXNRD1, AMIGO2, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, Rab-3, MTG16 (CBFA2T3), ATG9B, DNER, ZFH2, Ephrin-A receptor 5, IDUA, IP3KA, CRH receptor 2, CacyBP(SIP), Semaphorin 5A, Tomt, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, CECR2, Carbohydrate sulfotransferases, Rho GTPase, PDE4, Tensin 2, G-protein gamma, PRPS2, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ZNF267, A830006F12Rik, PP4R4, EGF, GlyRA2, ATP5B, Pro-CCK, Dynein, axonemal, heavy chains, BMPR1A, Semaphorin 3E, LOC283174, Myotrophin, NELL1, cPKC (conventional), DLL4, Serotonin receptor, Apelin, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, Sp8, WIF1, Osteopontin, ZNF238, SMRT, NHE6, M-Ras, CREB4, CHAMP, PKA-reg (cAMP-dependent), Lingo1, ANT, PP1-cat, |

|    |                                  |      |           |           |     |  |
|----|----------------------------------|------|-----------|-----------|-----|--|
|    |                                  |      |           |           |     | HMDH, PDLIM2, NR3A, HSBP1, Cables1, ECT2, IL3RA, GRM6, Histone H2, LIPA, LRR51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, HLF, BDH, HSP90 beta, Anillin, TXNIP (VDUP1), COL25A1, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PAK, BEX1, Glycine receptor, Fatty acid-binding protein, FOXP4, MAML1, SOHLH1, IZUMO1, GTL3, ASAH, LPPR4, DYNLT, BRK, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, RTL1, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, STARD7, Cyclin G1, SLC25A46, Glyoxalase I, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NCOA4 (ARA70), WDR47, Creatine kinase, DSCAML1, B-FABP, Azi1, DYNLL, Patched, XK, MEF2, HNMT, MEK4/7, Peg10, ACSL4, CEACAM1, ATF/CREB, RAI1, FN14(TNFRSF12A), Trim45, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, MRLC, eIF4A, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, ALAS1, ATP6V1B, PKD1L1, HSPC138, MPTP complex, ENC1, RHEB2, NKCC1, WDT2, Calmodulin, PGRMC1, Apo-2L(TNFSF10), LOXL2, Endophilin A1, BTBD1, Activin, C1orf43, Aquaporin 1, NME5, CLIC4, Calcyclin, Syntenin 1, SCOT, KCRS, ERK1/2, UGCG, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, SSTR2, SUR1, SLC25A4, K-cadherin (CDH6), MEF2C, SULT4A1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, MEK4(MAP2K4), DACH2, PRKAR1A, IGFALS, UFC1, Nephrocystin-4, DKK1, SSTR1, Guanine deaminase, PRPS, SOD1, KIAA1024, PPP4R2, SLC38A2, SAP102, FSTL5, CALM2, Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, PTCHD1, Galpha(s)-specific peptide GPCRs, ACTR3, ATP6AP2, CALB1, Pcdh19, CD166, DRIL2, NF-I, NPNT, Neuroserpin, Midkine, IRS6(DOK5), ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, SNX10 |
| 28 | regulation of molecular function | 4409 | 2.230E-17 | 6.110E-15 | 236 | Cyclin G, PP2A cat (alpha), HSP90, PAK3, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Alpha crystallin B, G3BP2, N-chimaerin, HPCA, RNF207, Peroxiredoxin, Endothelin-1, ARG2, GSKIP, NETO2, BRSK2, P2Y11, G-protein beta, JWA, Rab-6A, RGS8, BTBD12, CDC18L (CDC6), MOBKL1A, PSD2, MGF, PRKAR2B, MELC, NPFF receptor 2, UNRIP, HSP70, DDX3Y, CNR1, MAPBPIP, PPM1E, PRDX3, Thioredoxin, NDUFA4, HSPA4, Dynein, axonemal, light chains, PDE, Cystatin C, CNIH2, PPT1, SLC39A10, DKK3, NCKP1 subunit, Galpha(q)-specific Class A Orphan/other GPCRs, LMF1, SHISA7, KAL1, Aha1, RGS4, 14-3-3   |

|    |                     |     |           |           |    |   |
|----|---------------------|-----|-----------|-----------|----|---|
|    |                     |     |           |           |    | <p>beta/alpha, ORP-family, Myopodin, CEACAM, PKC-beta, G-protein beta/gamma, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, TORC1, S100, Rab-6, ORP8, Galpha(q)-specific nucleotide-like GPCRs, TIP41, Rab-3, Ephrin-A receptor 5, CRH receptor 2, DKK2, DOK7, Rho GTPase, PDE4, G-protein gamma, SOCS6, Dysferlin, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, PP4R4, Secretogranin V, EGF, Pro-CCK, BMPR1A, MMD, PKA-reg type II (cAMP-dependent), Myotrophin, CAP2, cPKC (conventional), Serotonin receptor, TRPC, COX VIa, ATP6V1H, SMRT, CysLT2 receptor, RGS11, PKA-reg (cAMP-dependent), ANT, PP1-cat, HMDH, TCP1-delta, NDFIP2, KIAA1110, ECT2, HBXIP, PSMD10 (Gankyrin), MID1IP1, CHTF18, CaIDAG-GEFII, ARHGAP18, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, NPR3, Galpha(i)-specific amine GPCRs, CCNI2, NCX1, HCN, Protein kinase G1, CAP1, HSP90 beta, TXNIP (VDUP1), CDK5, PAK, FLJ32001, BEX1, Fatty acid-binding protein, FOXF4, IZUMO1, DYNLT, SPOCK3, BEX2, eIF4A2, BRK, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Cyclin G1, SEC23A, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, Creatine kinase, ACAP1(CENTB1), TBC1D10C, DYNLL, Patched, MEF2, INCA1, NAPB, Sec23, APRIO, MEK4/7, RENBP, F262, CEACAM1, ATF/CREB, Hdj-2, DelGIP1, FEM1B, Acyl-CoA synthetase, PP2A catalytic, AP-4, eIF4A, BMI-1, SNAPS, OAZIN, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, COX VIa-1, PRNP, DNAJA2, TMS-1, MPTP complex, Malin, CAB39L, Calmodulin, DIRAS2, SUMO-3, Apo-2L(TNFSF10), FLJ45455, BTBD1, STAC2, SIPAR, Aquaporin 1, NDFIP1, Securin, ERK1/2, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, SUR1, HTR2A, SLC25A4, ATP1B3, ARPP-19, MEF2C, Protein kinase G, RIFK, ERK2 (MAPK1), Ran, MEK4(MAP2K4), PRKAR1A, TRIM23, DKK1, PARM-1, SOD1, TFIIIB, PPP4R2, SAP102, MAP1, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, CALML6, NF-I, NPNT, Neuroserpin, NRBF2, ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Myospryn, Glutaredoxin 1</p> |
| 29 | aerobic respiration | 211 | 2.285E-17 | 6.110E-15 | 37 | <p>COX VIc, ATP5C, SUCLG1, UQCRQPC, UQCRH, NDUFAB1, NDUFA1, PDH E2 subunit N6-lipoyllysine, NDUFB4, NDUFA8, NDUFA4, SDHB, NDUFB6, NDUFS4, UQCRB, ATP5E, COX VIIa, NDUFB3, ATP5B, NDUFB1, COX VIa, SUCB1, UQCR10, UQCRFS1, NDUFS6, MDH1, COX Va, ATP5A, PDH beta, NDUFA5, SCS-A, ODP2, COX VIa-1, Octanoyl-holo-acc, ATP5L, COX VIIa-2, COX VIIa-2L</p>  |

|    |                                 |      |           |           |    |  |
|----|---------------------------------|------|-----------|-----------|----|--|
| 30 | regulation of secretion by cell | 1045 | 2.351E-17 | 6.110E-15 | 89 | <p>NPY, PAM, Galpha(s)-specific nucleotide-like GPCRs, Rab-3B, Activin A, Endothelin-1, AP-1 gamma subunits, REV-ERBalpha, BRSK2, Synaptotagmin I, CNR1, Synaptotagmin IV, Synaptotagmin, Septin 1, PDE, NCKP1 subunit, Galpha(q)-specific Class A Orphan/other GPCRs, Kv3.3, ORP-family, CEACAM, PKC-beta, SUR, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, Ephrin-A receptor 5, IDUA, CRH receptor 2, NSF, GLRA, SYP, Rho GTPase, PDE4, Rap1GDS1, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, Apelin, Rab-27B, PPID, Osteopontin, Rab-3C, HMDH, NR3A, Substance P, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, Protein kinase G1, Activin beta A, CDK5, Glycine receptor, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, DYNLL, MEF2, ACSL4, F262, CEACAM1, ATF/CREB, DelGIP1, Acyl-CoA synthetase, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, NKCC1, Calmodulin, NELL2, Activin, Syntenin 1, SCOT, PKC, SUR1, HTR2A, MEF2C, Protein kinase G, Calcineurin A (beta), MPC2, CALM2, Cyclophilin A, Glutaredoxin 1</p> |
| 31 | regulation of system process    | 1019 | 4.781E-17 | 1.202E-14 | 87 | <p>HSP90, Galpha(s)-specific nucleotide-like GPCRs, GLSK, Smooth muscle myosin, RNF207, Activin A, Endothelin-1, ARG2, NETO2, MELC, Guanylate cyclase, HSP70, PDE, CNII2, IGSF9B, Guanylate cyclase alpha, Galpha(q)-specific Class A Orphan/other GPCRs, SHISA7, RGS4, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, S100, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, ZFH2, CRH receptor 2, GLRA, Rho GTPase, PDE4, Galpha(i)-specific metabotropic glutamate GPCRs, Pro-CCK, LOC283174, Myotrophin, cPKC (conventional), Serotonin receptor, Apelin, TRPC, PKA-reg (cAMP-dependent), ANT, HMDH, GUCY1A3, Substance P, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, PMCA1, NCX1, HCN, Protein kinase G1, Calponin-1, Activin beta A, PAK, Guanylate cyclase (alpha-1/beta-1), Glycine receptor, Fatty acid-binding protein, Calcineurin A (catalytic), Galpha(q)-specific peptide GPCRs, MAFbx, MEF2, MRLC, Galpha(s)-specific CRF GPCRs, MPTP complex, Calmodulin, FLJ45455, Activin, Aquaporin 1, CaMK II delta, PKC, SSTR2, SUR1, HTR2A, SLC25A4, Guanylate Cyclase 1, soluble, MEF2C, Protein kinase G, SOD1, CALM2, FOXP1/2/4 proteins, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, NPNT, 14-3-3, RAGE, ATP1beta subunit, Myospryn</p>                                      |

|    |                                    |      |           |           |    |   |
|----|------------------------------------|------|-----------|-----------|----|---|
| 32 | regulation of secretion            | 1159 | 6.467E-17 | 1.576E-14 | 94 | NPY, PAM, Galpha(s)-specific nucleotide-like GPCRs, Rab-3B, Activin A, Endothelin-1, AP-1 gamma subunits, REV-ERBalpha, BRSK2, Synaptotagmin I, Guanylate cyclase, CNR1, Synaptotagmin IV, Synaptotagmin, Septin 1, PDE, NCKP1 subunit, Galpha(q)-specific Class A Orphan/other GPCRs, Kv3.3, ORP-family, CEACAM, PKC-beta, SUR, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, S100, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, Ephrin-A receptor 5, IDUA, CRH receptor 2, NSF, GLRA, SYP, Rho GTPase, PDE4, Rap1GDS1, Galpha(i)-specific metabotropic glutamate GPCRs, Secretogranin V, EGF, Pro-CCK, cPKC (conventional), Serotonin receptor, Apelin, Rab-27B, PPID, Osteopontin, Rab-3C, HMDH, NR3A, Substance P, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, Protein kinase G1, Activin beta A, CDK5, Glycine receptor, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Galpha(q)-specific peptide GPCRs, DYNLL, MEF2, ACSL4, F262, CEACAM1, ATF/CREB, DelGIP1, Acyl-CoA synthetase, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, NKCC1, Calmodulin, NELL2, Activin, Aquaporin 1, Syntenin 1, SCOT, PKC, SUR1, HTR2A, MEF2C, Protein kinase G, Calcineurin A (beta), MPC2, CALM2, Cyclophilin A, Galpha(s)-specific peptide GPCRs, Glutaredoxin 1 |
| 33 | regulation of transporter activity | 485  | 7.543E-17 | 1.782E-14 | 56 | PP2A cat (alpha), HPCA, RNF207, Endothelin-1, NETO2, G-protein beta, HSP70, NDUFA4, PDE, CNIH2, SHISA7, G-protein beta/gamma, SUR, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, Galpha(q)-specific nucleotide-like GPCRs, PDE4, Dysferlin, cPKC (conventional), Serotonin receptor, TRPC, ANT, NDFIP2, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, HCN, Protein kinase G1, CDK5, SMIT, Galpha(q)-specific peptide GPCRs, MEF2, APRIO, PP2A catalytic, Glutaredoxin, Galpha(s)-specific CRF GPCRs, PRNP, MPTP complex, Calmodulin, FLJ45455, STAC2, NDFIP1, CaMK II delta, PKC, SUR1, SLC25A4, ATP1B3, MEF2C, Protein kinase G, CALM2, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1   |
| 34 | trans-synaptic signaling           | 702  | 9.199E-17 | 2.109E-14 | 69 | PLP1, NPY, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, GLSK, GAD1, Synaptotagmin I, Guanylate cyclase, CNR1, Synaptotagmin IV, Synaptotagmin, PDE, CNIH2, PPT1, Guanylate cyclase alpha, VDAC 3, GABA-A receptor alpha-1 subunit, GUCY1B1, SDFR1, Galpha(i)-specific peptide GPCRs, P/Q-type calcium channel alpha-1A subunit, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, GPR176, CaMK IV, GLRA, GABA-A  |



|    |  |      |           |           |     |  |
|----|--|------|-----------|-----------|-----|--|
|    |  |      |           |           |     | receptor beta-2 subunit, SYP, Rho GTPase, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, cPKC (conventional), Serotonin receptor, GABA-A receptor alpha-4 subunit, HTR5A, VDAC 1, GUCY1A3, Substance P, GRM6, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, GABA-A receptor alpha-5 subunit, CDK5, PAK, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, Glycine receptor, GABA-A receptor alpha-3 subunit, Glycine receptor beta chain, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, Galpha(q)-specific peptide GPCRs, MEF2, NAPB, SNAPs, Kv4.2 channel, MPTP complex, FLJ45455, Syntenin 1, ERK1/2, PKC, HTR2A, Guanylate Cyclase 1, soluble, MEF2C, ERK2 (MAPK1), PTCHD1, Galpha(s)-specific peptide GPCRs, GAD2   |
| 35 | regulation of transmembrane transporter activity | 443  | 1.140E-16 | 2.539E-14 | 53  | PP2A cat (alpha), HPCA, RNF207, Endothelin-1, NETO2, G-protein beta, HSP70, NDUFA4, PDE, CNIH2, SHISA7, G-protein beta/gamma, SUR, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, Galpha(q)-specific nucleotide-like GPCRs, PDE4, Dysferlin, cPKC (conventional), Serotonin receptor, TRPC, ANT, Galpha(q)-specific amine GPCRs, Galpha(i)-specific amine GPCRs, HCN, Protein kinase G1, CDK5, Galpha(q)-specific peptide GPCRs, MEF2, APRIO, PP2A catalytic, Glutaredoxin, Galpha(s)-specific CRF GPCRs, PRNP, MPTP complex, Calmodulin, FLJ45455, STAC2, CaMK II delta, PKC, SUR1, SLC25A4, ATP1B3, MEF2C, Protein kinase G, CALM2, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1  |
| 36 | regulation of signaling                          | 4708 | 1.321E-16 | 2.862E-14 | 245 | NPY, PP2A cat (alpha), HSP90, PAK3, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, IRF1, PTCH2, N-chimaerin, APJ, Peroxiredoxin, Activin A, Endothelin-1, GSKIP, NETO2, GHITM, REV-ERBalpha, BRSK2, JWA, ALDR, RGS8, CNOT7, MDS028, Importin (karyopherin)-alpha, GPR137C, NKIRAS1, PSD2, MGF, TIP47, PRKAR2B, NPFF receptor 2, UNRIP, Synaptotagmin I, Guanylate cyclase, ARL6, HSP70, SCRT2, DDX3Y, CNR1, MAPBPIP, Synaptotagmin IV, CITED2, DnaJB9, Synaptotagmin, Thioredoxin, Dynein, axonemal, light chains, PDE, CNIH2, PPT1, SLC39A10, IGSF9B, DKK3, NCKP1 subunit, Guanylate cyclase alpha, Galpha(q)-specific Class A Orphan/other GPCRs, GPR124, SHISA7, PTPN18, RGS4, 14-3-3 beta/alpha, Kv3.3, ORP-family, CEACAM, PKC-beta, PRDX1, G-protein beta/gamma, SDFR1, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, TORC1, CPT-1A, S100, ORP8, VWA2, Galpha(q)-specific nucleotide-like GPCRs, ZDH13, Aldose reductase, Rab-3, TM2D3, APOL3, Ephrin-A receptor 5, IP3KA, CRH receptor 2, Semaphorin |

|    |                            |      |           |           |     |   |
|----|----------------------------|------|-----------|-----------|-----|---|
|    |                            |      |           |           |     | 5A, Adropin, NSF, GLRA, DKK2, SYP, Rho GTPase, PDE4, Tensin 2, G-protein gamma, UBE2D1, SOCS6, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, A830006F12Rik, Secretogranin V, EGF, BMPR1A, LOC283174, PKA-reg type II (cAMP-dependent), cPKC (conventional), DLL4, Serotonin receptor, CHMP5, Apelin, TRPC, WIF1, Osteopontin, SMRT, CysLT2 receptor, NHE6, RGS11, PKA-reg (cAMP-dependent), RNF152, ANT, PP1-cat, HMDH, NDFIP2, NR3A, GUCY1A3, KIAA1110, ECT2, Substance P, HBXIP, PSMD10 (Gankyrin), GRM6, CalDAG-GEFII, Histone H2, MCT1 (SLC16A1), ARHGAP18, TMEM14A, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, DAT1, PMCA1, Rab-23, NCX1, HCN, HSP90 beta, Vinexin, Activin beta A, CDK5, PAK, Guanylate cyclase (alpha-1/beta-1), Glycine receptor, Fatty acid-binding protein, HINT, Sgk223, IZUMO1, LPPR4, DYNLT, BRK, Nek8, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, ATP6V1C, Histone H2B, TBC1D10C, MRAP2, VIP32, DYNLL, Patched, TNK1, MEF2, INCA1, APRIO, MEK4/7, Peg10, ACSL4, F262, CEACAM1, ATF/CREB, Hdj-2, FN14(TNFRSF12A), FEM1B, Acyl-CoA synthetase, PP2A catalytic, BMI-1, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, PRNP, TMS-1, MPTP complex, RHEB2, NKCC1, PDE4A, Calmodulin, DIRAS2, NELL2, FLJ31818, Apo-2L(TNFSF10), PDE11A, FLJ45455, Activin, NDFIP1, KCTD16, NME5, Syntenin 1, SCOT, ERK1/2, AATC, UGCG, CaMK II delta, PKC, SUR1, HTR2A, SLC25A4, ARPP-19, Guanylate Cyclase 1, soluble, MEF2C, ERK2 (MAPK1), Calcineurin A (beta), MEK4(MAP2K4), PRKAR1A, Nephrocystin-4, DKK1, MPC2, SOD1, KIAA1024, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, ATP6AP2, CALB1, NPNT, Midkine, IRS6(DOK5), PXDN, 14-3-3, RAGE, 14-3-3 eta, Myospryn, Glutaredoxin 1 |
| 37 | cellular metabolic process | 9304 | 1.494E-16 | 3.147E-14 | 409 | PLP1, FBXO45, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, HMGCLL1, ZYG11B, CPSF1, Angiopoietin 1, AEBP1, GLSK, Rab-3B, COX VIc, GAD1, C1D, TINP1, ZH11B, ATP5C, SUCLG1, FLJ12671, ELOVL5, Peroxiredoxin, Activin A, UBL5, Esterase D, Endothelin-1, SULT1A1, Trehalase, PSMB5, ARG2, DUOX1, REV-ERBalpha, BRSK2, UQCRQP, UBXD3, LAS1L, SC5D, JWA, ALDR, UQCRH, Rab-6A, SC4MOL, MRPS6, PSMA5, CNOT7, NFKBIL2, NDUFAB1, Importin (karyopherin)-alpha, BTBD12, NDUFA1, CDC18L (CDC6), MRPL1, TTLL9, MOBKL1A, DTX2, MCM6, DCMC, PDH E2 subunit N6-lipoyllysine, PRKAR2B, DPY19L1, NDUFB4, MC4R, UNRIP, NDUFA8, KLHL12, Guanylate   |

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|--|--|--|--|--|---|
|  |  |  |  |  | <p>cyclase, ARL6, HSP70, DDX3Y, Glycogen phosphorylase, PPM1E, NUDT4P1, GIMAP7, DnaJB9, Synaptotagmin, PRDX3, NDUFA4, ATP6V1A (70kD), JMJD3, PDE, Tcf15, PPT1, SDHB, MGAT4A, Karyopherin alpha 2, TM9SF2, Guanylate cyclase alpha, Galpha(q)-specific Class A Orphan/other GPCRs, LMF1, ATP5G, TPH2, RAB39B, PTPN18, BTBD18, TUSC3, UGT8, GUCY1B1, Exostosin-like 2, SEL1, ORP-family, B3GN6, Myopodin, PP1-cat gamma, PKC-beta, KIS, PRDX1, B3GN1, NDUFB6, ABO system transferase, NDUFS4, Galpha(i)-specific peptide GPCRs, CALM3, FUT2, KLHL13, UQCRB, ATP5E, CPT-1A, S100, Rab-6, TXNRD1, ORP8, LASS6, PIMT, PDK3, COX VIIa, ZDH13, Aldose reductase, NDUFB3, Rab-3, MTG16 (CBFA2T3), ATG9B, DNER, Ephrin-A receptor 5, IDUA, IP3KA, CRH receptor 2, AMDHD2, InsP6 kinase 3, GRAIL, UBA1L, RPL9, Tomt, CaMK IV, FBXO2, CECR2, Carbohydrate sulfotransferases, LACTB2, LPL1, MOCS2(small), Rho GTPase, PDE4, GTPBP3, Tensin 2, UBE2D1, PRPS2, SOCS6, Dysferlin, Ephrin-A receptor 4, TMEM86B, Secretogranin V, EGF, ATP5B, PPase (inorganic), SYTC, Dynein, axonemal, heavy chains, B3GALT, BMPR1A, MMADHC, MMD, PKA-reg type II (cAMP-dependent), B3GNT4, Myotrophin, cPKC (conventional), SF3A2, NDUFB1, ELOVL4, PSMA1, Serotonin receptor, CHMP5, ADSS, PPID, TRPC, PYGM, MOC2B, PDK4, VDAC 1, COX VIa, SUCB1, Osteopontin, ATP5G3, ABHD10, KCY, PC4, CHAMP, PKA-reg (cAMP-dependent), TRP-132, RNF152, ANT, PP1-cat, HMDH, UQCR10, NDFIP2, GUCY1A3, VTA1, Clathrin heavy chain, StARD4, CHTF18, Histone H2, LIPA, KLHL35, COPS4, LRRC51, Galpha(q)-specific amine GPCRs, UQCRFS1, Ephrin-A receptors, MRPL47, Histone H2A, Galpha(i)-specific amine GPCRs, Rab-23, SLBP, Protein kinase G1, HSP90 beta, PMS2L3, NDUFS6, Activin beta A, BRMS1L, CDK5, DUS3L, PAK, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, Fatty acid-binding protein, HINT, ENPP4, MAML1, KIAA0143, Sgk223, MDH1, GTL3, ASAH, GNT-IV, LPPR4, Atg101, TMEM74, SPOCK3, SPSY, COX Va, eIF4A2, BRK, ATP5A, Nek8, Selenoprotein P, Carbonic anhydrase XII, Calcineurin A (catalytic), LSM2, TOP1MT, 4833424O15Rik, B3GT2, SLC25A46, Glyoxalase I, DDX51, SMIT, FBI-1 (Pokemon), PDH beta, Galpha(q)-specific peptide GPCRs, MAFbx, SNAP190, NDUFA5, Tubulin alpha, Creatine kinase, DCK, MRAP2, PAP-II, NUDT4, DYNLL, TNK1, MEF2, ADAR3, PGAM1, HNMT, APRIO, SCS-A, MEK4/7, ACSL4, RENBP, F262, ATF/CREB, GLGB, ODP2, DelGIP1, Trim45, RSL24D1, FEM1B, Acyl-CoA synthetase, PP2A catalytic, GAS41, IDI1, ZFAND2A, eIF4A, BMI-1, OAZIN, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), RNF175, Galpha(s)-specific</p> |
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|    |  |     |           |           |    |   |
|----|--|-----|-----------|-----------|----|---|
|    |  |     |           |           |    | CRF GPCRs, LAMP2, COX VIa-1, KAD6, ALAS1, ATP6V1B, Quinone oxidoreductase, JKAMP, Protein kinase G 2, PRNP, DNAJA2, TMS-1, GKP3, MPTP complex, ENC1, Malin, C1orf59, PDE4A, Calmodulin, LPL, SUMO-3, PGRMC1, SET1B, LOXL2, KLHL2, NOLA3 (NOP10), BTBD1, Activin, SIPAR, NDFIP1, NME5, SCOT, Octanoyl-holo-acp, KCRS, Securin, ADHX, ERK1/2, Carboxypeptidase M, snRNP-G, AATC, UGCG, SLC29A4, TRUB1, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, ABTB1, PMM2, SLC25A4, Guanylate Cyclase 1, soluble, SULT4A1, MRPL33, Protein kinase G, RIFK, ERK2 (MAPK1), Calcineurin A (beta), DREV1, Ran, OAT, MEK4(MAP2K4), PRKAR1A, IMPA1, TRIM23, UFC1, MPC2, Guanine deaminase, PRPS, SOD1, TFIIB, YIPF5, dJ222E13.2, PPP4R2, GDE1, CALM2, Cyclophilin A, FOXP1/2/4 proteins, PI3K reg class IA, DCoHM, Galpha(s)-specific peptide GPCRs, ATP5L, ATP6AP2, SRm300, GAD2, SIAH3, PGM2L1, NF-I, MRPL3, B930041F14Rik, HXK3, COX VIIa-2, ACOXL, NRBF2, IRS6(DOK5), PXDN, 14-3-3, COX VIIa-2L, RAGE, Glutaredoxin 1, CMAS, CHST6 |
| 38 | ribose phosphate metabolic process     | 479 | 1.838E-16 | 3.770E-14 | 55 | PRPS1, ATP5C, SUCLG1, ELOVL5, SULT1A1, DCMC, PDH E2 subunit N6-lipoyllysine, Guanylate cyclase, Glycogen phosphorylase, NUDT4P1, GIMAP7, ATP6V1A (70kD), PDE, PPT1, Guanylate cyclase alpha, ATP5G, GUCY1B1, ATP5E, Rho GTPase, PDE4, PRPS2, ATP5B, ELOVL4, ADSS, PDK4, SUCB1, ATP5G3, KCY, HMDH, GUCY1A3, Ephrin-A receptors, Rab-23, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, HINT, ATP5A, PDH beta, NUDT4, PGAM1, SCS-A, ACSL4, F262, ODP2, Acyl-CoA synthetase, KAD6, PDE4A, NME5, Guanylate Cyclase 1, soluble, RIFK, Ran, MPC2, Guanine deaminase, PRPS, ATP5L, HXK3   |
| 39 | regulation of trans-synaptic signaling | 783 | 1.943E-16 | 3.884E-14 | 73 | Galpha(s)-specific nucleotide-like GPCRs, Endothelin-1, NETO2, PRKAR2B, Synaptotagmin I, CNR1, Synaptotagmin IV, Synaptotagmin, PDE, CNIH2, PPT1, SHISA7, RGS4, Kv3.3, PKC-beta, SDFR1, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, TORC1, S100, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, IP3KA, CRH receptor 2, GLRA, SYP, Rho GTPase, PDE4, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, PKA-reg type II (cAMP-dependent), cPKC (conventional), Serotonin receptor, PKA-reg (cAMP-dependent), NR3A, Substance P, GRM6, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, HCN, CDK5, PAK, Glycine receptor, Fatty acid-binding protein, LPPR4, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Galpha(q)-specific peptide GPCRs, MEF2, APRIO, ATF/CREB, Galpha(s)-specific CRF GPCRs, PRNP,  |

|    |                                  |      |           |           |     |  |
|----|----------------------------------|------|-----------|-----------|-----|--|
|    |                                  |      |           |           |     | RHEB2, NKCC1, PDE4A, Calmodulin, FLJ45455, ERK1/2, PKC, HTR2A, MEF2C, ERK2 (MAPK1), Calcineurin A (beta), DKK1, CALM2, CALB1, 14-3-3, RAGE, 14-3-3 eta   |
| 40 | ribonucleotide metabolic process | 468  | 2.821E-16 | 5.498E-14 | 54  | PRPS1, ATP5C, SUCLG1, ELOVL5, SULT1A1, DCMC, PDH E2 subunit N6-lipoyllysine, Guanylate cyclase, NUDT4P1, GIMAP7, ATP6V1A (70kD), PDE, PPT1, Guanylate cyclase alpha, ATP5G, GUCY1B1, ATP5E, Rho GTPase, PDE4, PRPS2, ATP5B, ELOVL4, ADSS, PDK4, SUCB1, ATP5G3, KCY, HMDH, GUCY1A3, Ephrin-A receptors, Rab-23, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, HINT, ATP5A, PDH beta, NUDT4, PGAM1, SCS-A, ACSL4, F262, ODP2, Acyl-CoA synthetase, KAD6, PDE4A, NME5, Guanylate Cyclase 1, soluble, RIFK, Ran, MPC2, Guanine deaminase, PRPS, ATP5L, HXK3  |
| 41 | proton transmembrane transport   | 192  | 3.347E-16 | 6.364E-14 | 34  | ATP5C, UQCRQPC, UQCRH, NDUFA4, ATP6V1A (70kD), ATP5G, ATP5E, COX VIIa, ATP6V1C1, ATP6M, V-ATPase E subunit, ATP5B, Dynein, axonemal, heavy chains, ATP6V1B2, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, UQCRFS1, COX Va, ATP5A, ATP6V1C, COX VIa-1, ATP6V1B, MPTP complex, ATP6V0B, ATP6V1E, SLC25A4, CLCN5, ATP5L, COX VIIa-2L   |
| 42 | developmental process            | 8639 | 3.590E-16 | 6.663E-14 | 385 | PLP1, Cyclin G, FBXO45, NPY, FAM3C, PP2A cat (alpha), PRPS1, HSP90, PAK3, PAM, Cadherin 8, Galpha(s)-specific nucleotide-like GPCRs, Angiopoietin 1, Semaphorin 3C, Alpha crystallin B, RhoN, IRF1, ILDR2, MAL2, SLC35E2B, MEGF10, PTCH2, N-chimaerin, HPCA, APJ, Smooth muscle myosin, EDIL3, Peroxiredoxin, Activin A, Endothelin-1, Trehalase, AP-1 gamma subunits, ARG2, T-plastin, DUOX1, REV-ERBalpha, BRSK2, UQCRQPC, G-protein beta, ALDR, CRTL1, RGS8, MDS028, Importin (karyopherin)-alpha, NckAP1, DNAH1, Lgi4, Pannexin-1, NKIRAS1, HPCAL4, PSD2, MGF, MEPE, MELC, UNRIP, KLHL12, Synaptotagmin I, Guanylate cyclase, ARL6, KCNK2, HSP70, DDX3Y, CNR1, MYL6, Synaptotagmin IV, CITED2, SLIRP, DnaJB9, Synaptotagmin, PRDX3, CNTN1 (F3), HSPA4, JMJD3, Dynein, axonemal, light chains, PDE, Cystatin C, Tcf5, PPT1, IGSF9B, DKK3, NCKP1 subunit, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, IMPG2, ATP5G, GPR124, KAL1, PTPN18, RGS4, BTBD18, GABA-A receptor alpha-1 subunit, UGT8, FLRT3, ORP-family, B3GN6, Tenascin-C, PP1-cat gamma, CEACAM, ODF3, TRPC5, KIS, PAFAH gamma, PRDX1, G-protein beta/gamma, B3GN1, SDFR1, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, S100, TXNRD1, ORP8, AMIGO2, PIMT, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, Rab-3, MTG16 (CBFA2T3), ATG9B, TM2D3, DNER, ZFH2, Ephrin-A receptor 5, |

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|--|--|--|--|--|---|
|  |  |  |  |  | <p>IDUA, IP3KA, CRH receptor 2, CacyBP(SIP), Semaphorin 5A, Tomt, CaMK IV, GLRA, DKK2, ZNF499, GABA-A receptor beta-2 subunit, CECR2, SYP, Carbohydrate sulfotransferases, Rho GTPase, PDE4, Tensin 2, G-protein gamma, PRPS2, Dysferlin, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, Elastin, ChREBP, ZNF267, A830006F12Rik, PP4R4, EGF, GlyRA2, ATP5B, Pro-CCK, XKR4, Dynein, axonemal, heavy chains, BMPR1A, Semaphorin 3E, LOC283174, Myotrophin, NELL1, CAP2, cPKC (conventional), DLL4, Serotonin receptor, Apelin, GABA-A receptor alpha-4 subunit, TRPC, HTR5A, Sp8, VDAC 1, WIF1, NDRG3, Osteopontin, ATP5G3, ZNF238, SMRT, NHE6, M-Ras, CREB4, CHAMP, PKA-reg (cAMP-dependent), Lingo1, ANT, PP1-cat, HMDH, PDLIM2, NR3A, HSBP1, Cables1, ECT2, Clathrin heavy chain, IL3RA, GRM6, CHTF18, CalDAG-GEFII, Histone H2, LIPA, LRRC51, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, NPR3, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, Rab-23, NCX1, HCN, Protein kinase G1, HLF, BDH, CAP1, HSP90 beta, Anillin, TXNIP (VDUP1), COL25A1, NDUFS6, Activin beta A, GABA-A receptor alpha-5 subunit, Zeta-sarcoglycan, CDK5, PAK, BEX1, Glycine receptor, Fatty acid-binding protein, FOXP4, MAML1, SOHLH1, IZUMO1, GTL3, ASAH, LPPR4, DYNLT, BRK, ATP5A, Glycine receptor beta chain, Nek8, Selenoprotein P, CAPZA, RTL1, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCR, STARD7, Cyclin G1, SLC25A46, Glyoxalase I, SMIT, FBI-1 (Pokemon), Galpha(q)-specific peptide GPCRs, H2AFZ, Histone H2B, NCOA4 (ARA70), WDR47, Creatine kinase, DSCAML1, B-FABP, Azi1, DYNLL, Patched, TNK1, XK, MEF2, HNMT, APRIO, MEK4/7, Peg10, ACSL4, CEACAM1, ATF/CREB, RAI1, Hdj-2, FN14(TNFRSF12A), Trim45, G-protein beta-4, FEM1B, Acyl-CoA synthetase, PP2A catalytic, MRLC, eIF4A, BMI-1, SNAPs, eIF2S1, Glutaredoxin, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, ALAS1, ATP6V1B, PKD1L1, PRNP, HSPC138, MPTP complex, ENC1, RHEB2, NKCC1, WDT2, Calmodulin, NELL2, PGRMC1, Apo-2L(TNFSF10), LOXL2, FLJ45455, Endophilin A1, BTBD1, Activin, C1orf43, Aquaporin 1, NME5, CLIC4, Calcyclin, Syntenin 1, SCOT, KCRS, Securin, ADHX, ERK1/2, Carboxypeptidase M, AATC, UGCG, Anks4b, NFIC, CaMK II delta, HSC70, PI3K reg class IA (p55-gamma), PKC, SSTR2, SUR1, HTR2A, SLC25A4, K-cadherin (CDH6), MEF2C, SULTA1, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), LISCH7, Ran, MEK4(MAP2K4), DACH2, PRKAR1A, IGFALS, UFC1, Nephrocystin-4, DKK1, SSTR1, Guanine deaminase, PRPS, SOD1, KIAA1024, PPP4R2, SLC38A2, SAP102, FSTL5, CALM2,</p> |
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|    |                         |      |           |           |     |  |
|----|-------------------------|------|-----------|-----------|-----|--|
|    |                         |      |           |           |     | Cyclophilin A, FOXP1/2/4 proteins, Aggrecanase-2, PI3K reg class IA, PTCHD1, Galpha(s)-specific peptide GPCRs, TCP1-alpha, ACTR3, ATP6AP2, CALB1, Pcdh19, CD166, DRIL2, NF-I, NPNT, Neuroserpin, Midkine, IRS6(DOK5), ARP3, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit, Glutaredoxin 1, SNX10  |
| 43 | head development        | 1457 | 3.957E-16 | 7.174E-14 | 107 | PLP1, Cyclin G, FBXO45, NPY, HPCA, Activin A, UQCRQPC, G-protein beta, RGS8, Synaptotagmin I, ARL6, HSP70, Synaptotagmin IV, Synaptotagmin, CNTN1 (F3), JMJD3, Cystatin C, PPT1, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, RGS4, FLRT3, PAFAH gamma, G-protein beta/gamma, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, AMIGO2, ZFH2, Ephrin-A receptor 5, CRH receptor 2, Semaphorin 5A, Rho GTPase, G-protein gamma, Dynein, axonemal, heavy chains, BMPR1A, Myotrophin, Serotonin receptor, HTR5A, ZNF238, SMRT, Histone H2, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, PMCA1, NCX1, HCN, Protein kinase G1, BDH, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, Fatty acid-binding protein, Selenoprotein P, Calcineurin A (catalytic), Cyclin G1, SLC25A46, Galpha(q)-specific peptide GPCRs, Histone H2B, Creatine kinase, DSCAML1, B-FABP, DYNLL, Patched, MEF2, HNMT, ATF/CREB, G-protein beta-4, Acyl-CoA synthetase, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)-specific CRF GPCRs, Calmodulin, Activin, Aquaporin 1, NME5, SCOT, ERK1/2, HSC70, SSTR2, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), Ran, UFC1, DKK1, SSTR1, SLC38A2, CALM2, FOXP1/2/4 proteins, PTCHD1, Galpha(s)-specific peptide GPCRs, ATP6AP2, Pcdh19, NF-I, Midkine, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit |
| 44 | transmembrane transport | 1628 | 4.478E-16 | 7.934E-14 | 115 | ZnT-2, SLC35E2B, SMVT, ATP5C, Endothelin-1, UQCRQPC, JWA, UQCRH, TMC4, LOC153328, Pannexin-1, KCNK2, HSP70, Tim17, NDUFA4, ATP6V1A (70kD), SLC39A10, HCN2, ATP5G, VDAC 3, GABA-A receptor alpha-1 subunit, TUSC3, Kv3.3, TRPC5, SLC25A45, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, ATP5E, CPT-1A, S100, KCNH5, TRPV1, COX VIIa, ATP6V1C1, ZDH13, ATP6M, FAM38B, SLC2A13, V-ATPase E subunit, GLRA, GABA-A receptor beta-2 subunit, TIMM17, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, ATP5B, Dynein, axonemal, heavy chains, ATP6V1B2, Serotonin receptor, GABA-A receptor alpha-4 subunit, TRPC, SLC7A5, VDAC 1, COX VIa, CLCN4, ATP6V1H, ATP5G3, NHE6, ANT, UQCR10, NR3A, MCT1 (SLC16A1), Galpha(q)-specific amine GPCRs, UQCRFS1, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, HCN, GABA-A receptor alpha-5  |

|    |  |      |           |           |     |  |
|----|--|------|-----------|-----------|-----|--|
|    |  |      |           |           |     | subunit, PANX2, Glycine receptor, Fatty acid-binding protein, TOM22, GABA-A receptor alpha-3 subunit, SLC16A13, COX Va, ATP5A, Glycine receptor beta chain, Kv9.3, SMIT, Galpha(q)-specific peptide GPCRs, ATP6V1C, COX VIa-1, ATP6V1B, Kv4.2 channel, PKD1L1, MPTP complex, NKCC1, ATP6V0B, Calmodulin, ATP6V1E, Aquaporin 1, CLIC4, Calcyclin, SLC29A4, HSC70, SLC35A5, PKC, SUR1, HTR2A, SLC25A4, ATP1B3, CLCN5, MPC2, SLC38A2, CALM2, ATP5L, 14-3-3, ACCN3 (ASIC3), COX VIIa-2L, ATP1beta subunit  |
| 45 | modulation of chemical synaptic transmission | 781  | 5.703E-16 | 9.880E-14 | 72  | Galpha(s)-specific nucleotide-like GPCRs, Endothelin-1, NETO2, PRKAR2B, Synaptotagmin I, CNR1, Synaptotagmin IV, Synaptotagmin, PDE, CNIH2, PPT1, SHISA7, RGS4, Kv3.3, PKC-beta, SDFR1, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, TORC1, S100, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, IP3KA, CRH receptor 2, GLRA, SYP, Rho GTPase, PDE4, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, PKA-reg type II (cAMP-dependent), cPKC (conventional), Serotonin receptor, PKA-reg (cAMP-dependent), NR3A, Substance P, GRM6, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Galpha(i)-specific amine GPCRs, HCN, CDK5, PAK, Glycine receptor, LPPR4, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Galpha(q)-specific peptide GPCRs, MEF2, APRIO, ATF/CREB, Galpha(s)-specific CRF GPCRs, PRNP, RHEB2, NKCC1, PDE4A, Calmodulin, FLJ45455, ERK1/2, PKC, HTR2A, MEF2C, ERK2 (MAPK1), Calcineurin A (beta), DKK1, CALM2, CALB1, 14-3-3, RAGE, 14-3-3 eta                        |
| 46 | brain development                            | 1385 | 6.591E-16 | 1.117E-13 | 103 | PLP1, Cyclin G, FBXO45, NPY, HPCA, Activin A, UQCRQPC, G-protein beta, RGS8, Synaptotagmin I, ARL6, HSP70, Synaptotagmin IV, Synaptotagmin, CNTN1 (F3), JMJD3, Cystatin C, PPT1, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, RGS4, PAFAH gamma, G-protein beta/gamma, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, AMIGO2, ZFH2, Ephrin-A receptor 5, CRH receptor 2, Semaphorin 5A, Rho GTPase, G-protein gamma, Dynein, axonemal, heavy chains, BMPR1A, Myotrophin, Serotonin receptor, HTR5A, ZNF238, SMRT, Histone H2, Ephrin-A receptors, Histone H2A, Galpha(i)-specific amine GPCRs, PMCA1, NCX1, HCN, Protein kinase G1, BDH, Activin beta A, GABA-A receptor alpha-5 subunit, CDK5, PAK, Fatty acid-binding protein, Selenoprotein P, Calcineurin A (catalytic), Cyclin G1, SLC25A46, Galpha(q)-specific peptide GPCRs, Histone H2B, Creatine kinase, DSCAML1, B-FABP, DYNLL, Patched, MEF2, HNMT, ATF/CREB, G-protein beta-4, Acyl-CoA synthetase, BMI-1, SNAPs, DLC1 (Dynein LC8a), Galpha(s)- |



|    |                               |      |           |           |     |  |
|----|-------------------------------|------|-----------|-----------|-----|--|
|    |                               |      |           |           |     | specific CRF GPCRs, Calmodulin, Activin, Aquaporin 1, NME5, SCOT, HSC70, SSTR2, MEF2C, Protein kinase G, Calcineurin A (beta), Ran, UFC1, DKK1, SSTR1, SLC38A2, CALM2, FOXP1/2/4 proteins, PTCHD1, Galpha(s)-specific peptide GPCRs, Pcdh19, NF-1, Midkine, 14-3-3, RAGE, 14-3-3 eta, ATP1beta subunit   |
| 47 | cellular homeostasis          | 1389 | 7.981E-16 | 1.324E-13 | 103 | PP2A cat (alpha), HSP90, Galpha(s)-specific nucleotide-like GPCRs, APJ, Peroxiredoxin, Endothelin-1, REV-ERBalpha, G-protein beta, CNR1, Glycogen phosphorylase, PRDX3, Thioredoxin, ATP6V1A (70kD), PDE, PPT1, SLC39A10, Galpha(q)-specific Class A Orphan/other GPCRs, TUSC3, TRPC5, PKC-beta, PRDX1, G-protein beta/gamma, SDFR1, SUR, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, S100, TXNRD1, TRPV1, PDK3, Galpha(q)-specific nucleotide-like GPCRs, Tensin 2, G-protein gamma, SOCS6, Rap1GDS1, ChREBP, ATP5B, cPKC (conventional), ATP6V1B2, Serotonin receptor, TRPC, PYGM, ATP6V1H, Osteopontin, NHE6, Substance P, Galpha(q)-specific amine GPCRs, GP-IB alpha, Galpha(i)-specific amine GPCRs, TRPC4, PMCA1, NCX1, Protein kinase G1, Zeta-sarcoglycan, CDK5, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPCRs, Galpha(q)-specific peptide GPCRs, NCOA4 (ARA70), Creatine kinase, XK, MEF2, APRIO, ATF/CREB, G-protein gamma 3, PP2A catalytic, Glutaredoxin, Galpha(s)-specific CRF GPCRs, LAMP2, ATP6V1B, Protein kinase G 2, PRNP, NKCC1, Calmodulin, NELL2, Aquaporin 1, NDFIP1, CLIC4, ERK1/2, CDw52, AATC, CaMK II delta, PKC, SUR1, HTR2A, ATP1B3, MEF2C, Protein kinase G, ERK2 (MAPK1), Calcineurin A (beta), SOD1, CALM2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, ATP6AP2, CALB1, HXK3, 14-3-3, RAGE, ATP1beta subunit, Glutaredoxin 1 |
| 48 | response to nitrogen compound | 2149 | 8.504E-16 | 1.381E-13 | 138 | Cyclin G, PP2A cat (alpha), HSP90, Galpha(s)-specific nucleotide-like GPCRs, IRF1, ATP5C, HPCA, Endothelin-1, ARG2, DUOX1, BRSK2, P2Y11, UBXD3, G-protein beta, ALDR, RGS8, CDC18L (CDC6), Pannexin-1, TIP47, PRKAR2B, MC4R, Guanylate cyclase, HSP70, CNR1, MAPBPIP, Glycogen phosphorylase, DnaJB9, Thioredoxin, PDE, HCN2, Galpha(q)-specific Class A Orphan/other GPCRs, ATP5G, RGS4, GABA-A receptor alpha-1 subunit, GUCY1B1, CEACAM, G-protein beta/gamma, SUR, NDUFS4, NCX, Galpha(i)-specific peptide GPCRs, CALM3, P/Q-type calcium channel alpha-1A subunit, CPT-1A, TRPV1, Galpha(q)-specific nucleotide-like GPCRs, Aldose reductase, CRH receptor 2, CacyBP(SIP), GLRA, GABA-A receptor beta-2 subunit, FBXO2, SYP, Rho GTPase, PDE4, G-protein gamma, Rap1GDS1, Ephrin-A receptor 4, Galpha(i)-specific metabotropic glutamate GPCRs, GlyRA2, ATP5B, PKA-reg type II (cAMP-dependent), cPKC   |

|    |   |     |           |           |    |   |
|----|---|-----|-----------|-----------|----|---|
|    |   |     |           |           |    | (conventional), AP3S1, Serotonin receptor, CHMP5, ADSS, TRPC, HTR5A, PYGM, PDK4, ATP5G3, SMRT, CysLT2 receptor, PKA-reg (cAMP-dependent), Substance P, AP-3 sigma subunits, HBXIP, Histone H2, Galpha(q)-specific amine GPCRs, Ephrin-A receptors, Histone H2A, HMP19, Galpha(i)-specific amine GPCRs, NCX1, HCN, BDH, HSP90 beta, CDK5, PAK, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, Glycine receptor, Fatty acid-binding protein, ATP5A, Glycine receptor beta chain, Calcineurin A (catalytic), Galpha(i)-specific cannabis GPSRs, Cyclin G1, Galpha(q)-specific peptide GPCRs, H2AFZ, MEF2, HNMT, APRIO, CEACAM1, ATF/CREB, Acyl-CoA synthetase, PP2A catalytic, RNF175, Galpha(s)-specific CRF GPCRs, ALAS1, JKAMP, PRNP, Calmodulin, LPL, Apo-2L(TNFSF10), Activin, Aquaporin 1, ERK1/2, AATC, PI3K reg class IA (p55-gamma), PKC, SUR1, HTR2A, ARPP-19, Guanylate Cyclase 1, soluble, MEF2C, ERK2 (MAPK1), Calcineurin A (beta), IGFALS, SOD1, CALM2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, ACTR3, ARP3, 14-3-3, RAGE |
| 49 | purine ribonucleotide metabolic process | 449 | 8.745E-16 | 1.391E-13 | 52 | PRPS1, ATP5C, SUCLG1, ELOVL5, SULT1A1, DCMC, PDH E2 subunit N6-lipoyllysine, Guanylate cyclase, NUDT4P1, GIMAP7, ATP6V1A (70kD), PDE, PPT1, Guanylate cyclase alpha, ATP5G, GUCY1B1, ATP5E, Rho GTPase, PDE4, PRPS2, ATP5B, ELOVL4, ADSS, PDK4, SUCB1, ATP5G3, HMDH, GUCY1A3, Ephrin-A receptors, Rab-23, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, HINT, ATP5A, PDH beta, NUDT4, PGAM1, SCS-A, ACSL4, F262, ODP2, Acyl-CoA synthetase, KAD6, PDE4A, NME5, Guanylate Cyclase 1, soluble, Ran, MPC2, Guanine deaminase, PRPS, ATP5L, HXK3  |
| 50 | purine nucleotide metabolic process     | 465 | 9.024E-16 | 1.407E-13 | 53 | PRPS1, ATP5C, SUCLG1, ELOVL5, SULT1A1, DCMC, PDH E2 subunit N6-lipoyllysine, Guanylate cyclase, NUDT4P1, GIMAP7, ATP6V1A (70kD), PDE, PPT1, Guanylate cyclase alpha, ATP5G, GUCY1B1, ATP5E, Rho GTPase, PDE4, PRPS2, ATP5B, ELOVL4, ADSS, PDK4, SUCB1, ATP5G3, HMDH, GUCY1A3, Ephrin-A receptors, Rab-23, Guanylate cyclase (alpha-1/beta-1), Guanylate cyclase beta, HINT, ATP5A, PDH beta, DCK, NUDT4, PGAM1, SCS-A, ACSL4, F262, ODP2, Acyl-CoA synthetase, KAD6, PDE4A, NME5, Guanylate Cyclase 1, soluble, Ran, MPC2, Guanine deaminase, PRPS, ATP5L, HXK3   |

Table A16. Top 50 KCL BrainBank Gene Ontology (GO) Biological Processes enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| # | Term Name                     | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names  |
|---|-------------------------------|-----------|-----------|------------------------|-------------------|--|
| 1 | phagocytosis, recognition     | 43        | 1.653E-12 | 5.115E-09              | 12                | Kappa chain (Ig light chain), KV139, COLEC12, IGHA1, MFGE8, Ficolin, IGKC, IGHG1, Fc gamma RII, Ficolin-1, Ig light chain, KVD16   |
| 2 | immune response               | 1463      | 2.644E-12 | 5.115E-09              | 60                | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, OASL, MxB, KV139, GZMH, COLEC12, C4A protein, Tubulin beta, Annexin I, IGHA1, PLA2, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HMGB2, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, H28, MxA, Galpha(i)-specific EDG GPCRs, Carbohydrate sulfotransferases, Ig light chain, OAS3, NALP3, GBP5, APRIL(TNFSF13), GBP4, IFI44, Oct-2, WNT, KVD16, Midkine, SEC14L1, HLAC, LIRB, ILT7                   |
| 3 | defense response to bacterium | 311       | 3.489E-12 | 5.115E-09              | 26                | HMG1,2, Kappa chain (Ig light chain), Histone H2, KV139, COLEC12, IGHA1, PLA2, MHC Class I alpha chain, Ficolin, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, GBP6, HIST2H2BE, Galpha(i)-specific peptide GPCRs, Lactoferrin, 2'-5'-oligoadenylate synthetase, Aquaporin 1, Ig light chain, OAS3, NALP3, GBP4, KVD16, HLAC   |
| 4 | defense response              | 1641      | 3.780E-12 | 5.115E-09              | 64                | HMG1,2, Kappa chain (Ig light chain), Histone H2, PBXIP1, A20, OASL, MxB, KV139, GZMH, COLEC12, CAT-2, C4A protein, Tubulin beta, Annexin I, VCAM1, IGHA1, PLA2, CD44, C4, MHC Class I alpha chain, Ficolin, RSAD2, GPR120, IGKC, LYPD1, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, Cystatin C, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, P2Y1, Carbohydrate sulfotransferases, Ig light chain, OAS3, NALP3, GBP5, GBP4, RXR, WNT, KVD16, Midkine, SEC14L1, HLAC, LIRB, ILT7 |

|   |                               |      |           |           |    |  |
|---|-------------------------------|------|-----------|-----------|----|--|
| 5 | innate immune response        | 799  | 4.298E-12 | 5.115E-09 | 42 | HMG1,2, Kappa chain (Ig light chain), Histone H2, OASL, MxB, KV139, GZMH, COLEC12, C4A protein, Tubulin beta, Annexin I, IGHA1, PLA2, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, GBP6, APOL1, IFI27, HIST2H2BE, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, 2'-5'-oligoadenylate synthetase, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, WNT, KVD16, SEC14L1, HLAC, ILT7   |
| 6 | response to bacterium         | 970  | 1.263E-11 | 1.253E-08 | 46 | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, KV139, COLEC12, GSTs, Connexin 30, C4A protein, VCAM1, IGHA1, PLA2, C4, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, GBP6, Fc gamma RII beta, ILT4, Fc gamma RII, Connexin 26, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, IFI44, WNT, KVD16, HLAC, LIRB, CCDC80   |
| 7 | response to external stimulus | 3141 | 1.711E-11 | 1.455E-08 | 95 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), LHX1, Histone H2, HGF, A20, OASL, MxB, KV139, GZMH, COLEC12, GSTs, Connexin 30, C4A protein, Tubulin beta, APH-1, SLC4A1, Neuropilin-2, Annexin I, VCAM1, IGHA1, PLA2, CD44, C4, WNT7B, PDK2, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, SDHL, LGR6, IGKC, DCPS, GPNMB (Osteoactivin), MC4R, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, Histone H2B, POMC, HMGB2, Cystatin C, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, GIPR, Connexin 26, CD147, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, Semaphorin 3D, CPT-1A, S1P1 receptor, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, PEA3, Galpha(i)-specific EDG GPCRs, P2Y1, Ig light chain, OAS3, NALP3, GBP5, WDR45L, NQO1, GBP4, RXR, IFI44, Dystroglycan, Galpha(s)-specific peptide GPCRs, Oct-2, HMGCL, WNT, CART, KVD16, Midkine, SEC14L1, HLAC, LIRB, RNF152, ILT7, CCDC80 |

|    |  |      |           |           |    |   |
|----|--|------|-----------|-----------|----|---|
| 8  | negative regulation of response to external stimulus | 540  | 2.159E-11 | 1.606E-08 | 33 | METRNL, HGF, A20, GSTs, APH-1, PLA2, CD44, Fatty acid-binding protein, MHC Class I alpha chain, GPR120, Galpha(s)-specific calcitonin GPCRs, EAT-2, Galpha(q)-specific peptide GPCRs, PLAT (TPA), Fc gamma RII beta, Fc gamma RII, CEACAM, PRSS11 (HtrA1), Galpha(i)-specific peptide GPCRs, Semaphorin 3D, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, OAS3, NALP3, MMP-28, PLA2G5, WNT, CART, Midkine, SEC14L1, HLAC, LIRB  |
| 9  | response to biotic stimulus                          | 1742 | 5.004E-11 | 3.309E-08 | 64 | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, OASL, MxB, KV139, GZMH, COLEC12, GSTs, Connexin 30, C4A protein, Tubulin beta, Annexin I, VCAM1, IGHA1, PLA2, C4, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, WFS1, HMGB2, GBP6, Fc gamma RII beta, Seprase, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, Connexin 26, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, IFI44, Oct-2, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7, CCDC80 |
| 10 | negative regulation of defense response              | 327  | 6.436E-11 | 3.830E-08 | 25 | METRNL, HGF, A20, GSTs, PLA2, CD44, MHC Class I alpha chain, GPR120, Galpha(s)-specific calcitonin GPCRs, EAT-2, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Fc gamma RII, CEACAM, PRSS11 (HtrA1), Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, OAS3, NALP3, PLA2G5, Midkine, SEC14L1, HLAC, LIRB  |

|    |   |      |           |           |    |  |
|----|---|------|-----------|-----------|----|--|
| 11 | response to other organism  | 1681 | 9.331E-11 | 4.885E-08 | 62 | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, OASL, MxB, KV139, GZMH, COLEC12, GSTs, Connexin 30, C4A protein, Tubulin beta, Annexin I, VCAM1, IGHA1, PLA2, C4, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HMGB2, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, Connexin 26, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, IFI44, Oct-2, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7, CCDC80   |
| 12 | response to external biotic stimulus                                      | 1685 | 1.029E-10 | 4.885E-08 | 62 | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, OASL, MxB, KV139, GZMH, COLEC12, GSTs, Connexin 30, C4A protein, Tubulin beta, Annexin I, VCAM1, IGHA1, PLA2, C4, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HMGB2, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, Connexin 26, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, IFI44, Oct-2, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7, CCDC80   |
| 13 | biological process involved in interspecies interaction between organisms | 1906 | 1.067E-10 | 4.885E-08 | 67 | HMG1,2, Kappa chain (Ig light chain), Histone H2, A20, OASL, MxB, KV139, GZMH, COLEC12, GSTs, Connexin 30, C4A protein, Tubulin beta, Annexin I, VCAM1, IGHA1, PLA2, C4, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, TPCN1, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HMGB2, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, Connexin 26, CD147, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Ig light chain, OAS3, NALP3, GBP5, ZBED1, GBP4, RXR, IFI44, Dystroglycan, Oct-2, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7, CCDC80 |

|    |   |      |           |           |    |  |
|----|---|------|-----------|-----------|----|--|
| 14 | negative regulation of cytokine production                          | 398  | 1.619E-10 | 6.521E-08 | 27 | HMG1,2, Angiopoietin 1, HGF, A20, GSTs, Annexin I, PLA2, MHC Class I alpha chain, GPR120, GPNMB (Osteoactivin), EAT-2, Galpha(q)-specific peptide GPCRs, POMC, PP2135, GBP6, Fc gamma RII beta, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, Lactoferrin, 2'-5'-oligoadenylate synthetase, OAS3, NALP3, Galpha(s)-specific peptide GPCRs, WNT, LIRB, ILT7   |
| 15 | defense response to other organism                                  | 1048 | 1.684E-10 | 6.521E-08 | 46 | HMG1,2, Kappa chain (Ig light chain), Histone H2, OASL, MxB, KV139, GZMH, COLEC12, C4A protein, Tubulin beta, Annexin I, IGHA1, PLA2, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, GBP6, APOL1, Perforin, IFI27, HIST2H2BE, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, 2'-5'-oligoadenylate synthetase, Aquaporin 1, H28, MxA, Ig light chain, OAS3, NALP3, GBP5, GBP4, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7   |
| 16 | regulation of response to external stimulus                         | 1246 | 1.753E-10 | 6.521E-08 | 51 | METRNL, HMG1,2, HGF, A20, OASL, GSTs, CAT-2, Tubulin beta, APH-1, Annexin I, PLA2, CD44, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, GPR120, Galpha(s)-specific calcitonin GPCRs, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, POMC, HMGB2, PLAT (TPA), GBP6, Fc gamma RII beta, Seprase, Fc gamma RII, CEACAM, PRSS11 (HtrA1), ZSWIM5, Galpha(i)-specific peptide GPCRs, Semaphorin 3D, S1P1 receptor, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Tubulin beta 2B, Galpha(i)-specific EDG GPCRs, OAS3, NALP3, GBP5, RXR, MMP-28, PLA2G5, WNT, CART, Midkine, SEC14L1, HLAC, LIRB |
| 17 | humoral immune response   | 272  | 3.249E-10 | 1.137E-07 | 22 | Kappa chain (Ig light chain), Histone H2, KV139, C4A protein, IGHA1, PLA2, C4, MHC Class I alpha chain, Ficolin, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HIST2H2BE, Galpha(i)-specific peptide GPCRs, I-TAC, Ficolin-1, Lactoferrin, Ig light chain, Oct-2, KVD16  |
| 18 | regulation of immune complex clearance by monocytes and macrophages | 8    | 3.752E-10 | 1.240E-07 | 6  | PLA2, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Fc gamma RII, Galpha(i)-specific peptide GPCRs, PLA2G5  |

|    |   |      |           |           |    |  |
|----|---|------|-----------|-----------|----|--|
| 19 | phagocytosis                                | 252  | 4.822E-10 | 1.510E-07 | 21 | HMG1,2, Kappa chain (Ig light chain), KV139, COLEC12, Annexin I, IGHA1, PLA2, MFGE8, Ficolin, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, Ficolin-1, Galpha(q)-specific nucleotide-like GPCRs, Ig light chain, PLA2G5, KVD16   |
| 20 | cell recognition                            | 193  | 1.445E-09 | 4.301E-07 | 18 | Kappa chain (Ig light chain), KV139, COLEC12, IGHA1, MFGE8, Ficolin, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Perforin, Fc gamma RII, CD147, Galpha(i)-specific peptide GPCRs, Ficolin-1, Ig light chain, CNTNAP3, WNT, KVD16  |
| 21 | defense response to Gram-positive bacterium | 123  | 7.797E-09 | 2.209E-06 | 14 | HMG1,2, Histone H2, PLA2, MHC Class I alpha chain, Ficolin, Galpha(q)-specific peptide GPCRs, Histone H2B, HMGB2, GBP6, HIST2H2BE, Galpha(i)-specific peptide GPCRs, Lactoferrin, NALP3, GBP4  |
| 22 | regulation of immune response               | 1068 | 9.712E-09 | 2.537E-06 | 43 | HMG1,2, Kappa chain (Ig light chain), A20, OASL, KV139, COLEC12, C4A protein, Annexin I, IGHA1, PLA2, CD44, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, HMGB2, PP2135, Fc gamma RII beta, ILT4, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, SUPT6H, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Ig light chain, OAS3, NALP3, GBP5, APRIL(TNFSF13), PLA2G5, WNT, KVD16, SEC14L1, HLAC, LIRB, ILT7 |
| 23 | regulation of defense response              | 834  | 9.805E-09 | 2.537E-06 | 37 | METRNL, HMG1,2, HGF, A20, GSTs, CAT-2, Annexin I, PLA2, CD44, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, GPR120, Galpha(s)-specific calcitonin GPCRs, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, POMC, HMGB2, GBP6, Fc gamma RII beta, Fc gamma RII, CEACAM, PRSS11 (HtrA1), Galpha(i)-specific peptide GPCRs, Ficolin-1, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, OAS3, NALP3, GBP5, PLA2G5, WNT, Midkine, SEC14L1, HLAC, LIRB                                  |



|    |  |     |           |           |    |  |
|----|--|-----|-----------|-----------|----|--|
| 24 | immune effector process                      | 521 | 1.343E-08 | 3.330E-06 | 28 | HMG1,2, Kappa chain (Ig light chain), A20, KV139, GZMH, C4A protein, Tubulin beta, IGHA1, PLA2, C4, MHC Class I alpha chain, Ficolin, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Perforin, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Ficolin-1, Galpha(q)-specific nucleotide-like GPCRs, Ig light chain, APRIL(TNFSF13), Oct-2, KVD16, Midkine, LIRB  |
| 25 | B cell mediated immunity                     | 174 | 1.478E-08 | 3.517E-06 | 16 | Kappa chain (Ig light chain), KV139, C4A protein, IGHA1, C4, MHC Class I alpha chain, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Fc gamma RII, Ig light chain, APRIL(TNFSF13), Oct-2, KVD16, LIRB   |
| 26 | immune response-regulating signaling pathway | 398 | 1.771E-08 | 4.053E-06 | 24 | HMG1,2, Kappa chain (Ig light chain), A20, KV139, COLEC12, IGHA1, PLA2, MHC Class I alpha chain, Ficolin, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, ILT4, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Ficolin-1, 2'-5'-oligoadenylate synthetase, Ig light chain, OAS3, KVD16, LIRB, ILT7   |
| 27 | complement activation                        | 74  | 1.933E-08 | 4.261E-06 | 11 | Kappa chain (Ig light chain), KV139, C4A protein, IGHA1, C4, Ficolin, IGKC, IGHG1, Ficolin-1, Ig light chain, KVD16  |
| 28 | regulation of cytokine production            | 977 | 2.168E-08 | 4.608E-06 | 40 | HMG1,2, Angiopoietin 1, HGF, A20, GSTs, Annexin I, PLA2, MHC Class I alpha chain, Ficolin, RSAD2, GPR120, SULF1, GPNMB (Osteoactivin), EAT-2, Galpha(q)-specific peptide GPCRs, POMC, HMGB2, PP2135, GBP6, Fc gamma RII beta, ILT4, Fc gamma RII, CD147, CEACAM, Galpha(i)-specific peptide GPCRs, Ficolin-1, Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, Galpha(i)-specific EDG GPCRs, OAS3, NALP3, GBP5, Galpha(s)-specific peptide GPCRs, Oct-2, WNT, Midkine, HLAC, LIRB, ILT7 |

|    |   |      |           |           |    |   |
|----|---|------|-----------|-----------|----|---|
| 29 | immune system process                       | 2517 | 2.655E-08 | 5.448E-06 | 74 | HMG1,2, Angiopoietin 1, Kappa chain (Ig light chain), Histone H2, PBXIP1, A20, OASL, MxB, KV139, GZMH, COLEC12, CAT-2, C4A protein, Tubulin beta, SLC4A1, Annexin I, VCAM1, IGHA1, PLA2, CD44, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, Galpha(s)-specific calcitonin GPCRs, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Histone H2B, POMC, HMGB2, GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, CD147, ALAS2, CD300E, CEACAM, HIST2H2BE, Galpha(i)-specific peptide GPCRs, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, H28, MxA, Galpha(i)-specific EDG GPCRs, P2Y1, Carbohydrate sulfotransferases, Ig light chain, OAS3, NALP3, GBP5, APRIL(TNFSF13), GBP4, IFI44, GALNT2, Oct-2, WNT, KVD16, Midkine, SEC14L1, HLAC, LIRB, ILT7 |
| 30 | lymphocyte mediated immunity                | 260  | 2.841E-08 | 5.635E-06 | 19 | Kappa chain (Ig light chain), KV139, GZMH, C4A protein, Tubulin beta, IGHA1, C4, MHC Class I alpha chain, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Perforin, Fc gamma RII, Ig light chain, APRIL(TNFSF13), Oct-2, KVD16, LIRB  |
| 31 | regulation of cell population proliferation | 2297 | 4.019E-08 | 7.715E-06 | 69 | HMG1,2, Angiopoietin 1, R-spondins, LHX1, Histone H2, PBXIP1, HGF, A20, Histone H2A, GSTs, FNIP2, Connexin 30, APJ, MCR, KiSS-1, SLC4A1, Neuropilin-2, Annexin I, VCAM1, PLA2, HIF-prolyl hydroxylase, CD44, MFGE8, WNT7B, SIX3, Fatty acid-binding protein, MHC Class I alpha chain, EGLN3, UHRF1, SULF1, Galpha(s)-specific calcitonin GPCRs, GPNMB (Osteoactivin), Galpha(q)-specific peptide GPCRs, HMGB2, Cystatin C, PP2135, Fc gamma RII beta, SOX17, Seprase, Clmn, ILT4, Fc gamma RII, CEACAM, PRSS11 (HtrA1), LRH1, Galpha(i)-specific peptide GPCRs, S1P1 receptor, I-TAC, Apo-2L(TNFSF10), Lactoferrin, Galpha(q)-specific nucleotide-like GPCRs, RASSF10, Aquaporin 1, PEA3, Galpha(i)-specific EDG GPCRs, PKHD1, MYEOV2, PLC-delta, EGF, APRIL(TNFSF13), GFAP, PR (membrane), POU class III, RXR, Galpha(s)-specific peptide GPCRs, WNT, PR (nuclear), Midkine, LIRB          |

|    |  |     |           |           |    |   |
|----|--|-----|-----------|-----------|----|---|
| 32 | leukocyte mediated immunity                    | 327 | 4.922E-08 | 9.075E-06 | 21 | Kappa chain (Ig light chain), KV139, GZMH, C4A protein, Tubulin beta, IGHA1, PLA2, C4, MHC Class I alpha chain, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Perforin, Fc gamma RII, Galpha(q)-specific nucleotide-like GPCRs, Ig light chain, APRIL(TNFSF13), Oct-2, KVD16, LIRB  |
| 33 | regulation of tumor necrosis factor production | 242 | 5.074E-08 | 9.075E-06 | 18 | HMG1,2, Angiopoietin 1, A20, GSTs, MHC Class I alpha chain, GPNMB (Osteoactivin), Galpha(q)-specific peptide GPCRs, POMC, PP2135, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Lactoferrin, 2'-5'-oligoadenylate synthetase, OAS3, Galpha(s)-specific peptide GPCRs, WNT, LIRB, ILT7   |
| 34 | positive regulation of immune response         | 662 | 5.185E-08 | 9.075E-06 | 31 | HMG1,2, Kappa chain (Ig light chain), KV139, C4A protein, Annexin I, IGHA1, PLA2, CD44, C4, MHC Class I alpha chain, Ficolin, RSAD2, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, HMGB2, Fc gamma RII beta, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Ficolin-1, Galpha(q)-specific nucleotide-like GPCRs, Ig light chain, NALP3, GBP5, APRIL(TNFSF13), PLA2G5, WNT, KVD16, HLAC, LIRB   |
| 35 | regulation of dendritic cell differentiation   | 24  | 5.795E-08 | 9.853E-06 | 7  | HMG1,2, MHC Class I alpha chain, Fc gamma RII beta, ILT4, Fc gamma RII, HLAC, LIRB  |
| 36 | regulation of neutrophil apoptotic process     | 15  | 6.116E-08 | 1.011E-05 | 6  | Annexin I, CD44, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Fc gamma RII, Galpha(i)-specific peptide GPCRs  |
| 37 | response to peptide                            | 857 | 6.319E-08 | 1.016E-05 | 36 | HMG1,2, Histone H2, A20, Histone H2A, GSTs, Annexin I, VCAM1, PLA2, PDK2, Fatty acid-binding protein, UHRF1, Galpha(s)-specific calcitonin GPCRs, MC4R, Galpha(q)-specific peptide GPCRs, ALDOB, POMC, PLAT (TPA), Fc gamma RII beta, Fc gamma RII, Connexin 26, CD147, CEACAM, Galpha(i)-specific peptide GPCRs, Apo-2L(TNFSF10), Calcitonin receptor, Galpha(q)-specific nucleotide-like GPCRs, DDX11, PLC-delta, PR (membrane), RXR, Dystroglycan, Galpha(s)-specific peptide GPCRs, AGRP, ACES, WNT, PR (nuclear) |

|    |   |      |           |           |     |   |
|----|---|------|-----------|-----------|-----|---|
| 38 | regulation of immune effector process                               | 494  | 6.918E-08 | 1.083E-05 | 26  | HMG1,2, Angiotensin 1, A20, Annexin I, PLA2, MHC Class I alpha chain, Ficolin, RSAD2, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, POMC, PP2135, Fc gamma RII beta, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, Ficolin-1, SUPT6H, Galpha(q)-specific nucleotide-like GPCRs, NALP3, APRIL(TNFSF13), PLA2G5, WNT, HLAC, LIRB  |
| 39 | regulation of tumor necrosis factor superfamily cytokine production | 249  | 7.833E-08 | 1.190E-05 | 18  | HMG1,2, Angiotensin 1, A20, GSTs, MHC Class I alpha chain, GPNMB (Osteoactivin), Galpha(q)-specific peptide GPCRs, POMC, PP2135, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Lactoferrin, 2'-5'-oligoadenylate synthetase, OAS3, Galpha(s)-specific peptide GPCRs, WNT, LIRB, ILT7  |
| 40 | regulation of response to biotic stimulus                           | 464  | 8.001E-08 | 1.190E-05 | 25  | HMG1,2, A20, OASL, PLA2, MHC Class I alpha chain, Ficolin, EAT-2, Galpha(q)-specific peptide GPCRs, POMC, HMGB2, GBP6, Fc gamma RII beta, Fc gamma RII, CEACAM, PRSS11 (HtrA1), Ficolin-1, Lactoferrin, 2'-5'-oligoadenylate synthetase, OAS3, GBP5, PLA2G5, WNT, SEC14L1, HLAC, LIRB   |
| 41 | response to stress  | 4173 | 9.203E-08 | 1.336E-05 | 104 | METRNL, HMG1,2, Angiotensin 1, Kappa chain (Ig light chain), Histone H2, PBXIP1, A20, OASL, Nk3R, MxB, Histone H2A, KV139, GZMH, COLEC12, GSTs, FNIP2, CAT-2, C4A protein, Tubulin beta, SLC4A1, Annexin I, VCAM1, IGHA1, PLA2, HIF-prolyl hydroxylase, CD44, C4, PDK2, Fatty acid-binding protein, MHC Class I alpha chain, Ficolin, RSAD2, GPR120, EGLN3, UHRF1, IGKC, GSTM3, LYPD1, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, ALDOB, Histone H2B, SOD3 (EC-SOD), POMC, WFS1, HMGB2, Cystatin C, PLAT (TPA), GBP6, Fc gamma RII beta, APOL1, ILT4, Perforin, Fc gamma RII, IFI27, GIPR, Connexin 26, ALAS2, CEACAM, L-FABP, HIST2H2BE, Galpha(i)-specific peptide GPCRs, DGK-kappa, I-TAC, Ficolin-1, Lactoferrin, STARD13, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, AGS8, Aquaporin 1, H28, MxA, Galpha(i)-specific EDG GPCRs, P2Y1, DDX11, Carbohydrate sulfotransferases, SLC12A1, Ig light chain, OAS3, PLC-delta, NALP3, GBP5, WDR45L, NQO1, CCDC88C, GBP4, AL3A2, GFAP, RXR, Dystroglycan, Galpha(s)-specific peptide GPCRs, HMGCL, WNT, Proline oxidase 1, CART, KVD16, Midkine, SEC14L1, HLAC, LIRB, RNF152, ILT7 |

|    |   |     |           |           |    |  |
|----|---|-----|-----------|-----------|----|--|
| 42 | regulation of lymphocyte activation   | 652 | 1.268E-07 | 1.781E-05 | 30 | HMG1,2, Kappa chain (Ig light chain), A20, KV139, SLC4A1, Annexin I, VCAM1, IGHA1, PLA2, CD44, MHC Class I alpha chain, IGKC, GPNMB (Osteoactivin), IGHG1, Galpha(q)-specific peptide GPCRs, PP2135, Fc gamma RII beta, ILT4, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, SUPT6H, Galpha(q)-specific nucleotide-like GPCRs, Ig light chain, NALP3, APRIL(TNFSF13), WNT, KVD16, Midkine, LIRB |
| 43 | regulation of adaptive immune response  | 286 | 1.287E-07 | 1.781E-05 | 19 | HMG1,2, A20, Annexin I, PLA2, CD44, MHC Class I alpha chain, RSAD2, IGHG1, Galpha(q)-specific peptide GPCRs, PP2135, Fc gamma RII beta, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, SUPT6H, NALP3, APRIL(TNFSF13), HLAC, LIRB  |
| 44 | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains               | 288 | 1.434E-07 | 1.940E-05 | 19 | HMG1,2, Kappa chain (Ig light chain), KV139, C4A protein, IGHA1, C4, MHC Class I alpha chain, IGKC, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, Perforin, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Ig light chain, APRIL(TNFSF13), Oct-2, KVD16, LIRB   |
| 45 | regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 261 | 1.592E-07 | 2.105E-05 | 18 | HMG1,2, A20, Annexin I, PLA2, MHC Class I alpha chain, RSAD2, IGHG1, Galpha(q)-specific peptide GPCRs, PP2135, Fc gamma RII beta, Fc gamma RII, CEACAM, Galpha(i)-specific peptide GPCRs, SUPT6H, NALP3, APRIL(TNFSF13), HLAC, LIRB  |
| 46 | regulation of innate immune response  | 293 | 1.875E-07 | 2.395E-05 | 19 | HMG1,2, A20, PLA2, MHC Class I alpha chain, Ficolin, EAT-2, Galpha(q)-specific peptide GPCRs, HMGB2, Fc gamma RII beta, Fc gamma RII, CEACAM, Ficolin-1, 2'-5'-oligoadenylate synthetase, OAS3, GBP5, PLA2G5, WNT, HLAC, LIRB  |

|    |  |      |           |           |     |   |
|----|--|------|-----------|-----------|-----|---|
| 47 | response to stimulus                     | 8783 | 1.892E-07 | 2.395E-05 | 179 | METRNL, DCHS1, HMG1,2, Angiopoietin 1, R-spondins, Kappa chain (Ig light chain), SLC6A11, LHX1, Histone H2, PBXIP1, HGF, A20, OASL, NK3R, MxB, Histone H2A, KV139, GZMH, COLEC12, GSTs, FNIP2, CAT-2, Connexin 30, C4A protein, APJ, MCR, Caspase-10, R-spondin 3, KiSS-1, Tubulin beta, SULT1A1, APH-1, SLC4A1, Neuropilin-2, Annexin I, VCAM1, IGHA1, PLA2, Rab-5C, HIF-prolyl hydroxylase, CD44, C4, MFGE8, CDGAP, WNT7B, PDK2, Fatty acid-binding protein, ARHI, MHC Class I alpha chain, Ficolin, RSAD2, G2A, SDHL, LGR6, GPR120, GPRC5C, EGLN3, UHRF1, SULF1, PAMCI, HYEP, IGKC, DCPS, GSTM3, LYPD1, Galpha(s)-specific calcitonin GPCRs, GPNMB (Osteoactivin), MC4R, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, RP13-102H20.1, ALDOB, Histone H2B, MAFbx, FLJ20625, Ccd1, SOD3 (EC-SOD), POMC, WFS1, HMGB2, XAF1, Cystatin C, RIS, PLAT (TPA), PP2135, GPR101, GBP6, Fc gamma RII beta, SOX17, Seprase, APOL1, ILT4, SLC13A5, Perforin, Fc gamma RII, ARRDC2, IFI27, GIPR, Connexin 26, CD147, ALAS2, CEACAM, L-FABP, LRH1, HIST2H2BE, Galpha(i)-specific peptide GPCRs, DGK-kappa, Semaphorin 3D, CPT-1A, S1P1 receptor, I-TAC, Ficolin-1, Apo-2L(TNFSF10), Lactoferrin, FLJ45455, Calcitonin receptor, STARD13, Galpha(q)-specific nucleotide-like GPCRs, 2'-5'-oligoadenylate synthetase, AGS8, RASSF10, Aquaporin 1, H28, MxA, PEA3, Galpha(i)-specific EDG GPCRs, P2Y1, THNSL2, DDX11, Carbohydrate sulfotransferases, MYEOV2, SLC12A1, Ig light chain, APH-1A, OAS3, PLC-delta, NALP3, EGF, GBP5, WDR45L, NQO1, CCDC88C, RAS4B, APRIL(TNFSF13), GBP4, AL3A2, GFAP, PR (membrane), POU class III, RXR, IFI44, Dystroglycan, ROPN1B, ECEL1, PLA2G5, CABYR, PLCD4, Galpha(s)-specific peptide GPCRs, Oct-2, CYP4V2, AGRP, ACES, HMGCL, WNT, Proline oxidase 1, WIF1, RXRG, CART, KVD16, PR (nuclear), Midkine, SEC14L1, HLAC, LIRB, RNF152, ILT7, CCDC80, APCDD1 |
| 48 | complement activation, classical pathway | 56   | 1.935E-07 | 2.399E-05 | 9   | Kappa chain (Ig light chain), KV139, C4A protein, IGHA1, C4, IGKC, IGHG1, Ig light chain, KVD16   |

|    |  |     |           |           |    |   |
|----|--|-----|-----------|-----------|----|---|
| 49 | immune response-regulating cell surface receptor signaling pathway | 299 | 2.566E-07 | 3.116E-05 | 19 | Kappa chain (Ig light chain), KV139, IGHA1, PLA2, MHC Class I alpha chain, Ficolin, IGKC, EAT-2, IGHG1, Galpha(q)-specific peptide GPCRs, Fc gamma RII beta, ILT4, Fc gamma RII, Galpha(i)-specific peptide GPCRs, Ficolin-1, Ig light chain, KVD16, LIRB, ILT7 |
| 50 | negative regulation of leukocyte cell-cell adhesion                | 190 | 3.140E-07 | 3.738E-05 | 15 | HMG1,2, GSTs, Annexin I, PLA2, CD44, MHC Class I alpha chain, GPNMB (Osteoactivin), PP2135, Fc gamma RII beta, ILT4, Fc gamma RII, CEACAM, Galpha(q)-specific nucleotide-like GPCRs, Midkine, LIRB  |

*Table A17. Top 50 TargetALS Gene Ontology (GO) Biological Processes enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.*

| # | Term Name   | Term ID                | Term Size | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|---|---|------------------------|-----------|------------------------|-------------------|---|
| 1 | The citric acid (TCA) cycle and respiratory electron transport  | REAC:<br>R-HSA-1428517 | 177       | 2.05E-14               | 39                | ENSG00000155380,ENSG00000004799,ENSG00000164258,ENSG00000164405,ENSG00000183648,ENSG00000168291,ENSG00000178741,ENSG00000165264,ENSG00000119421,ENSG00000164919,ENSG00000128609,ENSG00000173660,ENSG00000117118,ENSG00000145494,ENSG00000150768,ENSG00000163541,ENSG00000067992,ENSG00000124767,ENSG00000125356,ENSG00000213585,ENSG00000189043,ENSG00000165629,ENSG00000124172,ENSG00000115944,ENSG00000110955,ENSG00000065518,ENSG00000167283,ENSG00000143158,ENSG00000156467,ENSG00000154518,ENSG00000178449,ENSG00000123545,ENSG00000152234,ENSG00000184076,ENSG00000004779,ENSG00000119013,ENSG00000136143,ENSG00000169021,ENSG00000111775 |
| 2 | Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins. | REAC:<br>R-HSA-163200  | 127       | 9.56E-11               | 29                | ENSG00000164258,ENSG00000164405,ENSG00000183648,ENSG00000178741,ENSG00000165264,ENSG00000119421,ENSG00000164919,ENSG00000128609,ENSG00000173660,ENSG00000117118,ENSG00000145494,ENSG00000125356,ENSG00000189043,ENSG00000165629,ENSG00000124172,ENSG00000115944,ENSG00000110955,ENSG00000065518,ENSG00000167283,ENSG00000156467,ENSG00000154518,ENSG00000178449,ENSG00000123545,ENSG00000152234,ENSG00000184076,ENSG00000004779,ENSG00000119013,ENSG00000169021,ENSG00000111775   |
| 3 | Respiratory electron transport  | REAC:<br>R-HSA-611105  | 103       | 5.17E-08               | 23                | ENSG00000164258,ENSG00000164405,ENSG00000183648,ENSG00000178741,ENSG00000165264,ENSG00000119421,ENSG00000164919,ENSG00000128609,ENSG00000173660,ENSG00000117118,ENSG00000145494,ENSG00000125356,ENSG00000189043,ENSG00000115944,ENSG00000065518,ENSG00000156467,ENSG00000178449,ENSG00000123545,ENSG00000184076,ENSG00000004779,ENSG00000119013,ENSG00000169021,ENSG00000111775   |



|   |            |                                |      |          |     |   |
|---|------------|--------------------------------|------|----------|-----|---|
| 4 | Metabolism | REAC:<br>R-HSA-<br>143072<br>8 | 2075 | 7.41E-07 | 146 | <p>ENSG00000074410,ENSG00000160883,ENSG00000180089,ENSG00000152207,ENSG00000155380,ENSG00000004799,ENSG00000153093,ENSG00000138074,ENSG00000229894,ENSG00000196498,ENSG00000187566,ENSG00000103257,ENSG00000009950,ENSG00000196502,ENSG00000127415,ENSG00000176920,ENSG00000131730,ENSG00000110090,ENSG00000161267,ENSG00000006071,ENSG00000176383,ENSG00000141837,ENSG00000126368,ENSG00000137857,ENSG00000172292,ENSG00000164258,ENSG00000164405,ENSG00000183648,ENSG00000197894,ENSG00000168291,ENSG00000148154,ENSG00000132824,ENSG00000178741,ENSG00000005249,ENSG00000101843,ENSG00000035687,ENSG00000165264,ENSG00000119421,ENSG00000164919,ENSG00000120992,ENSG00000131238,ENSG00000128609,ENSG00000138018,ENSG00000138669,ENSG00000170340,ENSG00000171314,ENSG00000118402,ENSG00000104763,ENSG00000143106,ENSG00000130540,ENSG00000173660,ENSG00000163682,ENSG00000117118,ENSG00000145494,ENSG00000150768,ENSG00000186298,ENSG00000144827,ENSG00000163541,ENSG000000067992,ENSG00000081181,ENSG00000114480,ENSG00000124767,ENSG00000006007,ENSG00000085662,ENSG00000162368,ENSG00000136810,ENSG00000091039,ENSG00000023330,ENSG00000125356,ENSG00000109929,ENSG00000213585,ENSG00000173221,ENSG00000189043,ENSG00000165629,ENSG00000174684,ENSG00000133731,ENSG00000067064,ENSG00000115419,ENSG00000198431,ENSG00000124172,ENSG00000115944,ENSG00000110955,ENSG00000108946,ENSG00000150540,ENSG00000139684,ENSG00000105355,ENSG00000065518,ENSG00000155096,ENSG00000117461,ENSG00000164172,ENSG00000167283,ENSG00000143158,ENSG00000147224,ENSG00000156467,ENSG00000154518,ENSG00000129084,ENSG00000113575,ENSG000000084090,ENSG00000162630,ENSG00000102172,ENSG00000178449,ENSG00000165175,ENSG00000096384,ENSG00000123545,ENSG00000114450,ENSG00000146151,ENSG00000152234,ENSG00000168288,ENSG00000184076,ENSG00000012660,ENSG00000132341,ENSG00000100934,ENSG00000068366,ENSG00000004779,ENSG00000135002,ENSG00000119013,ENSG00000085231,ENSG00000137825,ENSG00000083720,ENSG00000180817,ENSG00000136143,ENSG00000139278,ENSG00000169021,ENSG00000173598,ENSG00000100804,ENSG0000014641,ENSG0000011</p> |
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|  |  |  |  |  |  | 1775,ENSG00000119125,ENSG00000156136,ENSG00000120053,ENSG00000052802,ENSG00000065154,ENSG00000162188,ENSG00000164211,ENSG000000688976,ENSG00000170745,ENSG00000101911,ENSG00000175445,ENSG00000123836,ENSG00000164434,ENSG00000165434,ENSG00000183196,ENSG00000174607,ENSG00000062096,ENSG00000139287,ENSG00000161896 |
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| 5 | Transmission across Chemical Synapses | REAC:<br>R-HSA-<br>112315 | 259 | 7.99E-05    | 32 | ENSG00000141837,ENSG00000005249,ENSG00000100030,ENSG00000109738,ENSG00000145864,ENSG00000156642,ENSG000000082458,ENSG00000067715,ENSG00000175175,ENSG00000166501,ENSG00000115419,ENSG00000108946,ENSG00000109158,ENSG00000011677,ENSG00000145349,ENSG00000114450,ENSG00000152495,ENSG00000127824,ENSG00000167552,ENSG000000022355,ENSG00000073969,ENSG00000109971,ENSG00000198785,ENSG00000144746,ENSG00000182481,ENSG00000104490,ENSG00000162188,ENSG00000128683,ENSG00000101958,ENSG00000186297,ENSG00000134294,ENSG00000136750   |
| 6 | Neuronal System                       | REAC:<br>R-HSA-<br>112316 | 400 | 0.000261829 | 41 | ENSG00000131398,ENSG00000073150,ENSG00000099822,ENSG0000006071,ENSG00000141837,ENSG00000005249,ENSG00000100030,ENSG00000109738,ENSG00000145864,ENSG00000156642,ENSG00000082458,ENSG00000067715,ENSG00000175175,ENSG00000166501,ENSG00000115419,ENSG00000184408,ENSG00000108946,ENSG00000109158,ENSG00000110218,ENSG00000140015,ENSG0000011677,ENSG00000145349,ENSG00000114450,ENSG00000152495,ENSG00000127824,ENSG00000167552,ENSG00000022355,ENSG00000073969,ENSG00000109971,ENSG00000082482,ENSG00000198785,ENSG00000144746,ENSG00000182481,ENSG00000104490,ENSG00000162188,ENSG00000170745,ENSG00000128683,ENSG00000101958,ENSG00000186297,ENSG00000134294,ENSG00000136750 |

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| 7 | Cellular responses to stress | REAC:<br>R-HSA-<br>226275<br>2 | 751 | 0.000347886 | 63 | ENSG00000265972,ENSG00000101213,ENSG00000143578,ENSG00000196498,ENSG00000105662,ENSG00000108557,ENSG00000184678,ENSG00000132510,ENSG00000111203,ENSG00000126368,ENSG00000164442,ENSG00000178741,ENSG00000106615,ENSG00000101843,ENSG00000162694,ENSG00000081189,ENSG00000164919,ENSG00000149196,ENSG00000155097,ENSG00000143106,ENSG00000069345,ENSG00000131966,ENSG00000100030,ENSG00000163682,ENSG00000134248,ENSG00000230989,ENSG00000128590,ENSG00000047249,ENSG00000088986,ENSG00000136810,ENSG00000100554,ENSG00000142168,ENSG00000189043,ENSG00000164603,ENSG00000134001,ENSG00000198431,ENSG00000115944,ENSG00000170606,ENSG00000129084,ENSG00000065559,ENSG00000145349,ENSG00000168283,ENSG00000147416,ENSG00000178449,ENSG00000096384,ENSG00000116586,ENSG00000117450,ENSG00000117410,ENSG00000072401,ENSG00000114573,ENSG00000127824,ENSG00000131100,ENSG00000167552,ENSG00000109971,ENSG00000233822,ENSG00000155304,ENSG00000086061,ENSG00000165672,ENSG00000198898,ENSG00000100804,ENSG00000111775,ENSG00000109846,ENSG00000164032 |
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| 8  | Cellular responses to stimuli  | REAC:<br>R-HSA-<br>895389<br>7 | 765 | 0.000657571 | 63 | ENSG00000265972,ENSG00000101213,ENSG00000143578,ENSG00000196498,ENSG00000105662,ENSG00000108557,ENSG00000184678,ENSG00000132510,ENSG00000111203,ENSG00000126368,ENSG00000164442,ENSG00000178741,ENSG00000106615,ENSG00000101843,ENSG00000162694,ENSG00000081189,ENSG00000164919,ENSG00000149196,ENSG00000155097,ENSG00000143106,ENSG00000069345,ENSG00000131966,ENSG00000100030,ENSG00000163682,ENSG00000134248,ENSG00000230989,ENSG00000128590,ENSG00000047249,ENSG00000088986,ENSG00000136810,ENSG00000100554,ENSG00000142168,ENSG00000189043,ENSG00000164603,ENSG00000134001,ENSG00000198431,ENSG00000115944,ENSG00000170606,ENSG00000129084,ENSG00000065559,ENSG00000145349,ENSG00000168283,ENSG00000147416,ENSG00000178449,ENSG00000096384,ENSG00000116586,ENSG00000117450,ENSG00000117410,ENSG00000072401,ENSG00000114573,ENSG00000127824,ENSG00000131100,ENSG00000167552,ENSG00000109971,ENSG00000233822,ENSG00000155304,ENSG00000086061,ENSG00000165672,ENSG00000198898,ENSG00000100804,ENSG00000111775,ENSG00000109846,ENSG00000164032 |
| 9  | TP53 Regulates Metabolic Genes | REAC:<br>R-HSA-<br>562889<br>7 | 84  | 0.002015317 | 15 | ENSG00000178741,ENSG00000106615,ENSG00000164919,ENSG00000134248,ENSG00000136810,ENSG00000189043,ENSG00000166913,ENSG00000115419,ENSG00000198431,ENSG00000115944,ENSG00000178449,ENSG00000116586,ENSG00000117450,ENSG00000111775,ENSG00000128245   |
| 10 | Amino acids regulate mTORC1    | REAC:<br>R-HSA-<br>963928<br>8 | 55  | 0.002169899 | 12 | ENSG00000111203,ENSG00000106615,ENSG00000155097,ENSG00000134248,ENSG00000047249,ENSG00000100554,ENSG00000164603,ENSG00000147416,ENSG00000116586,ENSG00000117410,ENSG00000114573,ENSG00000131100   |

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|----|--|------------------------|-----|-------------|----|--|
| 11 | Neurotransmitter receptors and postsynaptic signal transmission    | REAC:<br>R-HSA-112314  | 196 | 0.003430639 | 24 | ENSG0000005249,ENSG00000100030,ENSG00000109738,ENSG00000145864,ENSG00000156642,ENSG00000082458,ENSG00000175175,ENSG00000166501,ENSG00000108946,ENSG00000109158,ENSG0000011677,ENSG00000145349,ENSG00000114450,ENSG00000152495,ENSG00000127824,ENSG00000167552,ENSG0000022355,ENSG00000073969,ENSG00000198785,ENSG00000182481,ENSG00000104490,ENSG00000162188,ENSG00000101958,ENSG00000186297 |
| 12 | Pyruvate metabolism and Citric Acid (TCA) cycle                    | REAC:<br>R-HSA-71406   | 54  | 0.010976225 | 11 | ENSG00000155380,ENSG00000004799,ENSG00000168291,ENSG00000117118,ENSG00000150768,ENSG00000163541,ENSG00000067992,ENSG00000124767,ENSG00000213585,ENSG00000143158,ENSG00000136143  |
| 13 | Prefoldin mediated transfer of substrate to CCT/TriC               | REAC:<br>R-HSA-389957  | 28  | 0.011022993 | 8  | ENSG00000120438,ENSG00000156261,ENSG00000150753,ENSG00000135624,ENSG00000115484,ENSG00000127824,ENSG00000167552,ENSG00000155959  |
| 14 | Complex I biogenesis   | REAC:<br>R-HSA-6799198 | 57  | 0.018746131 | 11 | ENSG00000164258,ENSG00000183648,ENSG00000165264,ENSG00000119421,ENSG00000128609,ENSG00000145494,ENSG00000125356,ENSG00000065518,ENSG00000123545,ENSG0000004779,ENSG00000119013   |
| 15 | Folding of actin by CCT/TriC                                       | REAC:<br>R-HSA-390450  | 10  | 0.019165304 | 5  | ENSG00000120438,ENSG00000156261,ENSG00000150753,ENSG00000135624,ENSG00000115484  |
| 16 | Pyruvate metabolism  | REAC:<br>R-HSA-70268   | 30  | 0.019185317 | 8  | ENSG00000155380,ENSG00000004799,ENSG00000168291,ENSG00000150768,ENSG00000067992,ENSG00000124767,ENSG00000213585,ENSG00000143158  |
| 17 | Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding | REAC:<br>R-HSA-389958  | 33  | 0.040445511 | 8  | ENSG00000120438,ENSG00000156261,ENSG00000150753,ENSG00000135624,ENSG00000115484,ENSG00000127824,ENSG00000167552,ENSG00000155959  |
| 18 | Formation of ATP by chemiosmotic coupling                          | REAC:<br>R-HSA-163210  | 18  | 0.047422293 | 6  | ENSG00000165629,ENSG00000124172,ENSG00000110955,ENSG00000167283,ENSG00000154518,ENSG00000152234  |

Table A18. Significant KCL BrainBank Reactome enrichments (adjusted p-value (FDR) < 0.05) with gProfiler2. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| # | Term Name                       | Term ID                   | Term Size | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|---|---------------------------------|---------------------------|-----------|------------------------|-------------------|---|
| 1 | Interferon Signaling            | REAC:<br>R-HSA-<br>913531 | 193       | 0.00376404             | 13                | ENSG00000162654,ENSG00000026508,ENSG00000154451,ENSG00000157601,ENSG00000183347,ENSG00000135114,ENSG00000183486,ENSG00000165949,ENSG00000204525,ENSG00000132530,ENSG00000111331,ENSG00000134321,ENSG00000162692 |
| 2 | Interferon alpha/beta signaling | REAC:<br>R-HSA-<br>909733 | 68        | 0.00388184             | 8                 | ENSG00000157601,ENSG00000135114,ENSG00000183486,ENSG00000165949,ENSG00000204525,ENSG00000132530,ENSG00000111331,ENSG00000134321   |
| 3 | Interferon gamma signaling      | REAC:<br>R-HSA-<br>877300 | 87        | 0.02391092             | 8                 | ENSG00000162654,ENSG00000026508,ENSG00000154451,ENSG00000183347,ENSG00000135114,ENSG00000204525,ENSG00000111331,ENSG00000162692   |

Table A19. Significant TargetALS Reactome enrichments (adjusted p-value (FDR) < 0.05) with gProfiler2. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| #  | Term Name   | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|----|---|-----------|-----------|------------------------|-------------------|---|
| 1  | NRF2 regulation of oxidative stress response  | 54        | 2.681E-06 | 2.257E-03              | 10                | Thioredoxin, PRDX1, TXNRD1, SMRT, ENC1, PKC, ERK2 (MAPK1), MEK4(MAP2K4), SOD1, PI3K reg class IA  |
| 2  | Tinnitus-associated changes in auditory pathway   | 82        | 3.658E-06 | 2.257E-03              | 12                | GAD1, HCN2, GABA-A receptor alpha-1 subunit, GLRA, GABA-A receptor beta-2 subunit, GABA-A receptor alpha-4 subunit, GRM6, GABA-A receptor alpha-5 subunit, Glycine receptor, GABA-A receptor alpha-3 subunit, Glycine receptor beta chain, GAD2 |
| 3  | Neurophysiological process_Regulation of intrinsic membrane properties and excitability of cortical pyramidal neurons | 74        | 7.984E-06 | 2.463E-03              | 11                | HPCA, TRPC5, G-protein beta/gamma, cPKC (conventional), PKA-reg (cAMP-dependent), TRPC4, Calcineurin A (catalytic), Neurocalcin delta, Calmodulin, PKC, HTR2A   |
| 4  | Ubiquinone metabolism   | 74        | 7.984E-06 | 2.463E-03              | 11                | NDUFAB1, NDUFA1, NDUFB4, NDUFA8, NDUFA4, NDUFB6, NDUFS4, NDUFB3, NDUFB1, NDUFS6, NDUFA5   |
| 5  | G protein-coupled receptors signaling in lung cancer  | 76        | 1.039E-05 | 2.564E-03              | 11                | Endothelin-1, CNR1, G-protein beta/gamma, Galpha(i)-specific peptide GPCRs, EGF, PKA-reg (cAMP-dependent), Galpha(i)-specific cannabis GPSRs, Galpha(q)-specific peptide GPCRs, Calmodulin, ERK1/2, SSTR2                                       |
| 6  | Oxidative stress_Role of ASK1 under oxidative stress  | 54        | 2.087E-05 | 4.292E-03              | 9                 | UNRIP, Thioredoxin, PRDX1, TXNIP (VDUP1), PP2A catalytic, Glutaredoxin, MEK4(MAP2K4), SOD1, 14-3-3  |
| 7  | Signal transduction_Calcium-mediated signaling  | 72        | 3.791E-05 | 6.412E-03              | 10                | PKC-beta, CaMK IV, cPKC (conventional), Calcineurin A (catalytic), MEF2, Calmodulin, ERK1/2, PKC, MEK4(MAP2K4), 14-3-3  |
| 8  | Signal transduction_Erk Interactions: Inhibition of Erk   | 34        | 4.261E-05 | 6.412E-03              | 7                 | PKA-reg (cAMP-dependent), Calcineurin A (catalytic), PP2A catalytic, Calmodulin, ERK1/2, PKC, ERK2 (MAPK1)  |
| 9  | Signal transduction_Non-neuronal ACM1, ACM3 and ACM5 signaling  | 74        | 4.826E-05 | 6.412E-03              | 10                | MRLC2, PKA-reg (cAMP-dependent), MRLC, Calmodulin, ERK1/2, PKC, Guanylate Cyclase 1, soluble, MEF2C, Protein kinase G, PI3K reg class IA  |
| 10 | Altered Ca <sup>2+</sup> handling in heart failure  | 35        | 5.196E-05 | 6.412E-03              | 7                 | G-protein beta/gamma, PP1-cat, NCX1, Calcineurin A (catalytic), PP2A catalytic, Calmodulin, CaMK II delta   |
| 11 | Bipolar Disorder  | 76        | 6.094E-05 | 6.674E-03              | 10                | Synaptotagmin I, PKC-beta, G-protein beta/gamma, cPKC (conventional), Serotonin receptor, PKA-reg (cAMP-dependent), Calcineurin A (catalytic), Calmodulin, ERK1/2, PKC  |
| 12 | Development_Melanocyte development and pigmentation   | 49        | 7.031E-05 | 6.674E-03              | 8                 | MGF, PKC-beta, PKA-reg (cAMP-dependent), Protein kinase G1, Guanylate cyclase (alpha-1/beta-1), ERK1/2, PI3K reg class IA, Galpha(s)-specific peptide GPCRs   |



|    |  |    |           |           |   |   |
|----|--|----|-----------|-----------|---|---|
| 13 | Transcription_CREB signaling pathway   | 49 | 7.031E-05 | 6.674E-03 | 8 | CaMK IV, cPKC (conventional), PKA-reg (cAMP-dependent), PP1-cat, PP2A catalytic, Calmodulin, ERK1/2, PI3K reg class IA  |
| 14 | Neurophysiological process_Activity-dependent synaptic AMPA receptor removal   | 64 | 8.388E-05 | 7.371E-03 | 9 | HPCA, NSF, cPKC (conventional), PP1-cat, Calcineurin A (catalytic), NAPB, PP2A catalytic, Calmodulin, PKC   |
| 15 | LRRK2 in neuronal apoptosis in Parkinson's disease   | 17 | 8.960E-05 | 7.371E-03 | 5 | PRDX3, Thioredoxin, VDAC 1, ANT, MPTP complex   |
| 16 | Neurophysiological process_GABA-A receptor life cycle  | 27 | 9.701E-05 | 7.461E-03 | 6 | GABA-A receptor alpha-1 subunit, NSF, GABA-A receptor beta-2 subunit, PP1-cat, Clathrin heavy chain, Tubulin alpha  |
| 17 | Regulation of degradation of deltaF508-CFTR in CF  | 39 | 1.076E-04 | 7.461E-03 | 7 | HSP90, HSP70, Aha1, UBE2D1, Hdj-2, SUMO-3, HSC70  |
| 18 | Neurophysiological process_Synaptic vesicle fusion and recycling in nerve terminals  | 52 | 1.088E-04 | 7.461E-03 | 8 | Synaptotagmin I, P/Q-type calcium channel alpha-1A subunit, NSF, SYP, Calcineurin A (catalytic), Calmodulin, Endophilin A1, HSC70   |
| 19 | Development_Role of HDAC and calcium/calmodulin-dependent kinase (CaMK) in control of skeletal myogenesis                    | 53 | 1.250E-04 | 8.119E-03 | 8 | CaMK IV, Calcineurin A (catalytic), MEF2, RHEB2, Calmodulin, MEF2C, PI3K reg class IA, 14-3-3   |
| 20 | Apoptosis and survival_BAD phosphorylation   | 42 | 1.753E-04 | 1.030E-02 | 7 | G-protein beta/gamma, PKA-reg (cAMP-dependent), Calcineurin A (catalytic), PP2A catalytic, ERK1/2, PI3K reg class IA, 14-3-3  |
| 21 | Oxidative stress_Activation of NOX1, NOX5, DUOX1 and DUOX2 NADPH Oxidases  | 42 | 1.753E-04 | 1.030E-02 | 7 | DUOX1, PKC-beta, cPKC (conventional), PKA-reg (cAMP-dependent), Calmodulin, PKC, ERK2 (MAPK1)   |
| 22 | Ca(2+)-dependent NF-AT signaling in cardiac hypertrophy  | 57 | 2.109E-04 | 1.089E-02 | 8 | PKC-beta, G-protein beta/gamma, PKA-reg (cAMP-dependent), NCX1, Calcineurin A (catalytic), MEF2, Calmodulin, MEF2C  |
| 23 | Regulation of intrinsic membrane properties and excitability of striatopallidal medium spiny neurons in Huntington's disease | 57 | 2.109E-04 | 1.089E-02 | 8 | G-protein beta/gamma, P/Q-type calcium channel alpha-1A subunit, cPKC (conventional), Calcineurin A (catalytic), Kv4.2 channel, Calmodulin, PKC, Guanylate Cyclase 1, soluble |
| 24 | Angiotensin II Signaling in Cardiac Hypertrophy  | 72 | 2.118E-04 | 1.089E-02 | 9 | Thioredoxin, G-protein beta/gamma, CaMK IV, NCX1, Calcineurin A (catalytic), Calmodulin, ERK1/2, MEK4(MAP2K4), SOD1   |
| 25 | Neurophysiological process_Glutamic acid regulation of Dopamine D1A receptor signaling                                       | 45 | 2.738E-04 | 1.351E-02 | 7 | GABA-A receptor beta-2 subunit, PKA-reg (cAMP-dependent), PP1-cat, CDK5, Calcineurin A (catalytic), PP2A catalytic, Calmodulin  |
| 26 | A shift from oxidative to glycolytic muscle fiber phenotype in quadriceps muscles in COPD                                    | 60 | 3.029E-04 | 1.438E-02 | 8 | DCMC, CPT-1A, ATP5B, PDK4, Fatty acid-binding protein, MEF2, ALAS1, ERK2 (MAPK1)  |

|    |  |     |           |           |    |   |
|----|--|-----|-----------|-----------|----|---|
| 27 | Regulation of intrinsic membrane properties and excitability of striatonigral medium spiny neurons in Huntington's disease | 62  | 3.808E-04 | 1.740E-02 | 8  | P/Q-type calcium channel alpha-1A subunit, cPKC (conventional), PKA-reg (cAMP-dependent), PP1-cat, Kv4.2 channel, Calmodulin, PKC, Guanylate Cyclase 1, soluble |
| 28 | Transcription_ChREBP regulation pathway  | 23  | 4.225E-04 | 1.862E-02 | 5  | G-protein beta/gamma, ChREBP, PKA-reg (cAMP-dependent), Acyl-CoA synthetase, PP2A catalytic   |
| 29 | Neurophysiological process_Constitutive and regulated NMDA receptor trafficking  | 65  | 5.274E-04 | 2.014E-02 | 8  | cPKC (conventional), PKA-reg (cAMP-dependent), PP1-cat, CDK5, Calcineurin A (catalytic), Calmodulin, PKC, SAP102  |
| 30 | NF-AT signaling in cardiac hypertrophy   | 65  | 5.274E-04 | 2.014E-02 | 8  | Endothelin-1, G-protein beta/gamma, CaMK IV, NCX1, Calcineurin A (catalytic), Calmodulin, MEF2C, PI3K reg class IA  |
| 31 | Transport_The role of AVP in regulation of Aquaporin 2 and renal water reabsorption  | 50  | 5.328E-04 | 2.014E-02 | 7  | PRKAR2B, MRLC2, PKA-reg type II (cAMP-dependent), PKA-reg (cAMP-dependent), MRLC, Calmodulin, ERK1/2  |
| 32 | Immune response_Function of MEF2 in T lymphocytes  | 50  | 5.328E-04 | 2.014E-02 | 7  | CaMK IV, Calcineurin A (catalytic), MEF2, Calmodulin, MEF2C, Calcineurin A (beta), 14-3-3   |
| 33 | Transport_RAB3 regulation pathway  | 14  | 5.385E-04 | 2.014E-02 | 4  | Rab-3B, Rab-3, NSF, Slp5  |
| 34 | Immune response_Reactive oxygen species (ROS) in IL-4 signaling  | 66  | 5.854E-04 | 2.125E-02 | 8  | DUOX1, cPKC (conventional), PKA-reg (cAMP-dependent), Protein kinase G1, Guanylate cyclase (alpha-1/beta-1), PP2A catalytic, Calmodulin, PKC                    |
| 35 | Muscle contraction_GPCRs in the regulation of smooth muscle tone   | 83  | 6.197E-04 | 2.142E-02 | 9  | Endothelin-1, MELC, TRPC5, PKA-reg (cAMP-dependent), TRPC4, NCX1, MRLC, Calmodulin, HTR2A   |
| 36 | HSP70 and HSP40-dependent folding in Huntington's disease  | 25  | 6.363E-04 | 2.142E-02 | 5  | HSP90, HSP70, HSP90 beta, Hdj-2, HSC70  |
| 37 | Signal transduction_Activation of PKC via G-Protein coupled receptor   | 52  | 6.793E-04 | 2.142E-02 | 7  | MELC, PKC-beta, G-protein beta/gamma, Calcineurin A (catalytic), MEF2, Calmodulin, ERK1/2   |
| 38 | Nicotine signaling in cholinergic neurons  | 52  | 6.793E-04 | 2.142E-02 | 7  | G-protein beta/gamma, P/Q-type calcium channel alpha-1A subunit, Protein kinase G1, Calmodulin, Guanylate Cyclase 1, soluble, ERK2 (MAPK1), PI3K reg class IA   |
| 39 | Signal transduction_Cyclic AMP signaling   | 38  | 6.927E-04 | 2.142E-02 | 6  | G-protein beta/gamma, CaMK IV, PKA-reg (cAMP-dependent), Calcineurin A (catalytic), Calmodulin, PKC   |
| 40 | Epigenetic regulation of neuronal hyperexcitability in neuropathic pain  | 102 | 7.020E-04 | 2.142E-02 | 10 | PP2A cat (alpha), JMJD3, 14-3-3 beta/alpha, SYP, CDK5, Histone H2B, PP2A catalytic, Kv4.2 channel, Calmodulin, GAD2   |

|    |  |    |           |           |   |   |
|----|--|----|-----------|-----------|---|---|
| 41 | Calcium-dependent regulation of normal and asthmatic smooth muscle contraction | 68 | 7.168E-04 | 2.142E-02 | 8 | Endothelin-1, Substance P extracellular region, G-protein beta/gamma, Neurokinin A, TRPC4, NCX1, MRLC, Calmodulin   |
| 42 | ENaC regulation in normal and CF airways                                       | 53 | 7.636E-04 | 2.142E-02 | 7 | Endothelin-1, G-protein beta/gamma, cPKC (conventional), PKA-reg (cAMP-dependent), ERK1/2, Protein kinase G, PI3K reg class IA  |
| 43 | Neurophysiological process_Long-term depression in cerebellum                  | 53 | 7.636E-04 | 2.142E-02 | 7 | G-protein beta/gamma, P/Q-type calcium channel alpha-1A subunit, PP2A catalytic, Galpha(s)-specific CRF GPCRs, ERK1/2, Guanylate Cyclase 1, soluble, Protein kinase G |
| 44 | Translation_Regulation of EIF4F activity                                       | 53 | 7.636E-04 | 2.142E-02 | 7 | EGF, PP2A catalytic, eIF4A, RHEB2, ERK1/2, MEK4(MAP2K4), PI3K reg class IA  |
| 45 | Transcription_Negative regulation of HIF1A function                            | 69 | 7.908E-04 | 2.169E-02 | 8 | HSP90, HSP70, CITED2, HSPA4, MTG16 (CBFA2T3), HSP90 beta, LAMP2, HSC70  |
| 46 | HCV-dependent cytoplasmic signaling leading to HCC                             | 27 | 9.223E-04 | 2.474E-02 | 5 | 14-3-3 beta/alpha, eIF2S1, ERK1/2, PKC, ERK2 (MAPK1)  |
| 47 | Development_Oxytocin receptor signaling  | 41 | 1.049E-03 | 2.755E-02 | 6 | G-protein beta/gamma, cPKC (conventional), Protein kinase G1, Calmodulin, Guanylate Cyclase 1, soluble, MEF2C   |
| 48 | Signal transduction_NO synthesis   | 90 | 1.117E-03 | 2.840E-02 | 9 | HSP90, IRF1, Endothelin-1, G-protein beta/gamma, TRPC, PKA-reg (cAMP-dependent), Calmodulin, ERK1/2, MEF2C  |
| 49 | CHDI_Correlations from Discovery data_Causal network                           | 73 | 1.151E-03 | 2.840E-02 | 8 | Substance P extracellular region, G-protein beta/gamma, CaMK IV, CDK5, MEF2, RHEB2, Calmodulin, ERK1/2  |
| 50 | Neurophysiological process_Thyroliberin signaling                              | 73 | 1.151E-03 | 2.840E-02 | 8 | Endothelin-1, PKC-beta, G-protein beta/gamma, cPKC (conventional), PKA-reg (cAMP-dependent), Calmodulin, ERK1/2, PKC  |

Table A25. Top 50 KCL BrainBank Pathway Maps enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.

| #  | Term Name   | Term Size | p-value   | adjusted p-value (FDR) | Intersection Size | Intersection Gene Names   |
|----|---|-----------|-----------|------------------------|-------------------|---|
| 1  | Protein folding and maturation_POMC processing  | 22        | 3.761E-24 | 2.223E-21              | 17                | CLIP, ACTH, alpha-MSH, beta-Endorphin, proACTH, POMC, Joining peptide (JP), N-POMC, gamma-MSH, N-POC, beta-LPH, gamma-LPH, ACTH 1-17, DA-alphaMSH, gamma2-MSH, gamma3-MSH, beta-MSH |
| 2  | POMC, alpha-MSH and AGRP in regulation of food intake and energy expenditure in obesity in hypothalamus | 31        | 7.127E-06 | 2.106E-03              | 7                 | alpha-MSH, MC4R, proACTH, POMC, Beta-MSH / Beta-Endorphin, beta-LPH, AGRP   |
| 3  | Immune response_IFN-alpha/beta signaling via JAK/STAT   | 59        | 5.218E-04 | 1.028E-01              | 7                 | MxB, RSAD2, XAF1, IFI27, I-TAC, Apo-2L(TNFSF10), GBP4   |
| 4  | Development_Positive regulation of WNT/Beta-catenin signaling at the receptor level                     | 64        | 8.582E-04 | 1.268E-01              | 7                 | R-spondins, CD44, WNT7B, LGR6, Biglycan, RAB3IP, WNT  |
| 5  | Role of metalloproteases and heparanase in progression of pancreatic cancer                             | 29        | 4.986E-03 | 5.787E-01              | 4                 | CD44, CD44 soluble, CD147, CD44 (EXT)   |
| 6  | Dysregulation of germinal center response in SLE  | 51        | 7.630E-03 | 5.787E-01              | 5                 | VCAM1, MFGE8, Fc gamma RII beta, APRIL(TNFSF13), Oct-2  |
| 7  | Gamma-secretase regulation of osteogenesis  | 33        | 7.967E-03 | 5.787E-01              | 4                 | CD44, CD44 soluble, CD44 (ICD), CD44 (EXT)  |
| 8  | Role of osteoblasts in bone lesions formation in multiple myeloma                                       | 33        | 7.967E-03 | 5.787E-01              | 4                 | HGF, VCAM1, Apo-2L(TNFSF10), WNT  |
| 9  | Role of Nicotine-induced Leptin resistance in hypothalamus in development of obesity                    | 18        | 8.812E-03 | 5.787E-01              | 3                 | POMC, AGRP, CART  |
| 10 | L-Threonine metabolism  | 20        | 1.188E-02 | 5.890E-01              | 3                 | SDHL, ASCT1 (SLC1A4), SDSL  |
| 11 | Role of Leptin in regulation of eating behavior in obesity  | 20        | 1.188E-02 | 5.890E-01              | 3                 | POMC, AGRP, CART  |
| 12 | Renal secretion of inorganic electrolytes   | 21        | 1.362E-02 | 5.890E-01              | 3                 | SLC4A4, Aquaporin 1, SLC12A1  |
| 13 | Neurophysiological process_Glucose-excited neurons of arcuate nucleus (rodent model)                    | 21        | 1.362E-02 | 5.890E-01              | 3                 | HIF-prolyl hydroxylase, POMC, CART  |

|    |   |    |           |           |   |   |
|----|---|----|-----------|-----------|---|---|
| 14 | Type 2 diabetes (general schema)  | 8  | 1.495E-02 | 5.890E-01 | 2 | POMC, AGRP  |
| 15 | Cell adhesion_Gap junctions   | 22 | 1.549E-02 | 5.890E-01 | 3 | Connexin 30, Tubulin beta, Connexin 26                                |
| 16 | Inhibition of apoptosis in gastric cancer   | 41 | 1.698E-02 | 5.890E-01 | 4 | HGF, Caspase-10, XAF1, Apo-2L(TNFSF10)                                |
| 17 | Stem cells_Aberrant Wnt signaling in medulloblastoma stem cells                             | 23 | 1.750E-02 | 5.890E-01 | 3 | CD44, WNT, WIF1   |
| 18 | Transcription_Hypoxia- and receptor-mediated HIF-1 activation                               | 42 | 1.842E-02 | 5.890E-01 | 4 | HGF, HIF-prolyl hydroxylase, GPNMB (Osteoactivin), EGF                |
| 19 | Putative pathways of activation of classical complement system in major depressive disorder | 24 | 1.965E-02 | 5.890E-01 | 3 | C4A protein, C4, C4b  |
| 20 | Glycine and L-Serine metabolism   | 43 | 1.993E-02 | 5.890E-01 | 4 | PIPOX, SDHL, ASCT1 (SLC1A4), SDSL                                     |
| 21 | Development_Astrocyte differentiation (general schema)                                      | 25 | 2.194E-02 | 6.176E-01 | 3 | SLC6A11, CD44, GFAP   |
| 22 | Development_Signaling pathways in embryonic hepatocyte maturation                           | 45 | 2.318E-02 | 6.228E-01 | 4 | HGF, ALDOB, L-FABP, LRH1  |
| 23 | Role of tumor-infiltrating B cells in anti-tumor immunity                                   | 69 | 2.579E-02 | 6.628E-01 | 5 | Kappa chain (Ig light chain), Perforin, I-TAC, Apo-2L(TNFSF10), MLANA |
| 24 | Inter-cellular relations in COPD (general schema)   | 27 | 2.694E-02 | 6.634E-01 | 3 | Perforin, I-TAC, EGF  |
| 25 | Colorectal cancer (general schema)  | 28 | 2.965E-02 | 7.009E-01 | 3 | HGF, EGF, WNT   |
| 26 | Glomerular filtration and renal reabsorption of bile acids / Rodent version                 | 12 | 3.307E-02 | 7.517E-01 | 2 | HYEP, L-FABP  |
| 27 | WNT signaling in invasive-type melanoma cells   | 30 | 3.548E-02 | 7.766E-01 | 3 | KiSS-1, CD44, MLANA   |
| 28 | Gamma-secretase proteolytic targets   | 52 | 3.700E-02 | 7.810E-01 | 4 | CD44, CD44 soluble, CD44 (ICD), CD44 (EXT)                            |
| 29 | Disruption of epithelial layer restitution in asthma  | 31 | 3.860E-02 | 7.866E-01 | 3 | HGF, EGF, RXRG  |

|    |   |    |           |           |   |   |
|----|---|----|-----------|-----------|---|---|
| 30 | Role of red blood cell adhesion to endothelium in vaso-occlusion in Sickle cell disease | 32 | 4.185E-02 | 7.895E-01 | 3 | VCAM1, CD44, CD147                                |
| 31 | Cholehepatic circulation of bile acids / Rodent version                                 | 14 | 4.418E-02 | 7.895E-01 | 2 | HYEP, L-FABP                                      |
| 32 | Beta-catenin-dependent transcription regulation in colorectal cancer                    | 33 | 4.524E-02 | 7.895E-01 | 3 | CD44, CD44 soluble, CD44 (EXT)                    |
| 33 | Immune response_Antiviral actions of Interferons  | 33 | 4.524E-02 | 7.895E-01 | 3 | 2'-5'-oligoadenylate synthetase, MxA, OAS3        |
| 34 | E-cadherin signaling and its regulation in gastric cancer                               | 34 | 4.876E-02 | 7.895E-01 | 3 | HGF, EGF, WNT                                     |
| 35 | PR action in breast cancer: stimulation of metastasis                                   | 15 | 5.018E-02 | 7.895E-01 | 2 | PR (membrane), PR (nuclear)                       |
| 36 | Anandamide biosynthesis and metabolism  | 15 | 5.018E-02 | 7.895E-01 | 2 | PLC-delta, PLA2G5                                 |
| 37 | L-Lysine metabolism   | 35 | 5.241E-02 | 7.895E-01 | 3 | PIPOX, CAT-2, HCD2                                |
| 38 | HGF signaling in melanoma   | 36 | 5.619E-02 | 7.895E-01 | 3 | HGF, CD44, alpha-MSH                              |
| 39 | Development_Role of proteases in hematopoietic stem cell mobilization                   | 16 | 5.645E-02 | 7.895E-01 | 2 | VCAM1, CD44                                       |
| 40 | Enterohepatic circulation of bile acids / Rodent version                                | 16 | 5.645E-02 | 7.895E-01 | 2 | HYEP, L-FABP                                      |
| 41 | Mitochondrial beta-oxidation of long-chain saturated fatty acids                        | 37 | 6.010E-02 | 7.895E-01 | 3 | L-FABP, CPT-1A, HCD2                              |
| 42 | Influence of bone marrow cell environment on progression of multiple myeloma            | 37 | 6.010E-02 | 7.895E-01 | 3 | HGF, VCAM1, CD44                                  |
| 43 | Multiple sclerosis (general schema)   | 17 | 6.298E-02 | 7.895E-01 | 2 | VCAM1, Apo-2L(TNFSF10)                            |
| 44 | Development_Melanocyte development and pigmentation                                     | 38 | 6.413E-02 | 7.895E-01 | 3 | ACTH, alpha-MSH, Galpha(s)-specific peptide GPCRs |
| 45 | Signal transduction_Leptin signaling via JAK/STAT and MAPK cascade                      | 38 | 6.413E-02 | 7.895E-01 | 3 | POMC, AGRP, CART                                  |

|    |   |    |           |           |   |                                  |
|----|---|----|-----------|-----------|---|----------------------------------|
| 46 | WNT signaling in proliferative-type melanoma cells      | 38 | 6.413E-02 | 7.895E-01 | 3 | WNT7B, WNT, WIF1                 |
| 47 | Apoptosis and survival_Granzyme A signaling             | 38 | 6.413E-02 | 7.895E-01 | 3 | Histone H2B, HMGB2, Perforin     |
| 48 | Development_WNT/Beta-catenin signaling in embryogenesis | 38 | 6.413E-02 | 7.895E-01 | 3 | SOX17, LRH1, WNT                 |
| 49 | Breast cancer (general schema)                          | 39 | 6.828E-02 | 7.927E-01 | 3 | EGF, PR (membrane), PR (nuclear) |
| 50 | Immune response_Lectin induced complement pathway       | 39 | 6.828E-02 | 7.927E-01 | 3 | C4, C4a, C4b                     |

*Table A26. Top 50 TargetALS Pathway Maps enrichments with MetaCore. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term.*

| Clinical Phenotype        | Ensembl ID      | Gene Symbol   | KCL BrainBank |               |               | TargetALS (medial) |               |               | TargetALS (lateral) |               |               |
|---------------------------|-----------------|---------------|---------------|---------------|---------------|--------------------|---------------|---------------|---------------------|---------------|---------------|
|                           |                 |               | Pearson's r   | p-value       | p-value (adj) | Pearson's r        | p-value       | p-value (adj) | Pearson's r         | p-value       | p-value (adj) |
| Disease Duration (months) | ENSG00000006128 | <i>TAC1</i>   | 0.1815        | 0.0737        | 1.0           | 0.0384             | 0.7192        | 1.0           | 0.1036              | 0.3229        | 1.0           |
|                           | ENSG00000017427 | <i>IGF1</i>   | 0.0900        | 0.3783        | 1.0           | 0.0388             | 0.7166        | 1.0           | 0.2078              | <b>0.0456</b> | 1.0           |
|                           | ENSG00000049247 | <i>UTS2</i>   | -0.1975       | 0.0513        | 1.0           | -0.1057            | 0.3215        | 1.0           | -0.1596             | 0.1264        | 1.0           |
|                           | ENSG00000056291 | <i>NPFFR2</i> | -0.1236       | 0.2255        | 1.0           | 0.0271             | 0.8000        | 1.0           | -0.1015             | 0.3329        | 1.0           |
|                           | ENSG00000069482 | <i>GAL</i>    | 0.1076        | 0.2917        | 1.0           | -0.0451            | 0.6727        | 1.0           | 0.1017              | 0.3320        | 1.0           |
|                           | ENSG00000070031 | <i>SCT</i>    | -0.0149       | 0.8841        | 1.0           | 0.1510             | 0.1554        | 1.0           | 0.0956              | 0.3619        | 1.0           |
|                           | ENSG00000075073 | <i>TACR2</i>  | 0.0318        | 0.7561        | 1.0           | 0.1199             | 0.2605        | 1.0           | 0.0609              | 0.5622        | 1.0           |
|                           | ENSG00000078401 | <i>EDN1</i>   | 0.0073        | 0.9428        | 1.0           | 0.0756             | 0.4788        | 1.0           | -0.0616             | 0.5575        | 1.0           |
|                           | ENSG00000082556 | <i>OPRK1</i>  | -0.0529       | 0.6050        | 1.0           | -0.0561            | 0.5994        | 1.0           | 0.0510              | 0.6276        | 1.0           |
|                           | ENSG00000087494 | <i>PTHLH</i>  | 0.1521        | 0.1348        | 1.0           | 0.1445             | 0.1743        | 1.0           | 0.1739              | 0.0954        | 1.0           |
|                           | ENSG00000096395 | <i>MLN</i>    | -0.0067       | 0.9474        | 1.0           | 0.1168             | 0.2730        | 1.0           | -0.1418             | 0.1752        | 1.0           |
|                           | ENSG00000100604 | <i>CHGA</i>   | 0.0101        | 0.9211        | 1.0           | 0.0181             | 0.8653        | 1.0           | 0.0058              | 0.9561        | 1.0           |
|                           | ENSG00000100739 | <i>BDKRB1</i> | -0.0304       | 0.7666        | 1.0           | -0.1843            | 0.0821        | 1.0           | 0.1753              | 0.0928        | 1.0           |
|                           | ENSG00000101188 | <i>NTSR1</i>  | 0.0691        | 0.4990        | 1.0           | 0.2855             | <b>0.0064</b> | 0.6720        | 0.0337              | 0.7485        | 1.0           |
|                           | ENSG00000101200 | <i>AVP</i>    | NA            | NA            | NA            | 0.0928             | 0.3841        | 1.0           | 0.0653              | 0.5343        | 1.0           |
|                           | ENSG00000101327 | <i>PDYN</i>   | -0.0009       | 0.9933        | 1.0           | 0.1611             | 0.1294        | 1.0           | 0.0651              | 0.5350        | 1.0           |
|                           | ENSG00000102539 | <i>MLNR</i>   | -0.1471       | 0.1484        | 1.0           | 0.0488             | 0.6480        | 1.0           | -0.0344             | 0.7431        | 1.0           |
|                           | ENSG00000107014 | <i>RLN2</i>   | -0.0005       | 0.9965        | 1.0           | -0.0660            | 0.5363        | 1.0           | 0.0198              | 0.8505        | 1.0           |
|                           | ENSG00000107018 | <i>RLN1</i>   | 0.0989        | 0.3326        | 1.0           | -0.0701            | 0.5114        | 1.0           | -0.0024             | 0.9814        | 1.0           |
|                           | ENSG00000109163 | <i>GNRHR</i>  | 0.0356        | 0.7280        | 1.0           | -0.1190            | 0.2639        | 1.0           | -0.0563             | 0.5922        | 1.0           |
|                           | ENSG00000109255 | <i>NMU</i>    | 0.1481        | 0.1455        | 1.0           | -0.0484            | 0.6504        | 1.0           | 0.0588              | 0.5754        | 1.0           |
|                           | ENSG00000110148 | <i>CCKBR</i>  | 0.1223        | 0.2302        | 1.0           | 0.0809             | 0.4486        | 1.0           | 0.1342              | 0.1996        | 1.0           |
|                           | ENSG00000110680 | <i>CALCA</i>  | -0.0377       | 0.7127        | 1.0           | 0.2513             | <b>0.0169</b> | 1.0           | -0.0568             | 0.5887        | 1.0           |
|                           | ENSG00000112038 | <i>OPRM1</i>  | 0.1160        | 0.2552        | 1.0           | -0.0459            | 0.6676        | 1.0           | -0.0303             | 0.7728        | 1.0           |
|                           | ENSG00000113889 | <i>KNG1</i>   | -0.0556       | 0.5863        | 1.0           | -0.1042            | 0.3285        | 1.0           | 0.0214              | 0.8384        | 1.0           |
|                           | ENSG00000115138 | <i>POMC</i>   | -0.1024       | 0.3157        | 1.0           | 0.0342             | 0.7486        | 1.0           | -0.1015             | 0.3329        | 1.0           |
|                           | ENSG00000115353 | <i>TACR1</i>  | 0.2110        | <b>0.0370</b> | 1.0           | 0.1140             | 0.2848        | 1.0           | 0.2331              | <b>0.0245</b> | 1.0           |
|                           | ENSG00000116014 | <i>KISS1R</i> | 0.1325        | 0.1936        | 1.0           | 0.0840             | 0.4312        | 1.0           | -0.0502             | 0.6326        | 1.0           |
|                           | ENSG00000116329 | <i>OPRD1</i>  | -0.1212       | 0.2346        | 1.0           | 0.0173             | 0.8714        | 1.0           | 0.0147              | 0.8886        | 1.0           |
|                           | ENSG00000119973 | <i>PRLHR</i>  | 0.1400        | 0.1690        | 1.0           | 0.0857             | 0.4219        | 1.0           | 0.2083              | <b>0.0451</b> | 1.0           |
| ENSG00000120937           | <i>NPPB</i>     | 0.0934        | 0.3605        | 1.0           | NA            | NA                 | NA            | NA            | NA                  | NA            |               |
| ENSG00000121764           | <i>HCRTR1</i>   | -0.0368       | 0.7187        | 1.0           | 0.0450        | 0.6735             | 1.0           | 0.2409        | <b>0.0200</b>       | 1.0           |               |



|                 |                |         |               |        |         |               |     |         |               |     |
|-----------------|----------------|---------|---------------|--------|---------|---------------|-----|---------|---------------|-----|
| ENSG00000122585 | <i>NPY</i>     | 0.0448  | 0.6616        | 1.0    | 0.1185  | 0.2661        | 1.0 | -0.0445 | 0.6718        | 1.0 |
| ENSG00000124089 | <i>MC3R</i>    | NA      | NA            | NA     | 0.0514  | 0.6301        | 1.0 | 0.1424  | 0.1733        | 1.0 |
| ENSG00000124205 | <i>EDN3</i>    | -0.0173 | 0.8659        | 1.0    | 0.0197  | 0.8537        | 1.0 | -0.1067 | 0.3087        | 1.0 |
| ENSG00000125510 | <i>OPRL1</i>   | 0.0612  | 0.5495        | 1.0    | 0.1287  | 0.2267        | 1.0 | 0.0272  | 0.7959        | 1.0 |
| ENSG00000125522 | <i>NPBWR2</i>  | 0.1138  | 0.2646        | 1.0    | 0.0049  | 0.9636        | 1.0 | -0.0196 | 0.8522        | 1.0 |
| ENSG00000125787 | <i>GNRH2</i>   | -0.1234 | 0.2260        | 1.0    | 0.1036  | 0.3314        | 1.0 | -0.0928 | 0.3762        | 1.0 |
| ENSG00000126895 | <i>AVPR2</i>   | -0.3233 | <b>0.0012</b> | 0.1224 | 0.0397  | 0.7099        | 1.0 | -0.0608 | 0.5626        | 1.0 |
| ENSG00000128165 | <i>ADM2</i>    | -0.1500 | 0.1404        | 1.0    | 0.0627  | 0.5569        | 1.0 | 0.0008  | 0.9942        | 1.0 |
| ENSG00000128285 | <i>MCHR1</i>   | 0.1154  | 0.2579        | 1.0    | -0.0195 | 0.8553        | 1.0 | 0.0193  | 0.8545        | 1.0 |
| ENSG00000128310 | <i>GALR3</i>   | -0.0094 | 0.9269        | 1.0    | 0.0028  | 0.9790        | 1.0 | 0.0048  | 0.9635        | 1.0 |
| ENSG00000131096 | <i>PYY</i>     | 0.0847  | 0.4071        | 1.0    | 0.0215  | 0.8404        | 1.0 | 0.0636  | 0.5445        | 1.0 |
| ENSG00000132671 | <i>SSTR4</i>   | 0.1646  | 0.1054        | 1.0    | 0.1120  | 0.2933        | 1.0 | 0.1557  | 0.1361        | 1.0 |
| ENSG00000132911 | <i>NMUR2</i>   | -0.0494 | 0.6289        | 1.0    | -0.0782 | 0.4637        | 1.0 | -0.1404 | 0.1796        | 1.0 |
| ENSG00000133636 | <i>NTS</i>     | NA      | NA            | NA     | -0.0727 | 0.4957        | 1.0 | 0.0832  | 0.4278        | 1.0 |
| ENSG00000134443 | <i>GRP</i>     | 0.0054  | 0.9577        | 1.0    | 0.0464  | 0.6639        | 1.0 | -0.1242 | 0.2357        | 1.0 |
| ENSG00000135744 | <i>AGT</i>     | 0.0847  | 0.4072        | 1.0    | 0.2198  | <b>0.0374</b> | 1.0 | 0.0880  | 0.4014        | 1.0 |
| ENSG00000136160 | <i>EDNRB</i>   | 0.0497  | 0.6269        | 1.0    | 0.0136  | 0.8991        | 1.0 | -0.0649 | 0.5364        | 1.0 |
| ENSG00000137252 | <i>HCRTR2</i>  | 0.0853  | 0.4035        | 1.0    | 0.0403  | 0.7060        | 1.0 | 0.1035  | 0.3237        | 1.0 |
| ENSG00000139574 | <i>NPFF</i>    | -0.0754 | 0.4606        | 1.0    | -0.0697 | 0.5138        | 1.0 | -0.1424 | 0.1732        | 1.0 |
| ENSG00000139874 | <i>SSTR1</i>   | 0.0541  | 0.5965        | 1.0    | 0.1074  | 0.3135        | 1.0 | 0.0419  | 0.6899        | 1.0 |
| ENSG00000141433 | <i>ADCYAP1</i> | 0.1210  | 0.2351        | 1.0    | 0.1118  | 0.2942        | 1.0 | 0.1684  | 0.1067        | 1.0 |
| ENSG00000144891 | <i>AGTR1</i>   | -0.2372 | <b>0.0187</b> | 1.0    | -0.0541 | 0.6127        | 1.0 | -0.1301 | 0.2138        | 1.0 |
| ENSG00000145040 | <i>UCN2</i>    | 0.0169  | 0.8685        | 1.0    | -0.0236 | 0.8250        | 1.0 | -0.1320 | 0.2072        | 1.0 |
| ENSG00000146469 | <i>VIP</i>     | 0.1764  | 0.0824        | 1.0    | 0.0727  | 0.4962        | 1.0 | 0.1854  | 0.0753        | 1.0 |
| ENSG00000147437 | <i>GNRH1</i>   | -0.1891 | 0.0622        | 1.0    | -0.2565 | <b>0.0147</b> | 1.0 | -0.2138 | <b>0.0396</b> | 1.0 |
| ENSG00000147571 | <i>CRH</i>     | 0.1047  | 0.3048        | 1.0    | 0.1427  | 0.1796        | 1.0 | 0.1438  | 0.1691        | 1.0 |
| ENSG00000148734 | <i>NPFFR1</i>  | 0.0256  | 0.8021        | 1.0    | -0.1112 | 0.2967        | 1.0 | -0.1638 | 0.1166        | 1.0 |
| ENSG00000148926 | <i>ADM</i>     | -0.0558 | 0.5851        | 1.0    | 0.0401  | 0.7077        | 1.0 | 0.0673  | 0.5215        | 1.0 |
| ENSG00000151617 | <i>EDNRA</i>   | -0.1943 | 0.0552        | 1.0    | 0.0612  | 0.5667        | 1.0 | 0.1770  | 0.0897        | 1.0 |
| ENSG00000152034 | <i>MCHR2</i>   | 0.1232  | 0.2269        | 1.0    | -0.0395 | 0.7117        | 1.0 | 0.0376  | 0.7205        | 1.0 |
| ENSG00000157005 | <i>SST</i>     | 0.2060  | <b>0.0418</b> | 1.0    | 0.1386  | 0.1927        | 1.0 | 0.1291  | 0.2173        | 1.0 |
| ENSG00000157017 | <i>GHRL</i>    | -0.1210 | 0.2353        | 1.0    | 0.0463  | 0.6650        | 1.0 | -0.0624 | 0.5524        | 1.0 |
| ENSG00000159723 | <i>AGRP</i>    | -0.1807 | 0.0749        | 1.0    | -0.0014 | 0.9896        | 1.0 | -0.0762 | 0.4677        | 1.0 |
| ENSG00000161610 | <i>HCRT</i>    | -0.0527 | 0.6062        | 1.0    | NA      | NA            | NA  | NA      | NA            | NA  |

|                 |               |         |        |     |         |               |     |         |               |     |
|-----------------|---------------|---------|--------|-----|---------|---------------|-----|---------|---------------|-----|
| ENSG00000162009 | <i>SSTR5</i>  | NA      | NA     | NA  | 0.2161  | <b>0.0408</b> | 1.0 | 0.1433  | 0.1707        | 1.0 |
| ENSG00000163273 | <i>NPPC</i>   | 0.0876  | 0.3909 | 1.0 | 0.0587  | 0.5826        | 1.0 | 0.0660  | 0.5295        | 1.0 |
| ENSG00000163394 | <i>CCKAR</i>  | 0.0179  | 0.8608 | 1.0 | 0.0286  | 0.7893        | 1.0 | -0.2155 | <b>0.0380</b> | 1.0 |
| ENSG00000163794 | <i>UCN</i>    | -0.0228 | 0.8239 | 1.0 | 0.0410  | 0.7015        | 1.0 | 0.0102  | 0.9226        | 1.0 |
| ENSG00000164128 | <i>NPY1R</i>  | -0.1165 | 0.2531 | 1.0 | 0.0008  | 0.9943        | 1.0 | 0.0176  | 0.8667        | 1.0 |
| ENSG00000164129 | <i>NPY5R</i>  | 0.0968  | 0.3429 | 1.0 | 0.0166  | 0.8766        | 1.0 | 0.0064  | 0.9512        | 1.0 |
| ENSG00000166148 | <i>AVPR1A</i> | -0.0991 | 0.3316 | 1.0 | 0.2177  | <b>0.0393</b> | 1.0 | 0.0951  | 0.3646        | 1.0 |
| ENSG00000166573 | <i>GALR1</i>  | 0.0037  | 0.9713 | 1.0 | 0.1054  | 0.3229        | 1.0 | 0.1167  | 0.2653        | 1.0 |
| ENSG00000166603 | <i>MC4R</i>   | 0.1065  | 0.2965 | 1.0 | -0.1098 | 0.3028        | 1.0 | -0.0531 | 0.6133        | 1.0 |
| ENSG00000166863 | <i>TAC3</i>   | 0.1196  | 0.2408 | 1.0 | 0.0782  | 0.4639        | 1.0 | 0.2125  | <b>0.0409</b> | 1.0 |
| ENSG00000167244 | <i>IGF2</i>   | -0.0464 | 0.6502 | 1.0 | 0.0044  | 0.9671        | 1.0 | 0.0396  | 0.7062        | 1.0 |
| ENSG00000168081 | <i>PNOC</i>   | 0.0691  | 0.4991 | 1.0 | 0.2000  | 0.0587        | 1.0 | 0.2315  | <b>0.0256</b> | 1.0 |
| ENSG00000168398 | <i>BDKRB2</i> | 0.1000  | 0.3273 | 1.0 | -0.0307 | 0.7736        | 1.0 | 0.0200  | 0.8494        | 1.0 |
| ENSG00000169006 | <i>NTSR2</i>  | 0.1501  | 0.1400 | 1.0 | 0.0667  | 0.5321        | 1.0 | 0.0282  | 0.7888        | 1.0 |
| ENSG00000169836 | <i>TACR3</i>  | 0.0013  | 0.9899 | 1.0 | -0.1422 | 0.1811        | 1.0 | 0.0974  | 0.3529        | 1.0 |
| ENSG00000170498 | <i>KISS1</i>  | NA      | NA     | NA  | NA      | NA            | NA  | 0.2198  | <b>0.0342</b> | 1.0 |
| ENSG00000170893 | <i>TRH</i>    | 0.1858  | 0.0670 | 1.0 | 0.1824  | 0.0852        | 1.0 | 0.0973  | 0.3536        | 1.0 |
| ENSG00000171388 | <i>APLN</i>   | -0.0811 | 0.4273 | 1.0 | -0.0556 | 0.6028        | 1.0 | -0.0076 | 0.9426        | 1.0 |
| ENSG00000171596 | <i>NMUR1</i>  | -0.0789 | 0.4402 | 1.0 | 0.2664  | <b>0.0112</b> | 1.0 | 0.2215  | <b>0.0329</b> | 1.0 |
| ENSG00000174417 | <i>TRHR</i>   | -0.0020 | 0.9844 | 1.0 | -0.0412 | 0.6996        | 1.0 | -0.0264 | 0.8018        | 1.0 |
| ENSG00000174697 | <i>LEP</i>    | -0.0942 | 0.3561 | 1.0 | 0.0821  | 0.4419        | 1.0 | -0.0350 | 0.7391        | 1.0 |
| ENSG00000175206 | <i>NPPA</i>   | -0.1106 | 0.2785 | 1.0 | -0.1117 | 0.2946        | 1.0 | 0.0937  | 0.3718        | 1.0 |
| ENSG00000175868 | <i>CALCB</i>  | -0.1456 | 0.1526 | 1.0 | 0.0478  | 0.6548        | 1.0 | -0.0209 | 0.8421        | 1.0 |
| ENSG00000176136 | <i>MC5R</i>   | 0.0629  | 0.5385 | 1.0 | 0.0690  | 0.5181        | 1.0 | 0.1699  | 0.1034        | 1.0 |
| ENSG00000176358 | <i>TAC4</i>   | -0.0249 | 0.8075 | 1.0 | 0.0160  | 0.8811        | 1.0 | 0.0395  | 0.7067        | 1.0 |
| ENSG00000180616 | <i>SSTR2</i>  | 0.0732  | 0.4741 | 1.0 | 0.0264  | 0.8047        | 1.0 | -0.0563 | 0.5919        | 1.0 |
| ENSG00000180914 | <i>OXTR</i>   | -0.1290 | 0.2056 | 1.0 | -0.1326 | 0.2129        | 1.0 | -0.1716 | 0.1000        | 1.0 |
| ENSG00000181195 | <i>PENK</i>   | 0.1098  | 0.2819 | 1.0 | 0.0599  | 0.5746        | 1.0 | 0.1415  | 0.1761        | 1.0 |
| ENSG00000181408 | <i>UTS2R</i>  | -0.1650 | 0.1045 | 1.0 | 0.0794  | 0.4567        | 1.0 | 0.1567  | 0.1336        | 1.0 |
| ENSG00000182687 | <i>GALR2</i>  | -0.0956 | 0.3492 | 1.0 | 0.1189  | 0.2642        | 1.0 | -0.0959 | 0.3602        | 1.0 |
| ENSG00000183971 | <i>NPW</i>    | 0.0450  | 0.6601 | 1.0 | -0.1178 | 0.2687        | 1.0 | 0.1524  | 0.1448        | 1.0 |
| ENSG00000184502 | <i>GAST</i>   | NA      | NA     | NA  | -0.1530 | 0.1500        | 1.0 | 0.1348  | 0.1976        | 1.0 |
| ENSG00000185149 | <i>NPY2R</i>  | 0.0213  | 0.8353 | 1.0 | 0.0230  | 0.8297        | 1.0 | 0.0034  | 0.9742        | 1.0 |
| ENSG00000186867 | <i>QRFR</i>   | -0.0483 | 0.6369 | 1.0 | -0.0657 | 0.5381        | 1.0 | -0.0248 | 0.8134        | 1.0 |

|              |                 |               |         |                 |                |         |                |     |         |               |     |
|--------------|-----------------|---------------|---------|-----------------|----------------|---------|----------------|-----|---------|---------------|-----|
|              | ENSG00000187094 | <i>CCK</i>    | 0.0498  | 0.6264          | 1.0            | 0.0019  | 0.9861         | 1.0 | 0.0725  | 0.4900        | 1.0 |
|              | ENSG00000187258 | <i>NPSR1</i>  | 0.0818  | 0.4233          | 1.0            | 0.0802  | 0.4523         | 1.0 | -0.0401 | 0.7027        | 1.0 |
|              | ENSG00000198049 | <i>AVPR1B</i> | 0.0141  | 0.8905          | 1.0            | 0.1396  | 0.1895         | 1.0 | 0.0462  | 0.6601        | 1.0 |
|              | ENSG00000211451 | <i>GNRHR2</i> | 0.1613  | 0.1125          | 1.0            | -0.0754 | 0.4798         | 1.0 | 0.0129  | 0.9025        | 1.0 |
|              | ENSG00000226306 | <i>NPY6R</i>  | 0.1497  | 0.1412          | 1.0            | -0.0120 | 0.9108         | 1.0 | -0.0553 | 0.5985        | 1.0 |
|              | ENSG00000258839 | <i>MC1R</i>   | -0.1272 | 0.2118          | 1.0            | 0.1826  | 0.0850         | 1.0 | 0.0568  | 0.5885        | 1.0 |
|              | ENSG00000278195 | <i>SSTR3</i>  | -0.0127 | 0.9016          | 1.0            | 0.0651  | 0.5423         | 1.0 | 0.0980  | 0.3498        | 1.0 |
|              | ENSG00000288611 | <i>NPBWR1</i> | 0.0556  | 0.5866          | 1.0            | 0.0200  | 0.8515         | 1.0 | 0.2394  | <b>0.0208</b> | 1.0 |
| Age of Onset | ENSG00000006128 | <i>TAC1</i>   | -0.1357 | 0.1873          | 1.0            | -0.0021 | 0.9841         | 1.0 | -0.0373 | 0.7227        | 1.0 |
|              | ENSG00000017427 | <i>IGF1</i>   | -0.3803 | <b>0.000129</b> | <b>0.01357</b> | -0.0720 | 0.5003         | 1.0 | -0.2043 | <b>0.0495</b> | 1.0 |
|              | ENSG00000049247 | <i>UTS2</i>   | 0.2531  | <b>0.0129</b>   | 1.0            | 0.0690  | 0.5181         | 1.0 | 0.0833  | 0.4272        | 1.0 |
|              | ENSG00000056291 | <i>NPFFR2</i> | 0.0702  | 0.4967          | 1.0            | -0.0616 | 0.5640         | 1.0 | -0.0736 | 0.4831        | 1.0 |
|              | ENSG00000069482 | <i>GAL</i>    | -0.0817 | 0.4286          | 1.0            | 0.0033  | 0.9752         | 1.0 | -0.0418 | 0.6907        | 1.0 |
|              | ENSG00000070031 | <i>SCT</i>    | 0.0657  | 0.5247          | 1.0            | -0.0827 | 0.4383         | 1.0 | 0.0230  | 0.8267        | 1.0 |
|              | ENSG00000075073 | <i>TACR2</i>  | -0.1129 | 0.2736          | 1.0            | 0.0280  | 0.7932         | 1.0 | -0.0236 | 0.8221        | 1.0 |
|              | ENSG00000078401 | <i>EDN1</i>   | 0.2040  | <b>0.0462</b>   | 1.0            | -0.1328 | 0.2122         | 1.0 | 0.0085  | 0.9359        | 1.0 |
|              | ENSG00000082556 | <i>OPRK1</i>  | -0.0024 | 0.9812          | 1.0            | 0.1525  | 0.1513         | 1.0 | -0.0298 | 0.7769        | 1.0 |
|              | ENSG00000087494 | <i>PTHLH</i>  | -0.3846 | <b>0.000109</b> | <b>0.0111</b>  | 0.0196  | 0.8548         | 1.0 | -0.0614 | 0.5590        | 1.0 |
|              | ENSG00000096395 | <i>MLN</i>    | -0.0312 | 0.7628          | 1.0            | 0.0910  | 0.3938         | 1.0 | 0.0489  | 0.6419        | 1.0 |
|              | ENSG00000100604 | <i>CHGA</i>   | 0.1952  | 0.0566          | 1.0            | 0.1180  | 0.2681         | 1.0 | 0.0254  | 0.8088        | 1.0 |
|              | ENSG00000100739 | <i>BDKRB1</i> | -0.0276 | 0.7899          | 1.0            | -0.0703 | 0.5101         | 1.0 | -0.0350 | 0.7388        | 1.0 |
|              | ENSG00000101188 | <i>NTSR1</i>  | -0.0907 | 0.3796          | 1.0            | -0.0495 | 0.6430         | 1.0 | -0.1129 | 0.2813        | 1.0 |
|              | ENSG00000101200 | <i>AVP</i>    | NA      | NA              | NA             | 0.0236  | 0.8251         | 1.0 | 0.1641  | 0.1160        | 1.0 |
|              | ENSG00000101327 | <i>PDYN</i>   | -0.0955 | 0.3546          | 1.0            | -0.0339 | 0.7514         | 1.0 | -0.0569 | 0.5883        | 1.0 |
|              | ENSG00000102539 | <i>MLNR</i>   | -0.0148 | 0.8864          | 1.0            | -0.0057 | 0.9573         | 1.0 | -0.0721 | 0.4919        | 1.0 |
|              | ENSG00000107014 | <i>RLN2</i>   | -0.0843 | 0.4142          | 1.0            | 0.0459  | 0.6676         | 1.0 | 0.0931  | 0.3747        | 1.0 |
|              | ENSG00000107018 | <i>RLN1</i>   | -0.0444 | 0.6674          | 1.0            | -0.0440 | 0.6804         | 1.0 | -0.0158 | 0.8802        | 1.0 |
|              | ENSG00000109163 | <i>GNRHR</i>  | -0.1990 | 0.0520          | 1.0            | 0.1309  | 0.2189         | 1.0 | -0.0710 | 0.4988        | 1.0 |
|              | ENSG00000109255 | <i>NMU</i>    | -0.2021 | <b>0.0483</b>   | 1.0            | -0.0547 | 0.6085         | 1.0 | -0.0979 | 0.3505        | 1.0 |
|              | ENSG00000110148 | <i>CCKBR</i>  | -0.1890 | 0.0652          | 1.0            | -0.0347 | 0.7453         | 1.0 | -0.1088 | 0.2991        | 1.0 |
|              | ENSG00000110680 | <i>CALCA</i>  | 0.0907  | 0.3796          | 1.0            | -0.0398 | 0.7093         | 1.0 | 0.1060  | 0.3120        | 1.0 |
|              | ENSG00000112038 | <i>OPRM1</i>  | 0.0760  | 0.4615          | 1.0            | 0.2205  | <b>0.03674</b> | 1.0 | 0.0478  | 0.6490        | 1.0 |
|              | ENSG00000113889 | <i>KNG1</i>   | 0.1441  | 0.1612          | 1.0            | 0.0356  | 0.7392         | 1.0 | -0.0674 | 0.5211        | 1.0 |
|              | ENSG00000115138 | <i>POMC</i>   | -0.1645 | 0.1093          | 1.0            | -0.2047 | 0.0529         | 1.0 | -0.0315 | 0.7645        | 1.0 |

|                 |                |         |               |        |         |                 |        |         |               |     |
|-----------------|----------------|---------|---------------|--------|---------|-----------------|--------|---------|---------------|-----|
| ENSG00000115353 | <i>TACR1</i>   | -0.1094 | 0.2886        | 1.0    | -0.0115 | 0.9143          | 1.0    | -0.0955 | 0.3626        | 1.0 |
| ENSG00000116014 | <i>KISS1R</i>  | -0.1644 | 0.1094        | 1.0    | 0.0917  | 0.3899          | 1.0    | 0.1150  | 0.2726        | 1.0 |
| ENSG00000116329 | <i>OPRD1</i>   | 0.1236  | 0.2300        | 1.0    | 0.1277  | 0.2303          | 1.0    | -0.0459 | 0.6622        | 1.0 |
| ENSG00000119973 | <i>PRLHR</i>   | -0.2459 | <b>0.0157</b> | 1.0    | 0.0165  | 0.8774          | 1.0    | -0.0385 | 0.7142        | 1.0 |
| ENSG00000120937 | <i>NPPB</i>    | 0.1641  | 0.1102        | 1.0    | NA      | NA              | NA     | NA      | NA            | NA  |
| ENSG00000121764 | <i>HCRTR1</i>  | -0.1361 | 0.1861        | 1.0    | -0.0805 | 0.4507          | 1.0    | -0.2328 | <b>0.0247</b> | 1.0 |
| ENSG00000121853 | <i>GHSR</i>    | NA      | NA            | NA     | NA      | NA              | NA     | -0.0806 | 0.4422        | 1.0 |
| ENSG00000122585 | <i>NPY</i>     | -0.1055 | 0.3062        | 1.0    | -0.1413 | 0.1840          | 1.0    | -0.0287 | 0.7847        | 1.0 |
| ENSG00000124089 | <i>MC3R</i>    | NA      | NA            | NA     | -0.0312 | 0.7707          | 1.0    | NA      | NA            | NA  |
| ENSG00000124205 | <i>EDN3</i>    | -0.1654 | 0.1073        | 1.0    | -0.1443 | 0.1749          | 1.0    | -0.0592 | 0.5729        | 1.0 |
| ENSG00000125510 | <i>OPRL1</i>   | -0.1626 | 0.1134        | 1.0    | -0.1360 | 0.2012          | 1.0    | -0.0740 | 0.4807        | 1.0 |
| ENSG00000125522 | <i>NPBWR2</i>  | 0.0645  | 0.5323        | 1.0    | 0.1264  | 0.2350          | 1.0    | 0.0042  | 0.9682        | 1.0 |
| ENSG00000125787 | <i>GNRH2</i>   | 0.0027  | 0.9795        | 1.0    | 0.0153  | 0.8860          | 1.0    | 0.0504  | 0.6312        | 1.0 |
| ENSG00000126895 | <i>AVPR2</i>   | -0.0442 | 0.6690        | 1.0    | -0.0175 | 0.8699          | 1.0    | 0.0211  | 0.8411        | 1.0 |
| ENSG00000128165 | <i>ADM2</i>    | -0.0277 | 0.7884        | 1.0    | -0.0637 | 0.5510          | 1.0    | 0.0534  | 0.6110        | 1.0 |
| ENSG00000128285 | <i>MCHR1</i>   | -0.1521 | 0.1390        | 1.0    | 0.0221  | 0.8362          | 1.0    | -0.0815 | 0.4375        | 1.0 |
| ENSG00000128310 | <i>GALR3</i>   | 0.0454  | 0.6608        | 1.0    | -0.0116 | 0.9134          | 1.0    | 0.0144  | 0.8908        | 1.0 |
| ENSG00000131096 | <i>PYY</i>     | 0.1272  | 0.2169        | 1.0    | -0.0766 | 0.4728          | 1.0    | 0.1272  | 0.2244        | 1.0 |
| ENSG00000132671 | <i>SSTR4</i>   | -0.2106 | <b>0.0394</b> | 1.0    | -0.0826 | 0.4392          | 1.0    | -0.0776 | 0.4598        | 1.0 |
| ENSG00000132911 | <i>NMUR2</i>   | 0.2277  | <b>0.0257</b> | 1.0    | -0.0404 | 0.7055          | 1.0    | -0.0762 | 0.4681        | 1.0 |
| ENSG00000133636 | <i>NTS</i>     | NA      | NA            | NA     | 0.1286  | 0.2271          | 1.0    | -0.1354 | 0.1957        | 1.0 |
| ENSG00000134443 | <i>GRP</i>     | -0.2816 | <b>0.0054</b> | 0.5555 | 0.1126  | 0.2908          | 1.0    | 0.0530  | 0.6142        | 1.0 |
| ENSG00000135744 | <i>AGT</i>     | -0.1429 | 0.1647        | 1.0    | -0.0721 | 0.4997          | 1.0    | 0.0264  | 0.8017        | 1.0 |
| ENSG00000136160 | <i>EDNRB</i>   | -0.1339 | 0.1934        | 1.0    | -0.1359 | 0.2016          | 1.0    | -0.0864 | 0.4100        | 1.0 |
| ENSG00000137252 | <i>HCRTR2</i>  | -0.0949 | 0.3580        | 1.0    | 0.1082  | 0.3099          | 1.0    | 0.0451  | 0.6676        | 1.0 |
| ENSG00000139574 | <i>NPFF</i>    | 0.2074  | <b>0.0426</b> | 1.0    | 0.0377  | 0.7242          | 1.0    | -0.0171 | 0.8707        | 1.0 |
| ENSG00000139874 | <i>SSTR1</i>   | -0.3046 | <b>0.0026</b> | 0.2605 | -0.1458 | 0.1703          | 1.0    | -0.1456 | 0.1636        | 1.0 |
| ENSG00000141433 | <i>ADCYAP1</i> | -0.1075 | 0.2972        | 1.0    | 0.0470  | 0.6598          | 1.0    | -0.0334 | 0.7505        | 1.0 |
| ENSG00000144891 | <i>AGTR1</i>   | 0.0487  | 0.6376        | 1.0    | 0.0631  | 0.5548          | 1.0    | 0.0785  | 0.4547        | 1.0 |
| ENSG00000145040 | <i>UCN2</i>    | -0.1512 | 0.1413        | 1.0    | 0.3024  | <b>0.003771</b> | 0.3960 | 0.1408  | 0.1781        | 1.0 |
| ENSG00000146469 | <i>VIP</i>     | -0.3173 | <b>0.0016</b> | 0.1669 | -0.0154 | 0.8856          | 1.0    | -0.1737 | 0.0959        | 1.0 |
| ENSG00000147437 | <i>GNRH1</i>   | 0.2251  | <b>0.0275</b> | 1.0    | 0.1091  | 0.3060          | 1.0    | 0.0614  | 0.5588        | 1.0 |
| ENSG00000147571 | <i>CRH</i>     | -0.2499 | <b>0.0140</b> | 1.0    | -0.1290 | 0.2256          | 1.0    | -0.0999 | 0.3406        | 1.0 |
| ENSG00000148734 | <i>NPFFR1</i>  | 0.1346  | 0.1911        | 1.0    | 0.0676  | 0.5266          | 1.0    | -0.0276 | 0.7932        | 1.0 |

|                 |               |         |               |         |         |                        |                 |         |        |     |
|-----------------|---------------|---------|---------------|---------|---------|------------------------|-----------------|---------|--------|-----|
| ENSG00000148926 | <i>ADM</i>    | 0.2841  | <b>0.0050</b> | 0.5121  | -0.1494 | 0.1598                 | 1.0             | -0.1056 | 0.3137 | 1.0 |
| ENSG00000151617 | <i>EDNRA</i>  | -0.0844 | 0.4134        | 1.0     | -0.1591 | 0.1342                 | 1.0             | -0.1037 | 0.3226 | 1.0 |
| ENSG00000152034 | <i>MCHR2</i>  | -0.2794 | 0.0058        | 0.5952  | 0.0456  | 0.6693                 | 1.0             | -0.1445 | 0.1671 | 1.0 |
| ENSG00000157005 | <i>SST</i>    | -0.2875 | <b>0.0045</b> | 0.4599  | -0.0494 | 0.6439                 | 1.0             | -0.0444 | 0.6724 | 1.0 |
| ENSG00000157017 | <i>GHRL</i>   | -0.0143 | 0.8898        | 1.0     | -0.0259 | 0.8085                 | 1.0             | -0.0326 | 0.7566 | 1.0 |
| ENSG00000159723 | <i>AGRP</i>   | -0.0404 | 0.6960        | 1.0     | -0.0130 | 0.9029                 | 1.0             | 0.0536  | 0.6097 | 1.0 |
| ENSG00000161610 | <i>HCRT</i>   | -0.1026 | 0.3201        | 1.0     | NA      | NA                     | NA              | NA      | NA     | NA  |
| ENSG00000162009 | <i>SSTR5</i>  | NA      | NA            | NA      | -0.1674 | 0.1149                 | 1.0             | -0.1395 | 0.1822 | 1.0 |
| ENSG00000163273 | <i>NPPC</i>   | 0.0447  | 0.6653        | 1.0     | 0.0346  | 0.7459                 | 1.0             | 0.0535  | 0.6104 | 1.0 |
| ENSG00000163394 | <i>CCKAR</i>  | -0.0489 | 0.6362        | 1.0     | -0.0582 | 0.5860                 | 1.0             | -0.0224 | 0.8313 | 1.0 |
| ENSG00000163794 | <i>UCN</i>    | 0.2040  | <b>0.0462</b> | 1.0     | 0.0709  | 0.5064                 | 1.0             | 0.0290  | 0.7823 | 1.0 |
| ENSG00000164128 | <i>NPY1R</i>  | -0.1644 | 0.1095        | 1.0     | 0.0482  | 0.6517                 | 1.0             | -0.0779 | 0.4578 | 1.0 |
| ENSG00000164129 | <i>NPY5R</i>  | -0.1523 | 0.1385        | 1.0     | -0.0662 | 0.5355                 | 1.0             | -0.0716 | 0.4953 | 1.0 |
| ENSG00000166148 | <i>AVPR1A</i> | -0.1146 | 0.2661        | 1.0     | -0.3190 | <b>0.002182</b>        | 0.2291          | -0.1814 | 0.0818 | 1.0 |
| ENSG00000166573 | <i>GALR1</i>  | -0.2661 | <b>0.0088</b> | 0.8967  | -0.1302 | 0.2213                 | 1.0             | -0.1084 | 0.3010 | 1.0 |
| ENSG00000166603 | <i>MC4R</i>   | -0.0408 | 0.6929        | 1.0     | 0.0390  | 0.7150                 | 1.0             | 0.0224  | 0.8312 | 1.0 |
| ENSG00000166863 | <i>TAC3</i>   | -0.2816 | <b>0.0054</b> | 0.5556  | -0.0206 | 0.8473                 | 1.0             | -0.1746 | 0.0941 | 1.0 |
| ENSG00000167244 | <i>IGF2</i>   | 0.0924  | 0.3704        | 1.0     | -0.0037 | 0.9721                 | 1.0             | 0.0150  | 0.8864 | 1.0 |
| ENSG00000168081 | <i>PNOC</i>   | -0.3437 | <b>0.0006</b> | 0.06191 | -0.1428 | 0.1793                 | 1.0             | -0.1111 | 0.2891 | 1.0 |
| ENSG00000168398 | <i>BDKRB2</i> | -0.0239 | 0.8172        | 1.0     | -0.0383 | 0.7203                 | 1.0             | -0.1111 | 0.2892 | 1.0 |
| ENSG00000169006 | <i>NTSR2</i>  | -0.1129 | 0.2735        | 1.0     | -0.0912 | 0.3924                 | 1.0             | 0.0436  | 0.6783 | 1.0 |
| ENSG00000169836 | <i>TACR3</i>  | 0.0696  | 0.5006        | 1.0     | 0.0198  | 0.8530                 | 1.0             | -0.0876 | 0.4036 | 1.0 |
| ENSG00000170498 | <i>KISS1</i>  | NA      | NA            | NA      | NA      | NA                     | NA              | 0.1204  | 0.2504 | 1.0 |
| ENSG00000170893 | <i>TRH</i>    | -0.0334 | 0.7467        | 1.0     | -0.4667 | <b>0.000035<br/>34</b> | <b>0.000371</b> | -0.2000 | 0.0546 | 1.0 |
| ENSG00000171388 | <i>APLN</i>   | 0.2912  | <b>0.0040</b> | 0.4074  | -0.0612 | 0.5667                 | 1.0             | -0.0290 | 0.7829 | 1.0 |
| ENSG00000171596 | <i>NMUR1</i>  | -0.1836 | 0.0733        | 1.0     | -0.1833 | 0.0837                 | 1.0             | -0.0874 | 0.4049 | 1.0 |
| ENSG00000174417 | <i>TRHR</i>   | 0.1381  | 0.1798        | 1.0     | 0.0152  | 0.8867                 | 1.0             | -0.0738 | 0.4823 | 1.0 |
| ENSG00000174697 | <i>LEP</i>    | 0.0503  | 0.6262        | 1.0     | 0.1129  | 0.2893                 | 1.0             | 0.0916  | 0.3827 | 1.0 |
| ENSG00000175206 | <i>NPPA</i>   | -0.3044 | <b>0.0026</b> | 0.2615  | 0.0873  | 0.4133                 | 1.0             | 0.0266  | 0.8000 | 1.0 |
| ENSG00000175868 | <i>CALCB</i>  | 0.0423  | 0.6824        | 1.0     | 0.0450  | 0.6734                 | 1.0             | 0.0303  | 0.7732 | 1.0 |
| ENSG00000176136 | <i>MC5R</i>   | -0.1545 | 0.1329        | 1.0     | -0.1071 | 0.3150                 | 1.0             | -0.0580 | 0.5805 | 1.0 |
| ENSG00000176358 | <i>TAC4</i>   | 0.1046  | 0.3107        | 1.0     | 0.0601  | 0.5738                 | 1.0             | 0.0500  | 0.6338 | 1.0 |
| ENSG00000180616 | <i>SSTR2</i>  | -0.2460 | <b>0.0157</b> | 1.0     | -0.0379 | 0.7231                 | 1.0             | -0.0605 | 0.5648 | 1.0 |

|                 |               |         |               |         |         |        |     |         |                 |        |
|-----------------|---------------|---------|---------------|---------|---------|--------|-----|---------|-----------------|--------|
| ENSG00000180914 | <i>OXTR</i>   | 0.1973  | 0.0540        | 1.0     | -0.0058 | 0.9569 | 1.0 | 0.0219  | 0.8349          | 1.0    |
| ENSG00000181195 | <i>PENK</i>   | -0.2041 | <b>0.0461</b> | 1.0     | -0.0747 | 0.4840 | 1.0 | -0.1524 | 0.1447          | 1.0    |
| ENSG00000181408 | <i>UTS2R</i>  | 0.2228  | <b>0.0291</b> | 1.0     | 0.0880  | 0.4094 | 1.0 | -0.0062 | 0.9526          | 1.0    |
| ENSG00000182687 | <i>GALR2</i>  | 0.0792  | 0.4431        | 1.0     | -0.0837 | 0.4327 | 1.0 | 0.1472  | 0.1591          | 1.0    |
| ENSG00000183971 | <i>NPW</i>    | -0.1160 | 0.2605        | 1.0     | -0.0233 | 0.8276 | 1.0 | -0.0137 | 0.8963          | 1.0    |
| ENSG00000184502 | <i>GAST</i>   | NA      | NA            | NA      | 0.0023  | 0.9828 | 1.0 | -0.0216 | 0.8373          | 1.0    |
| ENSG00000185149 | <i>NPY2R</i>  | -0.1678 | 0.1022        | 1.0     | -0.0911 | 0.3931 | 1.0 | -0.1469 | 0.1599          | 1.0    |
| ENSG00000186867 | <i>QRFPR</i>  | -0.1669 | 0.1041        | 1.0     | 0.0539  | 0.6136 | 1.0 | 0.0069  | 0.9477          | 1.0    |
| ENSG00000187094 | <i>CCK</i>    | -0.1280 | 0.2141        | 1.0     | 0.0091  | 0.9318 | 1.0 | -0.0403 | 0.7010          | 1.0    |
| ENSG00000187258 | <i>NPSR1</i>  | -0.0828 | 0.4227        | 1.0     | 0.0357  | 0.7384 | 1.0 | 0.0712  | 0.4975          | 1.0    |
| ENSG00000198049 | <i>AVPR1B</i> | -0.0800 | 0.4385        | 1.0     | 0.1615  | 0.1282 | 1.0 | -0.0206 | 0.8449          | 1.0    |
| ENSG00000211451 | <i>GNRHR2</i> | -0.1188 | 0.2491        | 1.0     | 0.0011  | 0.9917 | 1.0 | -0.0935 | 0.3729          | 1.0    |
| ENSG00000226306 | <i>NPY6R</i>  | 0.0943  | 0.3606        | 1.0     | -0.0575 | 0.5906 | 1.0 | -0.0845 | 0.4206          | 1.0    |
| ENSG00000258839 | <i>MC1R</i>   | 0.1264  | 0.2196        | 1.0     | -0.0351 | 0.7426 | 1.0 | 0.0469  | 0.6556          | 1.0    |
| ENSG00000278195 | <i>SSTR3</i>  | 0.1343  | 0.1920        | 1.0     | 0.1144  | 0.2830 | 1.0 | -0.0486 | 0.6433          | 1.0    |
| ENSG00000288611 | <i>NPBWR1</i> | -0.3455 | <b>0.0006</b> | 0.05763 | -0.1121 | 0.2927 | 1.0 | -0.3360 | <b>0.000912</b> | 0.1050 |

Table A27. Results of the correlation analysis of neuropeptide receptors and ligand expression with disease duration or age of onset in people with ALS from either KCL BrainBank or medial and lateral samples from TargetALS. Adjusted p-values reflect the number of neuropeptide-related genes tested in each dataset (102 in KCL BrainBank, 105 in TargetALS medial and 106 in TargetALS lateral motor cortex). A p-value of < 0.05 denotes significance.

| Dataset             | Cell Type        | Median $\pm$ IQR (case) | Median $\pm$ IQR (control) | Levene's Test (F statistic; p-value) | ANCOVA (F statistic; p-value) |
|---------------------|------------------|-------------------------|----------------------------|--------------------------------------|-------------------------------|
| KCL BrainBank       | Neurons          | 0.662 $\pm$ 0.118       | 0.578 $\pm$ 0.179          | 4.213; <b>0.0417</b>                 | 15.295; <b>1.34E-04</b>       |
|                     | Astrocytes       | 0.191 $\pm$ 0.0748      | 0.279 $\pm$ 0.106          | 2.525; 0.114                         | 18.192; <b>3.34E-05</b>       |
|                     | Microglia        | 0.0159 $\pm$ 0.00972    | 0.0139 $\pm$ 0.0151        | 0.0275; 0.869                        | 0.0369; 0.848                 |
|                     | Endothelial      | 0.0146 $\pm$ 0.0128     | 0.0182 $\pm$ 0.0204        | 1.851; 0.175                         | 0.666; 0.416                  |
|                     | Oligodendrocytes | 0.0987 $\pm$ 0.0556     | 0.103 $\pm$ 0.0836         | 3.306; 0.0708                        | 2.688; 0.103                  |
| TargetALS (medial)  | Neurons          | 0.616 $\pm$ 0.187       | 0.602 $\pm$ 0.154          | 0.0278; 0.868                        | 0.0173; 0.896                 |
|                     | Astrocytes       | 0.235 $\pm$ 0.0936      | 0.242 $\pm$ 0.131          | 2.590; 0.110                         | 1.885; 0.173                  |
|                     | Microglia        | 0.0165 $\pm$ 0.0129     | 0.00976 $\pm$ 0.0103       | 0.0140; 0.906                        | 1.164; 0.283                  |
|                     | Endothelial      | 0.000924 $\pm$ 0.0101   | 0.00900 $\pm$ 0.00850      | 0.459; 0.499                         | 0.667; 0.416                  |
|                     | Oligodendrocytes | 0.114 $\pm$ 0.0934      | 0.0916 $\pm$ 0.0700        | 2.035; 0.157                         | 2.907; 0.091                  |
| TargetALS (lateral) | Neurons          | 0.630 $\pm$ 0.128       | 0.640 $\pm$ 0.143          | 0.131; 0.719                         | 0.0102; 0.920                 |
|                     | Astrocytes       | 0.227 $\pm$ 0.0808      | 0.228 $\pm$ 0.121          | 2.996; 0.086                         | 0.840; 0.361                  |
|                     | Microglia        | 0.0152 $\pm$ 0.0137     | 0.0121 $\pm$ 0.00775       | 0.322; 0.571                         | 0.968; 0.327                  |
|                     | Endothelial      | 0.00897 $\pm$ 0.00739   | 0.00838 $\pm$ 0.00712      | 0.0236; 0.878                        | 0.00180; 0.966                |
|                     | Oligodendrocytes | 0.0955 $\pm$ 0.110      | 0.0872 $\pm$ 0.0317        | 1.409; 0.238                         | 0.00770; 0.310                |

Table A28. Results of the case-control cell type deconvolution analysis with MuSiC2. Case and control median values represent the relative proportion of each cell type. Equality of variance was assessed using Levene's test, with significance in the proportions of cell types between disease status in each dataset assessed using ANCOVA corrected for age of death and sex. A p-value of  $< 0.05$ , highlighted in bold, denotes significance.

## Chapter 7

|                          | <b>KCL BrainBank<br/>(Cases)</b> | <b>TargetALS</b>    | <b>Zucca</b>    | <b>van Rheenen</b> | <b>KCL<br/>BrainBank<br/>(Controls)</b> | <b>van Rheenen<br/>(Controls)</b> | <b>TargetALS<br/>(Controls)</b> | <b>TargetALS<br/>(occipital<br/>cortex)</b> | <b>TargetALS<br/>(cerebellum)</b> |
|--------------------------|----------------------------------|---------------------|-----------------|--------------------|---|-----------------------------------|---------------------------------|---|-----------------------------------|
| Number of<br>Individuals | 112                              | 93 (168<br>samples) | 15              | 397                | 59                                      | 645                               | 19 (34 samples)                 | 45  | 123 (128<br>samples)              |
| Male (%)                 | 65 (58.0%)                       | 55 (59.1%)          | 7 (46.7%)       | 239 (60.2%)        | 26 (44.1%)                              | 360 (55.8%)                       | 9 (47.4%)                       | 22 (48.89%)                                 | 71 (57.72%)                       |
| Age (mean $\pm$ SD)      | 68.8 $\pm$ 12.7                  | 64.2 $\pm$ 10.2     | 66.4 $\pm$ 9.12 | 62.2 $\pm$ 12.0    | 76.2 $\pm$ 14.6                         | NA                                | 62.2 $\pm$ 12.0                 | 64.40 $\pm$<br>10.53                        | 63.66 $\pm$ 9.34                  |
| PMD (mean $\pm$ SD)      | 26.1 $\pm$ 12.1                  | 10.5 $\pm$ 6.96     | NA              | NA                 | 37.6 $\pm$ 19.3                         | NA                                | 21.8 $\pm$ 23.4                 | 10.00 $\pm$ 7.12                            | 10.12 $\pm$ 6.90                  |

*Table A29. Basic demographics of each of the nine datasets used in this study. PMD: postmortem delay, measured in hours. Age refers to age of death in KCL BrainBank and TargetALS, and age at last blood draw in Zucca and van Rheenen.*



|                                  | KCL BrainBank | TargetALS | Zucca | van Rheezen |
|----------------------------------|---------------|-----------|-------|-------------|
| <b>Clinical</b>                  |               |           |       |             |
| Age at Symptom Onset             | ✓             | ✓         | ✓     | ✓           |
| Age at Death                     | ✓             | ✓         | •     | •           |
| Disease Duration                 | ✓             | ✓         | •     | ✓           |
| Diagnostic Delay                 | ✓             | ✓         | •     | •           |
| Postmortem Delay                 | ✓             | ✓         | •     | •           |
| <b>Omics</b>                     |               |           |       |             |
| Telomere Length                  | ✓             | •         | •     | •           |
| Mitochondrial DNA Copy Number    | ✓             | •         | •     | •           |
| Transcriptional Age Acceleration | ✓             | ✓         | ✓     | ✓           |
| Biological Age Acceleration      | ✓             | •         | •     | •           |

Table A30. Breakdown of the phenotypic variables available for each of the 4 ALS datasets used in this study.

| Cluster | Gene ID         | Gene Symbol  | Feature Score | Probability |
|---------|-----------------|--------------|---------------|-------------|
| 1       | ENSG00000164600 | NEUROD6      | 0.2928        | 0.7002      |
| 1       | ENSG00000100362 | PVALB        | 0.2442        | 0.6736      |
| 1       | ENSG00000186081 | KRT5         | 0.2344        | 0.6725      |
| 1       | ENSG00000006128 | TAC1         | 0.2378        | 0.6502      |
| 1       | ENSG00000236714 | LINC01844    | 0.2060        | 0.6443      |
| 1       | ENSG00000141433 | ADCYAP1      | 0.1663        | 0.6258      |
| 1       | ENSG00000128564 | VGF          | 0.1616        | 0.6254      |
| 1       | ENSG00000147571 | CRH          | 0.1534        | 0.6083      |
| 1       | ENSG00000280776 | LINC01202    | 0.1441        | 0.6068      |
| 1       | ENSG00000205279 | CTXN3        | 0.1418        | 0.6043      |
| 1       | ENSG00000246363 | LINC02458    | 0.1693        | 0.6036      |
| 1       | ENSG00000164326 | CARTPT       | 0.2121        | 0.6029      |
| 1       | ENSG00000233123 | LINC01007    | 0.1434        | 0.5992      |
| 1       | ENSG00000157005 | SST          | 0.2557        | 0.5984      |
| 1       | ENSG00000223812 | PYDC2-AS1    | 0.1476        | 0.5963      |
| 1       | ENSG00000205634 | LINC00898    | 0.1320        | 0.5941      |
| 1       | ENSG00000224404 | Lnc-LARGE1-1 | 0.1353        | 0.5926      |
| 1       | ENSG00000151790 | TDO2         | 0.1494        | 0.5917      |
| 1       | ENSG00000122012 | SV2C         | 0.1272        | 0.5900      |
| 1       | ENSG00000144227 | NXPH2        | 0.1520        | 0.5897      |
| 1       | ENSG00000261757 | miR-1255     | 0.1283        | 0.5827      |
| 1       | ENSG00000254363 | LOC101929719 | 0.1810        | 0.5804      |
| 1       | ENSG00000183090 | FREM3        | 0.1174        | 0.5758      |
| 1       | ENSG00000188729 | OSTN         | 0.1506        | 0.5757      |
| 1       | ENSG00000159248 | GJD2         | 0.1175        | 0.5743      |
| 1       | ENSG00000285561 | None         | 0.1102        | 0.5732      |
| 1       | ENSG00000261738 | MIR3976HG    | 0.1128        | 0.5712      |
| 1       | ENSG00000131885 | KRT17P1      | 0.1079        | 0.5698      |

|   |                 |                |        |        |
|---|-----------------|----------------|--------|--------|
| 1 | ENSG00000261325 | LINC02192      | 0.1131 | 0.5683 |
| 1 | ENSG00000254561 | None           | 0.1068 | 0.5679 |
| 1 | ENSG00000237390 | Lnc-RHBG-1     | 0.1131 | 0.5645 |
| 1 | ENSG00000242159 | ABCF2P1        | 0.1116 | 0.5637 |
| 1 | ENSG00000256193 | LINC00507      | 0.1380 | 0.5636 |
| 1 | ENSG00000130701 | RBBP8NL        | 0.1008 | 0.5625 |
| 1 | ENSG00000265179 | Lnc-YES1-8     | 0.1087 | 0.5602 |
| 1 | ENSG00000169035 | KLK7           | 0.0983 | 0.5602 |
| 1 | ENSG00000150175 | FRMPD2B        | 0.0995 | 0.5592 |
| 1 | ENSG00000271538 | LINC02427      | 0.1744 | 0.5588 |
| 1 | ENSG00000104938 | CLEC4M         | 0.1060 | 0.5573 |
| 1 | ENSG00000228735 | LOC124901635   | 0.0935 | 0.5545 |
| 1 | ENSG00000170290 | SLN            | 0.1750 | 0.5544 |
| 1 | ENSG00000281383 | Lnc-KCNE1B-157 | 0.0933 | 0.5532 |
| 1 | ENSG00000143858 | SYT2           | 0.0924 | 0.5522 |
| 1 | ENSG00000228999 | LINC01830      | 0.1127 | 0.5497 |
| 1 | ENSG00000254101 | LINC02055      | 0.0925 | 0.5489 |
| 1 | ENSG00000285735 | LINC02717      | 0.0886 | 0.5486 |
| 1 | ENSG00000276462 | LINC03025      | 0.0907 | 0.5477 |
| 1 | ENSG00000286736 | None           | 0.0923 | 0.5462 |
| 1 | ENSG00000075673 | ATP12A         | 0.0913 | 0.5442 |
| 1 | ENSG00000174403 | MIR1-1HG-AS1   | 0.0865 | 0.5438 |
| 1 | ENSG00000287844 | None           | 0.0860 | 0.5438 |
| 1 | ENSG00000286063 | None           | 0.0889 | 0.5432 |
| 1 | ENSG00000111863 | ADTRP          | 0.1065 | 0.5421 |
| 1 | ENSG00000176697 | BDNF           | 0.0847 | 0.5415 |
| 1 | ENSG00000287611 | Lnc-HRH4-2     | 0.0847 | 0.5403 |
| 1 | ENSG00000279875 | None           | 0.0948 | 0.5391 |
| 1 | ENSG00000223930 | Lnc-ZMAT3-3    | 0.0928 | 0.5381 |
| 1 | ENSG00000160221 | GATD3A         | 0.0864 | 0.5375 |

|   |                 |                             |        |        |
|---|-----------------|-----------------------------|--------|--------|
| 1 | ENSG00000225493 | LINC01107                   | 0.0903 | 0.5375 |
| 1 | ENSG00000279952 | None                        | 0.0826 | 0.5373 |
| 1 | ENSG00000185149 | NPY2R                       | 0.1257 | 0.5354 |
| 1 | ENSG00000248837 | LOC105374524                | 0.0860 | 0.5341 |
| 1 | ENSG00000202048 | SNORD114-20                 | 0.0838 | 0.5338 |
| 1 | ENSG00000250634 | LINC01182                   | 0.0784 | 0.5329 |
| 1 | ENSG00000169676 | DRD5                        | 0.1015 | 0.5324 |
| 1 | ENSG00000268297 | CLEC4GP1                    | 0.0753 | 0.5315 |
| 1 | ENSG00000120875 | DUSP4                       | 0.0753 | 0.5310 |
| 1 | ENSG00000122025 | FLT3                        | 0.0920 | 0.5308 |
| 1 | ENSG00000231824 | AKAIN1                      | 0.0803 | 0.5303 |
| 1 | ENSG00000145708 | CRHBP                       | 0.1696 | 0.5296 |
| 1 | ENSG00000182632 | CCNYL2                      | 0.0952 | 0.5295 |
| 1 | ENSG00000174576 | NPAS4                       | 0.0765 | 0.5284 |
| 1 | ENSG00000241945 | PWP2                        | 0.0735 | 0.5259 |
| 1 | ENSG00000285578 | Lnc-DUSP22-2                | 0.0837 | 0.5259 |
| 1 | ENSG00000165899 | OTOGL                       | 0.0717 | 0.5256 |
| 1 | ENSG00000267623 | Cyclin Y-Like<br>Pseudogene | 0.0717 | 0.5248 |
| 1 | ENSG00000152595 | MEPE                        | 0.1049 | 0.5242 |
| 1 | ENSG00000138678 | GPAT3                       | 0.0725 | 0.5235 |
| 1 | ENSG00000239672 | NME1                        | 0.0979 | 0.5225 |
| 1 | ENSG00000179477 | ALOX12B                     | 0.0699 | 0.5218 |
| 1 | ENSG00000254510 | Lnc-NPAS4-1                 | 0.0688 | 0.5217 |
| 1 | ENSG00000286292 | None                        | 0.1351 | 0.5215 |
| 1 | ENSG00000274330 | ADAM20<br>Pseudogene        | 0.0686 | 0.5209 |
| 1 | ENSG00000106236 | NPTX2                       | 0.0749 | 0.5204 |
| 1 | ENSG00000285634 | LOC105376121                | 0.0825 | 0.5184 |
| 1 | ENSG00000170231 | FABP6                       | 0.1070 | 0.5184 |
| 1 | ENSG00000146469 | VIP                         | 0.0681 | 0.5180 |

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| 1 | ENSG00000117594 | HSD11B1                                 | 0.2147 | 0.5167 |
| 1 | ENSG00000254681 | PKD1P5                                  | 0.1017 | 0.5151 |
| 1 | ENSG00000258859 | LINC02296                               | 0.0909 | 0.5148 |
| 1 | ENSG00000260658 | Lnc-CDH8-10                             | 0.1106 | 0.5143 |
| 1 | ENSG00000286016 | None                                    | 0.0947 | 0.5108 |
| 1 | ENSG00000229618 | Lnc-ARL4A-54                            | 0.0836 | 0.5104 |
| 1 | ENSG00000132677 | RHBG                                    | 0.0677 | 0.5103 |
| 1 | ENSG00000287593 | Antisense to ADTRP                      | 0.0751 | 0.5091 |
| 1 | ENSG00000229722 | Lnc-SGK1-3                              | 0.1479 | 0.5090 |
| 1 | ENSG00000225280 | LOC105372558                            | 0.0998 | 0.5087 |
| 1 | ENSG00000227582 | ADGRF5P1                                | 0.1094 | 0.5078 |
| 1 | ENSG00000119888 | EPCAM                                   | 0.0706 | 0.5069 |
| 1 | ENSG00000156076 | WIF1                                    | 0.0761 | 0.5035 |
| 1 | ENSG00000174899 | SLC66A1L                                | 0.0722 | 0.5015 |
| 1 | ENSG00000229635 | Pseudogene Similar<br>to Part of FBXW1B | 0.0740 | 0.5011 |
| 1 | ENSG00000226405 | HSD17B12<br>Pseudogene                  | 0.1263 | 0.5006 |
| 1 | ENSG00000286109 | Lnc-KCNK1-1                             | 0.0681 | 0.5001 |
| 1 | ENSG00000287907 | None                                    | 0.0696 | 0.4981 |
| 1 | ENSG00000228772 | Lnc-PRL-3                               | 0.0822 | 0.4979 |
| 1 | ENSG00000255087 | LOC101929473                            | 0.0713 | 0.4973 |
| 1 | ENSG00000107165 | TYRP1                                   | 0.1184 | 0.4971 |
| 1 | ENSG00000126545 | CSN1S1                                  | 0.0804 | 0.4955 |
| 1 | ENSG00000184385 | UMODL1-AS1                              | 0.0734 | 0.4942 |
| 1 | ENSG00000261502 | Lnc-CDH8-10                             | 0.1012 | 0.4918 |
| 1 | ENSG00000225449 | RAB6C-AS1                               | 0.1405 | 0.4911 |
| 1 | ENSG00000137860 | SLC28A2                                 | 0.1007 | 0.4906 |
| 1 | ENSG00000259520 | SLC28A2-AS1                             | 0.1289 | 0.4866 |
| 1 | ENSG00000266573 | Lnc-HRH4-7                              | 0.0936 | 0.4845 |
| 1 | ENSG00000132744 | ACY3                                    | 0.0824 | 0.4835 |

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|---|-----------------|--------------|--------|--------|
| 1 | ENSG00000234665 | LERFS        | 0.0886 | 0.4825 |
| 1 | ENSG00000227723 | Lnc-MYB-5    | 0.1588 | 0.4812 |
| 1 | ENSG00000273214 | Lnc-POLR2F-1 | 0.1015 | 0.4796 |
| 1 | ENSG00000218772 | FAM8A6P      | 0.1215 | 0.4786 |
| 1 | ENSG00000286666 | None         | 0.0834 | 0.4784 |
| 1 | ENSG00000179520 | SLC17A8      | 0.0938 | 0.4775 |
| 1 | ENSG00000277918 | RNVU1-28     | 0.1078 | 0.4766 |
| 1 | ENSG00000216753 | HMGA1P7      | 0.1011 | 0.4670 |
| 1 | ENSG00000117322 | CR2          | 0.0698 | 0.4657 |
| 1 | ENSG00000256971 | LINC00508    | 0.0889 | 0.4610 |
| 1 | ENSG00000286810 | None         | 0.0805 | 0.4581 |
| 1 | ENSG00000178401 | DNAJC22      | 0.0983 | 0.4531 |
| 1 | ENSG00000223553 | SMPD4P1      | 0.0675 | 0.4308 |
| 1 | ENSG00000200959 | SNORA74A     | 0.0681 | 0.4273 |
| 1 | ENSG00000243323 | PTPRVP       | 0.0713 | 0.4221 |
| 2 | ENSG00000175084 | DES          | 0.8407 | 0.9591 |
| 2 | ENSG00000163017 | ACTG2        | 0.5157 | 0.8158 |
| 2 | ENSG00000105641 | SLC5A5       | 0.4185 | 0.7857 |
| 2 | ENSG00000168542 | COL3A1       | 0.4631 | 0.7699 |
| 2 | ENSG00000196616 | ADH1B        | 0.4705 | 0.7698 |
| 2 | ENSG00000108821 | COL1A1       | 0.4247 | 0.7545 |
| 2 | ENSG00000118271 | TTR          | 0.3322 | 0.7462 |
| 2 | ENSG00000096696 | DSP          | 0.3321 | 0.7450 |
| 2 | ENSG00000144810 | COL8A1       | 0.3937 | 0.7423 |
| 2 | ENSG00000111341 | MGP          | 0.3728 | 0.7233 |
| 2 | ENSG00000133392 | MYH11        | 0.3091 | 0.7219 |
| 2 | ENSG00000149596 | JPH2         | 0.2880 | 0.7045 |
| 2 | ENSG00000101335 | MYL9         | 0.2608 | 0.6917 |
| 2 | ENSG00000112214 | FHL5         | 0.2641 | 0.6903 |
| 2 | ENSG00000130176 | CNN1         | 0.2413 | 0.6892 |

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| 2 | ENSG00000198467 | TPM2       | 0.2413 | 0.6876 |
| 2 | ENSG00000187955 | COL14A1    | 0.2812 | 0.6777 |
| 2 | ENSG00000124253 | PCK1       | 0.3288 | 0.6772 |
| 2 | ENSG00000141052 | MYOCD      | 0.2321 | 0.6735 |
| 2 | ENSG0000013588  | GPRC5A     | 0.3677 | 0.6732 |
| 2 | ENSG00000163817 | SLC6A20    | 0.2255 | 0.6732 |
| 2 | ENSG00000143867 | OSR1       | 0.2179 | 0.6726 |
| 2 | ENSG00000115602 | IL1RL1     | 0.2727 | 0.6724 |
| 2 | ENSG00000054598 | FOXC1      | 0.2789 | 0.6712 |
| 2 | ENSG00000287338 | Lnc-TLR5-1 | 0.3582 | 0.6663 |
| 2 | ENSG00000107796 | ACTA2      | 0.2111 | 0.6644 |
| 2 | ENSG00000115590 | IL1R2      | 0.3469 | 0.6638 |
| 2 | ENSG00000115648 | MLPH       | 0.2497 | 0.6630 |
| 2 | ENSG00000112499 | SLC22A2    | 0.2091 | 0.6619 |
| 2 | ENSG00000205038 | PKHD1L1    | 0.2324 | 0.6579 |
| 2 | ENSG00000164692 | COL1A2     | 0.2609 | 0.6567 |
| 2 | ENSG00000162458 | FBLIM1     | 0.2227 | 0.6525 |
| 2 | ENSG00000269113 | TRABD2B    | 0.2354 | 0.6522 |
| 2 | ENSG00000112837 | TBX18      | 0.2049 | 0.6503 |
| 2 | ENSG00000152779 | SLC16A12   | 0.1988 | 0.6485 |
| 2 | ENSG00000131471 | AOC3       | 0.2022 | 0.6476 |
| 2 | ENSG00000241644 | INMT       | 0.1894 | 0.6471 |
| 2 | ENSG00000186564 | FOXD2      | 0.2019 | 0.6410 |
| 2 | ENSG00000107438 | PDLIM1     | 0.2306 | 0.6385 |
| 2 | ENSG00000161638 | ITGA5      | 0.2232 | 0.6385 |
| 2 | ENSG00000149257 | SERPINH1   | 0.3113 | 0.6370 |
| 2 | ENSG00000177575 | CD163      | 0.4013 | 0.6367 |
| 2 | ENSG00000164707 | SLC13A4    | 0.1768 | 0.6366 |
| 2 | ENSG00000149591 | TAGLN      | 0.1862 | 0.6346 |
| 2 | ENSG00000149573 | MPZL2      | 0.2436 | 0.6342 |

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|---|-----------------|-----------|--------|--------|
| 2 | ENSG00000112936 | C7        | 0.3239 | 0.6312 |
| 2 | ENSG00000237424 | FOXD2-AS1 | 0.1845 | 0.6312 |
| 2 | ENSG00000226390 | KCNQ2-AS1 | 0.1684 | 0.6311 |
| 2 | ENSG00000124107 | SLPI      | 0.1963 | 0.6308 |
| 2 | ENSG00000185585 | OLFML2A   | 0.1824 | 0.6269 |
| 2 | ENSG00000176692 | FOXC2     | 0.1617 | 0.6250 |
| 2 | ENSG00000152049 | KCNE4     | 0.2716 | 0.6242 |
| 2 | ENSG00000000971 | CFH       | 0.2495 | 0.6231 |
| 2 | ENSG00000173597 | SULT1B1   | 0.2169 | 0.6223 |
| 2 | ENSG00000144837 | PLA1A     | 0.2179 | 0.6212 |
| 2 | ENSG00000115604 | IL18R1    | 0.1820 | 0.6208 |
| 2 | ENSG00000279821 | None      | 0.1868 | 0.6201 |
| 2 | ENSG00000112175 | BMP5      | 0.1541 | 0.6177 |
| 2 | ENSG00000173530 | TNFRSF10D | 0.2506 | 0.6163 |
| 2 | ENSG00000015520 | NPC1L1    | 0.1809 | 0.6157 |
| 2 | ENSG00000142173 | COL6A2    | 0.1894 | 0.6138 |
| 2 | ENSG00000027644 | INSRR     | 0.1484 | 0.6127 |
| 2 | ENSG00000102802 | MEDAG     | 0.1481 | 0.6126 |
| 2 | ENSG00000099994 | SUSD2     | 0.1962 | 0.6125 |
| 2 | ENSG00000198848 | CES1      | 0.1597 | 0.6098 |
| 2 | ENSG00000198959 | TGM2      | 0.1946 | 0.6095 |
| 2 | ENSG00000143546 | S100A8    | 0.3517 | 0.6077 |
| 2 | ENSG00000184811 | TRARG1    | 0.1404 | 0.6053 |
| 2 | ENSG00000130635 | COL5A1    | 0.1363 | 0.6012 |
| 2 | ENSG00000163736 | PPBP      | 0.1520 | 0.6009 |
| 2 | ENSG00000163220 | S100A9    | 0.3857 | 0.6009 |
| 2 | ENSG00000172935 | MRGPRF    | 0.1409 | 0.5978 |
| 2 | ENSG00000166523 | CLEC4E    | 0.1432 | 0.5978 |
| 2 | ENSG00000118729 | CASQ2     | 0.1389 | 0.5977 |
| 2 | ENSG00000265107 | GJA5      | 0.1532 | 0.5977 |

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|---|-----------------|---------------|--------|--------|
| 2 | ENSG00000115594 | IL1R1         | 0.2082 | 0.5974 |
| 2 | ENSG00000124212 | PTGIS         | 0.1438 | 0.5956 |
| 2 | ENSG00000165474 | GJB2          | 0.1371 | 0.5954 |
| 2 | ENSG00000196154 | S100A4        | 0.2512 | 0.5943 |
| 2 | ENSG00000128274 | A4GALT        | 0.2053 | 0.5942 |
| 2 | ENSG00000173110 | HSPA6         | 0.3594 | 0.5917 |
| 2 | ENSG00000164761 | TNFRSF11B     | 0.2011 | 0.5914 |
| 2 | ENSG00000163431 | LMOD1         | 0.1365 | 0.5912 |
| 2 | ENSG00000135842 | NIBAN1        | 0.2978 | 0.5905 |
| 2 | ENSG00000167244 | IGF2          | 0.1261 | 0.5904 |
| 2 | ENSG00000106366 | SERPINE1      | 0.1559 | 0.5904 |
| 2 | ENSG00000174348 | PODN          | 0.1846 | 0.5897 |
| 2 | ENSG00000206538 | VGLL3         | 0.1305 | 0.5883 |
| 2 | ENSG00000122176 | FMOD          | 0.1288 | 0.5881 |
| 2 | ENSG00000088882 | CPXM1         | 0.1336 | 0.5870 |
| 2 | ENSG00000221869 | CEBPD         | 0.1630 | 0.5867 |
| 2 | ENSG00000074219 | TEAD2         | 0.1467 | 0.5861 |
| 2 | ENSG00000153404 | PLEKHG4B      | 0.1228 | 0.5853 |
| 2 | ENSG00000120708 | TGFBI         | 0.2404 | 0.5845 |
| 2 | ENSG00000047617 | ANO2          | 0.1433 | 0.5842 |
| 2 | ENSG00000142973 | CYP4B1        | 0.1186 | 0.5828 |
| 2 | ENSG00000260337 | Lnc-FAM174B-1 | 0.1209 | 0.5816 |
| 2 | ENSG00000125733 | TRIP10        | 0.1981 | 0.5798 |
| 2 | ENSG00000244734 | HBB           | 0.1650 | 0.5781 |
| 2 | ENSG00000138722 | MMRN1         | 0.1785 | 0.5778 |
| 2 | ENSG00000110852 | CLEC2B        | 0.2295 | 0.5774 |
| 2 | ENSG00000166482 | MFAP4         | 0.1255 | 0.5773 |
| 2 | ENSG00000101187 | SLCO4A1       | 0.1270 | 0.5771 |
| 2 | ENSG00000106211 | HSPB1         | 0.1555 | 0.5770 |
| 2 | ENSG00000137834 | SMAD6         | 0.1622 | 0.5762 |

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|---|-----------------|---------------------------------|--------|--------|
| 2 | ENSG0000073792  | IGF2BP2                         | 0.1389 | 0.5754 |
| 2 | ENSG00000164294 | GPX8                            | 0.1488 | 0.5753 |
| 2 | ENSG00000142798 | HSPG2                           | 0.1443 | 0.5747 |
| 2 | ENSG00000137507 | LRRC32                          | 0.1669 | 0.5745 |
| 2 | ENSG00000140682 | TGFB11                          | 0.1366 | 0.5739 |
| 2 | ENSG00000187498 | COL4A1                          | 0.1411 | 0.5727 |
| 2 | ENSG00000188536 | HBA2                            | 0.1400 | 0.5720 |
| 2 | ENSG00000279142 | None                            | 0.1117 | 0.5718 |
| 2 | ENSG00000125810 | CD93                            | 0.3224 | 0.5718 |
| 2 | ENSG00000184058 | TBX1                            | 0.1091 | 0.5717 |
| 2 | ENSG00000281732 | LOC284933                       | 0.1097 | 0.5715 |
| 2 | ENSG00000287652 | Antisense to DGCR8<br>and CDC45 | 0.1736 | 0.5709 |
| 2 | ENSG00000173641 | HSPB7                           | 0.1194 | 0.5700 |
| 2 | ENSG00000159403 | C1R                             | 0.2205 | 0.5690 |
| 2 | ENSG00000206172 | HBA1                            | 0.1478 | 0.5680 |
| 2 | ENSG00000159212 | CLIC6                           | 0.1114 | 0.5659 |
| 2 | ENSG00000100985 | MMP9                            | 0.1078 | 0.5650 |
| 2 | ENSG00000250863 | Lnc-KCTD8-1                     | 0.2379 | 0.5643 |
| 2 | ENSG00000169429 | CXCL8                           | 0.1011 | 0.5636 |
| 2 | ENSG00000177464 | GPR4                            | 0.1500 | 0.5636 |
| 2 | ENSG00000162998 | FRZB                            | 0.1011 | 0.5635 |
| 2 | ENSG00000160183 | TMPRSS3                         | 0.1281 | 0.5617 |
| 2 | ENSG00000109758 | HGFAC                           | 0.0997 | 0.5615 |
| 2 | ENSG00000233117 | LINC00702                       | 0.1065 | 0.5614 |
| 2 | ENSG00000183508 | TENT5C                          | 0.1446 | 0.5602 |
| 2 | ENSG00000258647 | LINC00930                       | 0.0996 | 0.5592 |
| 2 | ENSG00000173421 | IHO1                            | 0.1189 | 0.5576 |
| 2 | ENSG00000111057 | KRT18                           | 0.1250 | 0.5570 |
| 2 | ENSG00000060138 | YBX3                            | 0.1784 | 0.5568 |

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|---|-----------------|--------------|--------|--------|
| 2 | ENSG00000128917 | DLL4         | 0.1135 | 0.5567 |
| 2 | ENSG00000124762 | CDKN1A       | 0.1752 | 0.5554 |
| 2 | ENSG00000239677 | PDZRN3-AS1   | 0.0937 | 0.5545 |
| 2 | ENSG00000243620 | Lnc-ZIC4-3   | 0.1434 | 0.5534 |
| 2 | ENSG00000249307 | LINC01088    | 0.1275 | 0.5529 |
| 2 | ENSG00000115607 | IL18RAP      | 0.1272 | 0.5526 |
| 2 | ENSG00000261170 | LOC107984827 | 0.1218 | 0.5520 |
| 2 | ENSG00000138061 | CYP1B1       | 0.1214 | 0.5517 |
| 2 | ENSG00000106624 | AEBP1        | 0.1317 | 0.5514 |
| 2 | ENSG00000117595 | IRF6         | 0.0949 | 0.5510 |
| 2 | ENSG00000187479 | C11orf96     | 0.0954 | 0.5504 |
| 2 | ENSG00000179023 | KLHDC7A      | 0.0897 | 0.5499 |
| 2 | ENSG00000168427 | KLHL30       | 0.0902 | 0.5498 |
| 2 | ENSG00000250033 | SLC7A11-AS1  | 0.1174 | 0.5488 |
| 2 | ENSG00000183888 | SRARP        | 0.0986 | 0.5487 |
| 2 | ENSG00000162383 | SLC1A7       | 0.2594 | 0.5470 |
| 2 | ENSG00000185201 | IFITM2       | 0.2451 | 0.5458 |
| 2 | ENSG00000125430 | HS3ST3B1     | 0.1002 | 0.5457 |
| 2 | ENSG00000182718 | ANXA2        | 0.2208 | 0.5457 |
| 2 | ENSG00000253123 | LOC100507403 | 0.0915 | 0.5454 |
| 2 | ENSG00000094963 | FMO2         | 0.1120 | 0.5448 |
| 2 | ENSG00000229380 | PRKAR1B-AS2  | 0.0871 | 0.5447 |
| 2 | ENSG00000285938 | BCL6-AS1     | 0.1633 | 0.5444 |
| 2 | ENSG00000149452 | SLC22A8      | 0.1339 | 0.5427 |
| 2 | ENSG00000163739 | CXCL1        | 0.0862 | 0.5420 |
| 2 | ENSG00000196954 | CASP4        | 0.2211 | 0.5413 |
| 2 | ENSG00000173068 | BNC2         | 0.2439 | 0.5410 |
| 2 | ENSG00000003436 | TFPI         | 0.1344 | 0.5407 |
| 2 | ENSG00000171345 | KRT19        | 0.0834 | 0.5407 |
| 2 | ENSG00000253686 | LINC01484    | 0.1257 | 0.5405 |

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|---|-----------------|-----------------------|--------|--------|
| 2 | ENSG0000004939  | SLC4A1                | 0.1226 | 0.5398 |
| 2 | ENSG00000112303 | VNN2                  | 0.1302 | 0.5396 |
| 2 | ENSG00000106034 | CPED1                 | 0.1185 | 0.5393 |
| 2 | ENSG00000204389 | HSPA1A                | 0.1690 | 0.5393 |
| 2 | ENSG00000262152 | GREP1                 | 0.0831 | 0.5389 |
| 2 | ENSG00000148604 | RGR                   | 0.0865 | 0.5387 |
| 2 | ENSG00000187922 | LCN10                 | 0.0839 | 0.5387 |
| 2 | ENSG00000126778 | SIX1                  | 0.1048 | 0.5384 |
| 2 | ENSG00000174226 | SNX31                 | 0.0937 | 0.5383 |
| 2 | ENSG00000164867 | NOS3                  | 0.1047 | 0.5379 |
| 2 | ENSG00000187513 | GJA4                  | 0.0914 | 0.5377 |
| 2 | ENSG00000229926 | IL9RP1                | 0.0889 | 0.5374 |
| 2 | ENSG00000276317 | Lnc-GATA5-10          | 0.0815 | 0.5371 |
| 2 | ENSG00000173918 | C1QTNF1               | 0.1052 | 0.5369 |
| 2 | ENSG00000256955 | Lnc-MMP17-1           | 0.0837 | 0.5357 |
| 2 | ENSG00000163638 | ADAMTS9               | 0.1670 | 0.5355 |
| 2 | ENSG00000077238 | IL4R                  | 0.1918 | 0.5351 |
| 2 | ENSG00000100336 | APOL4                 | 0.3160 | 0.5349 |
| 2 | ENSG00000047457 | CP                    | 0.3633 | 0.5349 |
| 2 | ENSG00000162747 | FCGR3B                | 0.1056 | 0.5344 |
| 2 | ENSG00000278130 | FAM166A<br>Pseudogene | 0.0809 | 0.5335 |
| 2 | ENSG00000151929 | BAG3                  | 0.1593 | 0.5334 |
| 2 | ENSG00000272512 | Lnc-HES4-2            | 0.0765 | 0.5332 |
| 2 | ENSG00000165507 | DEPP1                 | 0.1676 | 0.5330 |
| 2 | ENSG00000186150 | UBL4B                 | 0.0873 | 0.5326 |
| 2 | ENSG00000129654 | FOXJ1                 | 0.1860 | 0.5320 |
| 2 | ENSG00000168079 | SCARA5                | 0.0786 | 0.5318 |
| 2 | ENSG00000230122 | ECEL1P3               | 0.0777 | 0.5313 |
| 2 | ENSG00000241158 | ADAMTS9-AS1           | 0.1303 | 0.5305 |

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|---|-----------------|-------------------------|--------|--------|
| 2 | ENSG00000122862 | SRGN                    | 0.1557 | 0.5294 |
| 2 | ENSG00000135245 | HILPDA                  | 0.1222 | 0.5294 |
| 2 | ENSG00000050327 | ARHGEF5                 | 0.0878 | 0.5292 |
| 2 | ENSG00000233588 | CYP51A1P2               | 0.1109 | 0.5285 |
| 2 | ENSG00000232803 | SLCO4A1-AS1             | 0.0783 | 0.5282 |
| 2 | ENSG00000184557 | SOCS3                   | 0.3501 | 0.5275 |
| 2 | ENSG00000287656 | Antisense to<br>SLC22A3 | 0.0726 | 0.5271 |
| 2 | ENSG00000170577 | SIX2                    | 0.0784 | 0.5270 |
| 2 | ENSG00000137801 | THBS1                   | 0.0703 | 0.5243 |
| 2 | ENSG00000185561 | TLCD2                   | 0.1310 | 0.5236 |
| 2 | ENSG00000197405 | C5AR1                   | 0.2152 | 0.5233 |
| 2 | ENSG00000249669 | CARMN                   | 0.0902 | 0.5231 |
| 2 | ENSG00000182885 | ADGRG3                  | 0.0785 | 0.5222 |
| 2 | ENSG00000163623 | NKX6-1                  | 0.0762 | 0.5212 |
| 2 | ENSG00000163464 | CXCR1                   | 0.0771 | 0.5210 |
| 2 | ENSG00000267304 | Lnc-TJP3-2              | 0.0679 | 0.5210 |
| 2 | ENSG00000267065 | LINC02080               | 0.0687 | 0.5208 |
| 2 | ENSG00000258676 | Lnc-ST8SIA2-1           | 0.0683 | 0.5202 |
| 2 | ENSG00000130600 | H19                     | 0.0842 | 0.5194 |
| 2 | ENSG00000160593 | JAML                    | 0.0916 | 0.5190 |
| 2 | ENSG00000141574 | SECTM1                  | 0.1016 | 0.5185 |
| 2 | ENSG00000251493 | FOXD1                   | 0.0706 | 0.5185 |
| 2 | ENSG00000228133 | LOC105371485            | 0.0710 | 0.5178 |
| 2 | ENSG00000074047 | GLI2                    | 0.0794 | 0.5177 |
| 2 | ENSG00000262003 | LOC101927727            | 0.0716 | 0.5171 |
| 2 | ENSG00000254362 | Lnc-PPP2R2A-2           | 0.0734 | 0.5165 |
| 2 | ENSG00000198542 | ITGBL1                  | 0.0744 | 0.5158 |
| 2 | ENSG00000150048 | CLEC1A                  | 0.1016 | 0.5149 |
| 2 | ENSG00000197901 | SLC22A6                 | 0.1006 | 0.5148 |

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| 2 | ENSG00000188511 | MIR3667HG    | 0.0821 | 0.5145 |
| 2 | ENSG00000145623 | OSMR         | 0.1585 | 0.5141 |
| 2 | ENSG00000163395 | IGFN1        | 0.1503 | 0.5121 |
| 2 | ENSG00000117318 | ID3          | 0.1579 | 0.5119 |
| 2 | ENSG00000270640 | Lnc-BABAM2-2 | 0.0681 | 0.5117 |
| 2 | ENSG00000140839 | CLEC18B      | 0.0926 | 0.5105 |
| 2 | ENSG00000168404 | MLKL         | 0.1351 | 0.5098 |
| 2 | ENSG00000125144 | MT1G         | 0.0702 | 0.5098 |
| 2 | ENSG00000169894 | MUC3A        | 0.0727 | 0.5086 |
| 2 | ENSG00000170801 | HTRA3        | 0.0950 | 0.5082 |
| 2 | ENSG00000171049 | FPR2         | 0.0841 | 0.5080 |
| 2 | ENSG00000148926 | ADM          | 0.1033 | 0.5077 |
| 2 | ENSG00000000938 | FGR          | 0.1132 | 0.5075 |
| 2 | ENSG00000279320 | None         | 0.0784 | 0.5070 |
| 2 | ENSG00000213719 | CLIC1        | 0.1690 | 0.5068 |
| 2 | ENSG00000169908 | TM4SF1       | 0.1260 | 0.5067 |
| 2 | ENSG00000108823 | SGCA         | 0.0927 | 0.5051 |
| 2 | ENSG00000205592 | MUC19        | 0.0809 | 0.5050 |
| 2 | ENSG00000112299 | VNN1         | 0.1115 | 0.5050 |
| 2 | ENSG00000134531 | EMP1         | 0.1952 | 0.5048 |
| 2 | ENSG00000136732 | GYPC         | 0.1909 | 0.5046 |
| 2 | ENSG00000256443 | Lnc-CPSF7-3  | 0.0683 | 0.5023 |
| 2 | ENSG00000162692 | VCAM1        | 0.1084 | 0.5019 |
| 2 | ENSG00000123374 | CDK2         | 0.1392 | 0.4990 |
| 2 | ENSG00000187634 | SAMD11       | 0.1889 | 0.4974 |
| 2 | ENSG00000205364 | MT1M         | 0.0792 | 0.4971 |
| 2 | ENSG00000142089 | IFITM3       | 0.1127 | 0.4960 |
| 2 | ENSG00000205358 | MT1H         | 0.0677 | 0.4953 |
| 2 | ENSG00000280109 | PLAC4        | 0.0771 | 0.4950 |
| 2 | ENSG00000125731 | SH2D3A       | 0.0905 | 0.4942 |

|   |                 |                 |        |        |
|---|-----------------|-----------------|--------|--------|
| 2 | ENSG00000235750 | KIAA0040        | 0.1544 | 0.4933 |
| 2 | ENSG00000268388 | FENDRR          | 0.0698 | 0.4933 |
| 2 | ENSG00000115165 | CYTIP           | 0.1310 | 0.4923 |
| 2 | ENSG00000152977 | ZIC1            | 0.0967 | 0.4917 |
| 2 | ENSG00000159167 | STC1            | 0.2229 | 0.4904 |
| 2 | ENSG00000185885 | IFITM1          | 0.1422 | 0.4897 |
| 2 | ENSG00000100060 | MFNG            | 0.1947 | 0.4889 |
| 2 | ENSG00000132357 | CARD6           | 0.1124 | 0.4887 |
| 2 | ENSG00000145779 | TNFAIP8         | 0.1175 | 0.4887 |
| 2 | ENSG00000183615 | FAM167B         | 0.1053 | 0.4886 |
| 2 | ENSG00000124549 | BTN2A3P         | 0.1080 | 0.4876 |
| 2 | ENSG00000110719 | TCIRG1          | 0.1600 | 0.4860 |
| 2 | ENSG00000276412 | Lnc-CNTNAP3B-13 | 0.0763 | 0.4851 |
| 2 | ENSG00000028137 | TNFRSF1B        | 0.2047 | 0.4815 |
| 2 | ENSG00000281327 | LINC01338       | 0.1457 | 0.4808 |
| 2 | ENSG00000185499 | MUC1            | 0.0847 | 0.4793 |
| 2 | ENSG00000186431 | FCAR            | 0.0737 | 0.4782 |
| 2 | ENSG00000105559 | PLEKHA4         | 0.1353 | 0.4772 |
| 2 | ENSG00000118503 | TNFAIP3         | 0.0913 | 0.4767 |
| 2 | ENSG00000231246 | LINC02884       | 0.0746 | 0.4754 |
| 2 | ENSG00000160111 | CPAMD8          | 0.1501 | 0.4751 |
| 2 | ENSG00000070729 | CNGB1           | 0.1294 | 0.4748 |
| 2 | ENSG00000011422 | PLAUR           | 0.1129 | 0.4747 |
| 2 | ENSG00000236908 | LINC02827       | 0.0676 | 0.4702 |
| 2 | ENSG00000176046 | NUPR1           | 0.1310 | 0.4701 |
| 2 | ENSG00000090339 | ICAM1           | 0.1558 | 0.4689 |
| 2 | ENSG00000105974 | CAV1            | 0.0781 | 0.4680 |
| 2 | ENSG00000100504 | PYGL            | 0.0952 | 0.4621 |
| 2 | ENSG00000166592 | RRAD            | 0.0733 | 0.4614 |
| 2 | ENSG00000103710 | RASL12          | 0.1499 | 0.4578 |



|   |                 |          |        |        |
|---|-----------------|----------|--------|--------|
| 2 | ENSG00000128016 | ZFP36    | 0.1257 | 0.4530 |
| 2 | ENSG00000170345 | FOS      | 0.0876 | 0.4526 |
| 2 | ENSG00000167772 | ANGPTL4  | 0.1161 | 0.4514 |
| 2 | ENSG00000142102 | PGGHG    | 0.0681 | 0.4497 |
| 2 | ENSG00000175591 | P2RY2    | 0.0895 | 0.4371 |
| 2 | ENSG00000020633 | RUNX3    | 0.0743 | 0.4361 |
| 2 | ENSG00000156463 | SH3RF2   | 0.0891 | 0.4310 |
| 2 | ENSG00000287689 | None     | 0.0712 | 0.4284 |
| 2 | ENSG00000154188 | ANGPT1   | 0.0687 | 0.4277 |
| 3 | ENSG00000064886 | CHI3L2   | 0.4444 | 0.7458 |
| 3 | ENSG00000006747 | SCIN     | 0.4155 | 0.6644 |
| 3 | ENSG00000095970 | TREM2    | 0.2306 | 0.6507 |
| 3 | ENSG00000038945 | MSR1     | 0.3232 | 0.6468 |
| 3 | ENSG00000118785 | SPP1     | 0.1842 | 0.6451 |
| 3 | ENSG00000224189 | HAGLR    | 0.2821 | 0.6409 |
| 3 | ENSG00000012223 | LTF      | 0.1864 | 0.6378 |
| 3 | ENSG00000163823 | CCR1     | 0.2533 | 0.6327 |
| 3 | ENSG00000196136 | SERPINA3 | 0.3858 | 0.6323 |
| 3 | ENSG00000173391 | OLR1     | 0.1675 | 0.6306 |
| 3 | ENSG00000026508 | CD44     | 0.3408 | 0.6300 |
| 3 | ENSG00000203747 | FCGR3A   | 0.2844 | 0.6260 |
| 3 | ENSG00000150337 | FCGR1A   | 0.1995 | 0.6243 |
| 3 | ENSG00000066294 | CD84     | 0.1908 | 0.6191 |
| 3 | ENSG00000168329 | CX3CR1   | 0.1554 | 0.6083 |
| 3 | ENSG00000173369 | C1QB     | 0.3041 | 0.6062 |
| 3 | ENSG00000005844 | ITGAL    | 0.2456 | 0.6054 |
| 3 | ENSG00000155307 | SAMSN1   | 0.2182 | 0.6042 |
| 3 | ENSG00000108691 | CCL2     | 0.2850 | 0.6042 |
| 3 | ENSG00000240583 | AQP1     | 0.2052 | 0.6041 |
| 3 | ENSG00000166927 | MS4A7    | 0.2270 | 0.6031 |

|   |                 |              |        |        |
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| 3 | ENSG00000185811 | IKZF1        | 0.2204 | 0.6021 |
| 3 | ENSG00000148773 | MKI67        | 0.3404 | 0.6020 |
| 3 | ENSG00000077420 | APBB1IP      | 0.1666 | 0.5975 |
| 3 | ENSG00000158869 | FCER1G       | 0.2290 | 0.5966 |
| 3 | ENSG00000204287 | HLA-DRA      | 0.1752 | 0.5957 |
| 3 | ENSG00000011600 | TYROBP       | 0.1881 | 0.5945 |
| 3 | ENSG00000082074 | FYB1         | 0.2092 | 0.5931 |
| 3 | ENSG00000167613 | LAIR1        | 0.2646 | 0.5931 |
| 3 | ENSG00000105697 | HAMP         | 0.1858 | 0.5916 |
| 3 | ENSG00000258342 | LINC00609    | 0.2780 | 0.5912 |
| 3 | ENSG00000239961 | LILRA4       | 0.1370 | 0.5882 |
| 3 | ENSG00000160255 | ITGB2        | 0.2669 | 0.5882 |
| 3 | ENSG00000104972 | LILRB1       | 0.2167 | 0.5874 |
| 3 | ENSG00000125730 | C3           | 0.1568 | 0.5841 |
| 3 | ENSG00000159189 | C1QC         | 0.2604 | 0.5840 |
| 3 | ENSG00000162511 | LAPTM5       | 0.1968 | 0.5834 |
| 3 | ENSG00000134061 | CD180        | 0.2625 | 0.5832 |
| 3 | ENSG00000140968 | IRF8         | 0.1710 | 0.5831 |
| 3 | ENSG00000018280 | SLC11A1      | 0.2388 | 0.5819 |
| 3 | ENSG00000271605 | MILR1        | 0.1310 | 0.5815 |
| 3 | ENSG00000204472 | AIF1         | 0.1678 | 0.5814 |
| 3 | ENSG00000129450 | SIGLEC9      | 0.2089 | 0.5802 |
| 3 | ENSG00000239998 | LILRA2       | 0.1916 | 0.5801 |
| 3 | ENSG00000242574 | HLA-DMB      | 0.1448 | 0.5797 |
| 3 | ENSG00000184574 | LPAR5        | 0.1204 | 0.5796 |
| 3 | ENSG00000173988 | LRRRC63      | 0.1636 | 0.5787 |
| 3 | ENSG00000226496 | LINC00323    | 0.2143 | 0.5778 |
| 3 | ENSG00000257585 | LINC00609    | 0.1563 | 0.5776 |
| 3 | ENSG00000257826 | Lnc-MBIP-3   | 0.2340 | 0.5772 |
| 3 | ENSG00000276980 | Lnc-GPR108-3 | 0.1544 | 0.5759 |

|   |                 |                 |        |        |
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| 3 | ENSG00000132965 | ALOX5AP         | 0.2384 | 0.5757 |
| 3 | ENSG00000165025 | SYK             | 0.1635 | 0.5747 |
| 3 | ENSG00000121933 | TMIGD3          | 0.1161 | 0.5733 |
| 3 | ENSG00000131747 | TOP2A           | 0.2065 | 0.5730 |
| 3 | ENSG00000233670 | PIRT            | 0.1656 | 0.5724 |
| 3 | ENSG00000250771 | TLR2 Pseudogene | 0.1736 | 0.5723 |
| 3 | ENSG00000115956 | PLEK            | 0.1586 | 0.5708 |
| 3 | ENSG00000100292 | HMOX1           | 0.2271 | 0.5693 |
| 3 | ENSG00000167755 | KLK6            | 0.3529 | 0.5686 |
| 3 | ENSG00000173372 | C1QA            | 0.2941 | 0.5682 |
| 3 | ENSG00000158715 | SLC45A3         | 0.1833 | 0.5679 |
| 3 | ENSG00000155629 | PIK3AP1         | 0.2317 | 0.5677 |
| 3 | ENSG00000086205 | FOLH1           | 0.3113 | 0.5675 |
| 3 | ENSG00000261795 | Lnc-PDGFA-4     | 0.1338 | 0.5672 |
| 3 | ENSG00000204252 | HLA-DOA         | 0.1157 | 0.5669 |
| 3 | ENSG00000175567 | UCP2            | 0.1424 | 0.5666 |
| 3 | ENSG00000204161 | TMEM273         | 0.1158 | 0.5659 |
| 3 | ENSG00000175785 | PRIMA1          | 0.1161 | 0.5650 |
| 3 | ENSG00000265531 | FCGR1CP         | 0.1028 | 0.5650 |
| 3 | ENSG00000253924 | Lnc-NPBWR1-8    | 0.2240 | 0.5648 |
| 3 | ENSG00000167851 | CD300A          | 0.2093 | 0.5647 |
| 3 | ENSG00000228392 | None            | 0.2104 | 0.5645 |
| 3 | ENSG00000169403 | PTAFR           | 0.1752 | 0.5639 |
| 3 | ENSG00000105366 | SIGLEC8         | 0.1177 | 0.5639 |
| 3 | ENSG00000269553 | Lnc-MAG-2       | 0.1194 | 0.5636 |
| 3 | ENSG00000016602 | CLCA4           | 0.1681 | 0.5630 |
| 3 | ENSG00000013297 | CLDN11          | 0.1882 | 0.5627 |
| 3 | ENSG00000186417 | GLDN            | 0.2349 | 0.5612 |
| 3 | ENSG00000259104 | PTCSC3          | 0.1650 | 0.5609 |
| 3 | ENSG00000105967 | TFEC            | 0.1231 | 0.5609 |

|   |                 |              |        |        |
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| 3 | ENSG00000110077 | MS4A6A       | 0.3586 | 0.5605 |
| 3 | ENSG00000232310 | LINC03002    | 0.1724 | 0.5599 |
| 3 | ENSG00000158865 | SLC5A11      | 0.2242 | 0.5596 |
| 3 | ENSG00000101336 | HCK          | 0.1635 | 0.5594 |
| 3 | ENSG00000090104 | RGS1         | 0.1631 | 0.5578 |
| 3 | ENSG00000041982 | TNC          | 0.0966 | 0.5564 |
| 3 | ENSG00000255216 | Lnc-TRIM29-2 | 0.2158 | 0.5560 |
| 3 | ENSG00000138964 | PARVG        | 0.1641 | 0.5553 |
| 3 | ENSG00000171860 | C3AR1        | 0.1675 | 0.5548 |
| 3 | ENSG00000275395 | FCGBP        | 0.3690 | 0.5546 |
| 3 | ENSG00000204655 | MOG          | 0.2646 | 0.5546 |
| 3 | ENSG00000197249 | SERPINA1     | 0.3593 | 0.5541 |
| 3 | ENSG00000187908 | DMBT1        | 0.2145 | 0.5540 |
| 3 | ENSG00000254314 | Lnc-NPBWR1-9 | 0.1663 | 0.5539 |
| 3 | ENSG00000081237 | PTPRC        | 0.1697 | 0.5526 |
| 3 | ENSG00000231389 | HLA-DPA1     | 0.1207 | 0.5513 |
| 3 | ENSG00000250072 | SH3TC2-DT    | 0.2859 | 0.5506 |
| 3 | ENSG00000154864 | PIEZO2       | 0.1379 | 0.5501 |
| 3 | ENSG00000134817 | APLNR        | 0.1656 | 0.5494 |
| 3 | ENSG00000139292 | LGR5         | 0.1987 | 0.5487 |
| 3 | ENSG00000183160 | TMEM119      | 0.0974 | 0.5479 |
| 3 | ENSG00000225781 | OR6V1        | 0.1580 | 0.5472 |
| 3 | ENSG00000152689 | RASGRP3      | 0.1192 | 0.5470 |
| 3 | ENSG00000251138 | LINC02882    | 0.3034 | 0.5470 |
| 3 | ENSG00000174607 | UGT8         | 0.2070 | 0.5466 |
| 3 | ENSG00000197471 | SPN          | 0.1518 | 0.5465 |
| 3 | ENSG00000267432 | DNAH17-AS1   | 0.2638 | 0.5465 |
| 3 | ENSG00000213186 | TRIM59       | 0.2357 | 0.5465 |
| 3 | ENSG00000071991 | CDH19        | 0.1692 | 0.5465 |
| 3 | ENSG00000171051 | FPR1         | 0.1661 | 0.5464 |

|   |                 |                  |        |        |
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| 3 | ENSG00000136167 | LCP1             | 0.2126 | 0.5462 |
| 3 | ENSG00000228789 | HCG22            | 0.1308 | 0.5458 |
| 3 | ENSG00000142583 | SLC2A5           | 0.1205 | 0.5456 |
| 3 | ENSG00000277494 | GPIHBP1          | 0.1423 | 0.5446 |
| 3 | ENSG00000286558 | None             | 0.2273 | 0.5445 |
| 3 | ENSG00000114013 | CD86             | 0.1466 | 0.5440 |
| 3 | ENSG00000081479 | LRP2             | 0.1365 | 0.5439 |
| 3 | ENSG00000148908 | RGS10            | 0.0901 | 0.5436 |
| 3 | ENSG00000042493 | CAPG             | 0.1489 | 0.5434 |
| 3 | ENSG00000105383 | CD33             | 0.1443 | 0.5428 |
| 3 | ENSG00000204482 | LST1             | 0.0920 | 0.5425 |
| 3 | ENSG00000205116 | TMEM88B          | 0.1989 | 0.5423 |
| 3 | ENSG00000161896 | IP6K3            | 0.1400 | 0.5423 |
| 3 | ENSG00000231131 | LNCAROD          | 0.1219 | 0.5419 |
| 3 | ENSG00000134516 | DOCK2            | 0.1101 | 0.5418 |
| 3 | ENSG00000104974 | LILRA1           | 0.0889 | 0.5414 |
| 3 | ENSG00000207955 | MIR219A2HG       | 0.3251 | 0.5414 |
| 3 | ENSG00000126860 | EVI2A            | 0.1890 | 0.5402 |
| 3 | ENSG00000268758 | ADGRE4P          | 0.0917 | 0.5401 |
| 3 | ENSG00000279419 | None             | 0.2489 | 0.5400 |
| 3 | ENSG00000244062 | ACSL3 Pseudogene | 0.2810 | 0.5397 |
| 3 | ENSG00000261121 | LINC02473        | 0.1756 | 0.5397 |
| 3 | ENSG00000143226 | FCGR2A           | 0.2433 | 0.5395 |
| 3 | ENSG00000172243 | CLEC7A           | 0.0942 | 0.5394 |
| 3 | ENSG00000080031 | PTPRH            | 0.1945 | 0.5393 |
| 3 | ENSG00000019582 | CD74             | 0.1044 | 0.5391 |
| 3 | ENSG00000103089 | FA2H             | 0.2255 | 0.5390 |
| 3 | ENSG00000166091 | CMTM5            | 0.2567 | 0.5389 |
| 3 | ENSG00000198502 | HLA-DRB5         | 0.1264 | 0.5383 |
| 3 | ENSG00000170458 | CD14             | 0.2002 | 0.5383 |

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|---|-----------------|---------------|--------|--------|
| 3 | ENSG00000127412 | TRPV5         | 0.1333 | 0.5382 |
| 3 | ENSG00000148826 | NKX6-2        | 0.0973 | 0.5366 |
| 3 | ENSG00000105695 | MAG           | 0.2540 | 0.5362 |
| 3 | ENSG00000188488 | SERPINA5      | 0.1245 | 0.5360 |
| 3 | ENSG00000112799 | LY86          | 0.1109 | 0.5355 |
| 3 | ENSG00000142512 | SIGLEC10      | 0.0913 | 0.5349 |
| 3 | ENSG00000160791 | CCR5          | 0.1243 | 0.5345 |
| 3 | ENSG00000261997 | None          | 0.0881 | 0.5342 |
| 3 | ENSG00000270547 | LINC01235     | 0.0773 | 0.5341 |
| 3 | ENSG00000197993 | KEL           | 0.1067 | 0.5334 |
| 3 | ENSG00000179178 | TMEM125       | 0.3213 | 0.5328 |
| 3 | ENSG00000204644 | ZFP57         | 0.1625 | 0.5326 |
| 3 | ENSG00000139629 | GALNT6        | 0.1594 | 0.5326 |
| 3 | ENSG00000286279 | Lnc-SLC16A7-4 | 0.2188 | 0.5319 |
| 3 | ENSG00000251429 | AIDAP2        | 0.1537 | 0.5318 |
| 3 | ENSG00000012124 | CD22          | 0.1227 | 0.5311 |
| 3 | ENSG00000140030 | GPR65         | 0.1490 | 0.5307 |
| 3 | ENSG00000180739 | S1PR5         | 0.1704 | 0.5297 |
| 3 | ENSG00000163694 | RBM47         | 0.2062 | 0.5297 |
| 3 | ENSG00000228058 | LINC01736     | 0.0948 | 0.5295 |
| 3 | ENSG00000204278 | TMEM235       | 0.1819 | 0.5292 |
| 3 | ENSG00000198019 | FCGR1B        | 0.0741 | 0.5287 |
| 3 | ENSG00000172578 | KLHL6         | 0.2254 | 0.5286 |
| 3 | ENSG00000282608 | ADORA3        | 0.1216 | 0.5285 |
| 3 | ENSG00000233828 | MIR4280HG     | 0.2797 | 0.5284 |
| 3 | ENSG00000116774 | OLFML3        | 0.0919 | 0.5284 |
| 3 | ENSG00000250198 | LINC02199     | 0.1212 | 0.5280 |
| 3 | ENSG00000169896 | ITGAM         | 0.1538 | 0.5278 |
| 3 | ENSG00000268170 | Lnc-FAM131B-2 | 0.1720 | 0.5275 |
| 3 | ENSG00000127507 | ADGRE2        | 0.0830 | 0.5275 |

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| 3 | ENSG00000187912 | CLEC17A            | 0.0857 | 0.5272 |
| 3 | ENSG00000287372 | None               | 0.0722 | 0.5271 |
| 3 | ENSG00000286749 | Antisense to NMUR2 | 0.1255 | 0.5271 |
| 3 | ENSG00000158859 | ADAMTS4            | 0.1169 | 0.5270 |
| 3 | ENSG00000174125 | TLR1               | 0.1138 | 0.5270 |
| 3 | ENSG00000171840 | NINJ2              | 0.1958 | 0.5261 |
| 3 | ENSG00000272808 | GCAWKR             | 0.2691 | 0.5258 |
| 3 | ENSG00000064300 | NGFR               | 0.0736 | 0.5257 |
| 3 | ENSG00000126266 | FFAR1              | 0.1173 | 0.5257 |
| 3 | ENSG00000236398 | TAS2R39            | 0.0990 | 0.5254 |
| 3 | ENSG00000228408 | Lnc-TAB2-1         | 0.3106 | 0.5246 |
| 3 | ENSG00000130300 | PLVAP              | 0.0702 | 0.5246 |
| 3 | ENSG00000086730 | LAT2               | 0.1724 | 0.5242 |
| 3 | ENSG00000167641 | PPP1R14A           | 0.1141 | 0.5234 |
| 3 | ENSG00000184357 | H1-5               | 0.2146 | 0.5231 |
| 3 | ENSG00000133321 | PLAAT4             | 0.1197 | 0.5230 |
| 3 | ENSG00000231427 | LINC01445          | 0.1206 | 0.5228 |
| 3 | ENSG00000162444 | RBP7               | 0.2111 | 0.5224 |
| 3 | ENSG00000159216 | RUNX1              | 0.1434 | 0.5221 |
| 3 | ENSG00000110934 | BIN2               | 0.1052 | 0.5219 |
| 3 | ENSG00000174123 | TLR10              | 0.0753 | 0.5211 |
| 3 | ENSG00000136960 | ENPP2              | 0.2141 | 0.5210 |
| 3 | ENSG00000254415 | SIGLEC14           | 0.0754 | 0.5208 |
| 3 | ENSG00000011426 | ANLN               | 0.1141 | 0.5207 |
| 3 | ENSG00000287939 | None               | 0.0793 | 0.5203 |
| 3 | ENSG00000241345 | LOC105375483       | 0.1202 | 0.5200 |
| 3 | ENSG00000169413 | RNASE6             | 0.0759 | 0.5195 |
| 3 | ENSG00000178082 | TWF1P1             | 0.1148 | 0.5192 |
| 3 | ENSG00000124915 | MYRF-AS1           | 0.0889 | 0.5184 |
| 3 | ENSG00000256618 | MTRNR2L1           | 0.1613 | 0.5184 |

|   |                 |             |        |        |
|---|-----------------|-------------|--------|--------|
| 3 | ENSG00000162949 | CAPN13      | 0.1591 | 0.5183 |
| 3 | ENSG00000249484 | LINC01470   | 0.1220 | 0.5183 |
| 3 | ENSG00000073737 | DHRS9       | 0.0817 | 0.5182 |
| 3 | ENSG00000146192 | FGD2        | 0.0924 | 0.5179 |
| 3 | ENSG00000244682 | FCGR2C      | 0.1287 | 0.5177 |
| 3 | ENSG00000286403 | None        | 0.1016 | 0.5177 |
| 3 | ENSG00000179468 | OR9A2       | 0.1493 | 0.5176 |
| 3 | ENSG00000101049 | SGK2        | 0.1796 | 0.5174 |
| 3 | ENSG00000051523 | CYBA        | 0.1548 | 0.5162 |
| 3 | ENSG00000225217 | HSPA7       | 0.2140 | 0.5161 |
| 3 | ENSG00000183196 | CHST6       | 0.0768 | 0.5160 |
| 3 | ENSG00000180353 | HCLS1       | 0.1249 | 0.5154 |
| 3 | ENSG00000138316 | ADAMTS14    | 0.1382 | 0.5153 |
| 3 | ENSG00000175489 | LRRC25      | 0.1485 | 0.5151 |
| 3 | ENSG00000070190 | DAPP1       | 0.0724 | 0.5148 |
| 3 | ENSG00000107099 | DOCK8       | 0.0916 | 0.5146 |
| 3 | ENSG00000108798 | ABI3        | 0.0964 | 0.5144 |
| 3 | ENSG00000136867 | SLC31A2     | 0.1023 | 0.5144 |
| 3 | ENSG00000163191 | S100A11     | 0.3018 | 0.5140 |
| 3 | ENSG00000283608 | Lnc-SUMO4-6 | 0.1398 | 0.5131 |
| 3 | ENSG00000240534 | RPL34P17    | 0.2349 | 0.5130 |
| 3 | ENSG00000229391 | HLA-DRB6    | 0.0948 | 0.5126 |
| 3 | ENSG00000224389 | C4B         | 0.2260 | 0.5119 |
| 3 | ENSG00000154642 | C21orf91    | 0.1296 | 0.5118 |
| 3 | ENSG00000180929 | GPR62       | 0.1292 | 0.5116 |
| 3 | ENSG00000125735 | TNFSF14     | 0.1245 | 0.5113 |
| 3 | ENSG00000167588 | GPD1        | 0.3039 | 0.5112 |
| 3 | ENSG00000137462 | TLR2        | 0.1196 | 0.5096 |
| 3 | ENSG00000262188 | LINC01978   | 0.1429 | 0.5092 |
| 3 | ENSG00000196126 | HLA-DRB1    | 0.0822 | 0.5089 |

|   |                 |               |        |        |
|---|-----------------|---------------|--------|--------|
| 3 | ENSG00000226448 | RPL7AP51      | 0.1549 | 0.5088 |
| 3 | ENSG00000184730 | APOBR         | 0.1201 | 0.5084 |
| 3 | ENSG00000237166 | LINC01792     | 0.1283 | 0.5082 |
| 3 | ENSG00000227544 | LINC03013     | 0.1727 | 0.5080 |
| 3 | ENSG00000183760 | ACP7          | 0.1075 | 0.5079 |
| 3 | ENSG00000006042 | TMEM98        | 0.0994 | 0.5073 |
| 3 | ENSG00000235568 | NFAM1         | 0.1035 | 0.5073 |
| 3 | ENSG00000228793 | LOC100507336  | 0.0786 | 0.5072 |
| 3 | ENSG00000286522 | H3C2          | 0.1474 | 0.5070 |
| 3 | ENSG00000158714 | SLAMF8        | 0.2027 | 0.5063 |
| 3 | ENSG00000225924 | TAB2-AS1      | 0.0742 | 0.5062 |
| 3 | ENSG00000248208 | WDR45P1       | 0.0856 | 0.5059 |
| 3 | ENSG00000131401 | NAPSB         | 0.1100 | 0.5053 |
| 3 | ENSG00000226994 | Lnc-RASGRP3-5 | 0.2097 | 0.5051 |
| 3 | ENSG00000159399 | HK2           | 0.1393 | 0.5048 |
| 3 | ENSG00000231840 | TMEM139-AS1   | 0.0943 | 0.5047 |
| 3 | ENSG00000166923 | GREM1         | 0.2348 | 0.5042 |
| 3 | ENSG00000128283 | CDC42EP1      | 0.0740 | 0.5041 |
| 3 | ENSG00000105122 | RASAL3        | 0.0911 | 0.5039 |
| 3 | ENSG00000167208 | SNX20         | 0.1051 | 0.5034 |
| 3 | ENSG00000150656 | CNDP1         | 0.2512 | 0.5034 |
| 3 | ENSG00000287609 | None          | 0.0942 | 0.5025 |
| 3 | ENSG00000113396 | SLC27A6       | 0.1071 | 0.5021 |
| 3 | ENSG00000140379 | BCL2A1        | 0.1602 | 0.5020 |
| 3 | ENSG00000129757 | CDKN1C        | 0.0953 | 0.5013 |
| 3 | ENSG00000283462 | LOC101930276  | 0.1841 | 0.5010 |
| 3 | ENSG00000169385 | RNASE2        | 0.0788 | 0.5005 |
| 3 | ENSG00000236700 | LINC01010     | 0.0749 | 0.5005 |
| 3 | ENSG00000136286 | MYO1G         | 0.0689 | 0.5000 |
| 3 | ENSG00000221937 | TAS2R40       | 0.0786 | 0.4998 |

|   |                 |              |        |        |
|---|-----------------|--------------|--------|--------|
| 3 | ENSG00000176381 | PRR18        | 0.1319 | 0.4988 |
| 3 | ENSG00000137869 | CYP19A1      | 0.0816 | 0.4979 |
| 3 | ENSG00000173253 | DMRT2        | 0.1261 | 0.4975 |
| 3 | ENSG00000172005 | MAL          | 0.1617 | 0.4968 |
| 3 | ENSG00000197430 | OPALIN       | 0.2467 | 0.4965 |
| 3 | ENSG00000100365 | NCF4         | 0.1516 | 0.4964 |
| 3 | ENSG00000171631 | P2RY6        | 0.1131 | 0.4951 |
| 3 | ENSG00000119535 | CSF3R        | 0.1157 | 0.4950 |
| 3 | ENSG00000232560 | LINC01549    | 0.0799 | 0.4948 |
| 3 | ENSG00000014257 | ACP3         | 0.0803 | 0.4948 |
| 3 | ENSG00000244301 | AOX3P        | 0.1489 | 0.4939 |
| 3 | ENSG00000140873 | ADAMTS18     | 0.1981 | 0.4934 |
| 3 | ENSG00000129667 | RHBDF2       | 0.1048 | 0.4932 |
| 3 | ENSG00000253877 | LINC01608    | 0.1697 | 0.4931 |
| 3 | ENSG00000172548 | NIPAL4       | 0.1423 | 0.4930 |
| 3 | ENSG00000128645 | HOXD1        | 0.1054 | 0.4924 |
| 3 | ENSG00000163565 | IFI16        | 0.1153 | 0.4920 |
| 3 | ENSG00000286625 | None         | 0.1128 | 0.4916 |
| 3 | ENSG00000250215 | CIR1P2       | 0.2653 | 0.4913 |
| 3 | ENSG00000170775 | GPR37        | 0.1659 | 0.4912 |
| 3 | ENSG00000130592 | LSP1         | 0.1076 | 0.4910 |
| 3 | ENSG00000251442 | LINC01094    | 0.1477 | 0.4909 |
| 3 | ENSG00000110079 | MS4A4A       | 0.2060 | 0.4905 |
| 3 | ENSG00000232474 | NCKAP5-IT1   | 0.0993 | 0.4901 |
| 3 | ENSG00000254081 | LINC01299    | 0.2365 | 0.4899 |
| 3 | ENSG00000152766 | ANKRD22      | 0.1144 | 0.4899 |
| 3 | ENSG00000221887 | HMSD         | 0.1194 | 0.4898 |
| 3 | ENSG00000277117 | LOC102723996 | 0.0830 | 0.4898 |
| 3 | ENSG00000237082 | COX5BP6      | 0.1287 | 0.4893 |
| 3 | ENSG00000025708 | TYMP         | 0.1410 | 0.4891 |

|   |                 |                                |        |        |
|---|-----------------|--------------------------------|--------|--------|
| 3 | ENSG0000012779  | ALOX5                          | 0.1019 | 0.4890 |
| 3 | ENSG00000275713 | H2BC9                          | 0.1015 | 0.4889 |
| 3 | ENSG00000122367 | LDB3                           | 0.1561 | 0.4886 |
| 3 | ENSG00000165131 | LLCFC1                         | 0.0803 | 0.4877 |
| 3 | ENSG00000285269 | SLC35D2-HSD17B3<br>readthrough | 0.0822 | 0.4877 |
| 3 | ENSG00000227088 | Lnc-LRRTM4-1                   | 0.1546 | 0.4877 |
| 3 | ENSG00000252312 | RN7SKP21                       | 0.0857 | 0.4874 |
| 3 | ENSG00000179420 | OR6W1P                         | 0.1194 | 0.4869 |
| 3 | ENSG00000258948 | KRT8P1                         | 0.0795 | 0.4866 |
| 3 | ENSG00000198774 | RASSF9                         | 0.1114 | 0.4862 |
| 3 | ENSG00000288533 | Antisense to TYMS<br>and CLUL1 | 0.1653 | 0.4860 |
| 3 | ENSG00000127324 | TSPAN8                         | 0.0709 | 0.4858 |
| 3 | ENSG00000254863 | LINC02744                      | 0.1007 | 0.4851 |
| 3 | ENSG00000279223 | None                           | 0.0911 | 0.4846 |
| 3 | ENSG00000285712 | None                           | 0.1039 | 0.4836 |
| 3 | ENSG00000128652 | HOXD3                          | 0.0765 | 0.4825 |
| 3 | ENSG00000231171 | LINC01098                      | 0.1112 | 0.4816 |
| 3 | ENSG00000229140 | CCDC26                         | 0.0901 | 0.4812 |
| 3 | ENSG00000155926 | SLA                            | 0.1026 | 0.4811 |
| 3 | ENSG00000133048 | CHI3L1                         | 0.1678 | 0.4809 |
| 3 | ENSG00000164342 | TLR3                           | 0.0717 | 0.4808 |
| 3 | ENSG00000273259 | Thioesterase                   | 0.1471 | 0.4808 |
| 3 | ENSG00000286569 | None                           | 0.0794 | 0.4806 |
| 3 | ENSG00000157227 | MMP14                          | 0.2251 | 0.4805 |
| 3 | ENSG00000257720 | ILF2P2                         | 0.1511 | 0.4801 |
| 3 | ENSG00000100368 | CSF2RB                         | 0.1802 | 0.4799 |
| 3 | ENSG00000174837 | ADGRE1                         | 0.0964 | 0.4799 |
| 3 | ENSG00000259764 | PCSK6-AS1                      | 0.1262 | 0.4791 |
| 3 | ENSG00000244738 | Lnc-CLDN11-2                   | 0.0942 | 0.4785 |

|   |                 |              |        |        |
|---|-----------------|--------------|--------|--------|
| 3 | ENSG00000160223 | ICOSLG       | 0.0727 | 0.4773 |
| 3 | ENSG00000115523 | GNLY         | 0.0901 | 0.4770 |
| 3 | ENSG00000244731 | C4A          | 0.1582 | 0.4768 |
| 3 | ENSG00000118640 | VAMP8        | 0.1102 | 0.4767 |
| 3 | ENSG00000105281 | SLC1A5       | 0.1965 | 0.4765 |
| 3 | ENSG00000066336 | SPI1         | 0.1143 | 0.4761 |
| 3 | ENSG00000248529 | LOC101928651 | 0.1135 | 0.4756 |
| 3 | ENSG00000166928 | MS4A14       | 0.1456 | 0.4753 |
| 3 | ENSG00000166473 | PKD1L2       | 0.0930 | 0.4750 |
| 3 | ENSG00000163563 | MNDA         | 0.1076 | 0.4747 |
| 3 | ENSG0000010327  | STAB1        | 0.2132 | 0.4740 |
| 3 | ENSG00000277775 | H3C7         | 0.0732 | 0.4734 |
| 3 | ENSG00000187554 | TLR5         | 0.0922 | 0.4718 |
| 3 | ENSG00000232504 | ST3GAL5-AS1  | 0.1183 | 0.4707 |
| 3 | ENSG00000132702 | HAPLN2       | 0.1061 | 0.4696 |
| 3 | ENSG00000129465 | RIPK3        | 0.0762 | 0.4676 |
| 3 | ENSG00000287538 | None         | 0.1149 | 0.4666 |
| 3 | ENSG00000153551 | CMTM7        | 0.0872 | 0.4662 |
| 3 | ENSG00000205403 | CFI          | 0.1287 | 0.4656 |
| 3 | ENSG00000207736 | MIR657       | 0.0843 | 0.4652 |
| 3 | ENSG00000137752 | CASP1        | 0.1240 | 0.4649 |
| 3 | ENSG00000128340 | RAC2         | 0.0997 | 0.4643 |
| 3 | ENSG00000287736 | PTCSC1       | 0.0953 | 0.4643 |
| 3 | ENSG00000145287 | PLAC8        | 0.1238 | 0.4637 |
| 3 | ENSG00000263154 | Lnc-BAHCC1-1 | 0.0776 | 0.4619 |
| 3 | ENSG00000203710 | CR1          | 0.0840 | 0.4616 |
| 3 | ENSG00000198835 | GJC2         | 0.0819 | 0.4607 |
| 3 | ENSG00000258227 | CLEC5A       | 0.0896 | 0.4606 |
| 3 | ENSG00000090382 | LYZ          | 0.1161 | 0.4600 |

|   |                 |                                      |        |        |
|---|-----------------|--------------------------------------|--------|--------|
| 3 | ENSG00000260922 | Antisense to ADAMTS18                | 0.0977 | 0.4583 |
| 3 | ENSG00000285885 | Antisense to MOBP                    | 0.0999 | 0.4581 |
| 3 | ENSG00000214688 | C10orf105                            | 0.0833 | 0.4551 |
| 3 | ENSG00000286048 | Antisense to ITGA2                   | 0.0949 | 0.4543 |
| 3 | ENSG00000229494 | LOC101927948                         | 0.1134 | 0.4542 |
| 3 | ENSG00000197747 | S100A10                              | 0.1026 | 0.4542 |
| 3 | ENSG00000136235 | GPNMB                                | 0.0836 | 0.4536 |
| 3 | ENSG00000267287 | Lnc-NFATC1-1                         | 0.0916 | 0.4532 |
| 3 | ENSG00000185905 | C16orf54                             | 0.0831 | 0.4531 |
| 3 | ENSG00000257183 | Lnc-KCNC2-2                          | 0.1148 | 0.4526 |
| 3 | ENSG00000152804 | HHEX                                 | 0.0788 | 0.4524 |
| 3 | ENSG00000129810 | SGO1                                 | 0.0700 | 0.4517 |
| 3 | ENSG00000132854 | KANK4                                | 0.0883 | 0.4501 |
| 3 | ENSG00000286541 | None                                 | 0.0795 | 0.4495 |
| 3 | ENSG00000283431 | Novel Zinc Finger Protein Pseudogene | 0.0805 | 0.4477 |
| 3 | ENSG00000117228 | GBP1                                 | 0.0698 | 0.4451 |
| 3 | ENSG00000122585 | NPY                                  | 0.0969 | 0.4421 |
| 3 | ENSG00000101670 | LIPG                                 | 0.0778 | 0.4418 |
| 3 | ENSG00000224397 | PELATON                              | 0.0792 | 0.4413 |
| 3 | ENSG00000261710 | Lnc-ADGRB1-3                         | 0.0753 | 0.4369 |
| 3 | ENSG00000141526 | SLC16A3                              | 0.0949 | 0.4368 |
| 3 | ENSG00000128262 | POM121L9P                            | 0.0709 | 0.4355 |
| 3 | ENSG00000283787 | PRR33                                | 0.0741 | 0.4291 |

*Table A31. Genetic Composition of KCL BrainBank case-derived clusters. Feature score refers to the basis components which contribute the most to the samples mapped to each cluster, whilst probability refers to the probability that the gene belongs to that cluster, where the baseline probability is 0.3333.*

| Source | Term Name   | Term ID            | Term Size | p adjusted | Intersection Size |
|--------|---|--------------------|-----------|------------|-------------------|
| GO:MF  | neuropeptide hormone activity                     | GO:0005184         | 22        | 9.90E-06   | 5                 |
| GO:MF  | hormone activity                                  | GO:0005179         | 78        | 1.10E-05   | 7                 |
| GO:BP  | chemical synaptic transmission                    | GO:0007268         | 663       | 4.00E-04   | 14                |
| GO:BP  | anterograde trans-synaptic signaling              | GO:0098916         | 663       | 4.00E-04   | 14                |
| GO:BP  | trans-synaptic signaling                          | GO:0099537         | 671       | 4.60E-04   | 14                |
| REAC   | MECP2 regulates transcription of neuronal ligands | REAC:R-HSA-9022702 | 7         | 6.30E-04   | 3                 |
| GO:BP  | synaptic signaling                                | GO:0099536         | 694       | 6.90E-04   | 14                |
| GO:BP  | regulation of epinephrine secretion               | GO:0014060         | 7         | 3.60E-03   | 3                 |
| GO:BP  | epinephrine secretion                             | GO:0048242         | 8         | 5.70E-03   | 3                 |
| KEGG   | cAMP signaling pathway                            | KEGG:04024         | 203       | 8.00E-03   | 6                 |
| KEGG   | neuroactive ligand-receptor interaction           | KEGG:04080         | 301       | 9.60E-03   | 7                 |
| GO:BP  | epinephrine transport                             | GO:0048241         | 11        | 1.70E-02   | 3                 |
| GO:BP  | mating  | GO:0007618         | 35        | 1.80E-02   | 4                 |
| GO:CC  | neuronal cell body                                | GO:0043025         | 471       | 2.10E-02   | 9                 |
| REAC   | Transcriptional Regulation by MECP2               | REAC:R-HSA-8986944 | 58        | 2.40E-02   | 4                 |
| GO:BP  | positive regulation of epinephrine secretion      | GO:0032812         | 2         | 2.80E-02   | 2                 |
| GO:MF  | receptor ligand activity                          | GO:0048018         | 356       | 3.50E-02   | 8                 |
| TF     | NRSF<br>TTCAGCACCCACGGACAGMGCC                    | TF:M00256_1        | 13        | 3.70E-02   | 3                 |
| REAC   | GPCR ligand binding                               | REAC:R-HSA-500792  | 388       | 3.90E-02   | 8                 |
| GO:MF  | signaling receptor activator activity             | GO:0030546         | 363       | 4.10E-02   | 8                 |
| GO:BP  | neuropeptide signaling pathway                    | GO:0007218         | 89        | 4.40E-02   | 5                 |

Table A32. KCL BrainBank enrichment for Cluster 1 with gProfiler2. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term. GO:BP – Gene Ontology Biological Process, GO:CC – Gene Ontology Cellular Components, GO:MF – Gene Ontology Molecular Function, KEGG: Kyoto Encyclopaedia of Genes and Genomes, REAC: Reactome, TF: Transfac.



| Source | Term Name                                    | Term ID     | Term Size | p adjusted | Intersection Size |
|--------|--|-------------|-----------|------------|-------------------|
| GO:CC  | cell periphery                               | GO:0071944  | 5188      | 1.70E-39   | 140               |
| GO:BP  | response to stimulus                         | GO:0050896  | 7482      | 7.30E-37   | 165               |
| GO:CC  | extracellular region                         | GO:0005576  | 3516      | 7.40E-34   | 109               |
| GO:BP  | biological regulation                        | GO:0065007  | 10837     | 1.60E-33   | 194               |
| TF     | Factor: Kid3; motif: CCACN                   | TF:M01160   | 17056     | 3.70E-31   | 241               |
| TF     | Factor: Spi-B; motif: TTCYBC                 | TF:M03851   | 17110     | 6.80E-31   | 241               |
| TF     | Transfac                                     | TF:M00000   | 17114     | 7.10E-31   | 241               |
| GO:BP  | response to chemical                         | GO:0042221  | 3698      | 2.30E-30   | 108               |
| TF     | Factor: Spi-B; motif: TTCYBC; match class: 1 | TF:M03851_1 | 17095     | 2.90E-30   | 240               |
| GO:BP  | cellular response to chemical stimulus       | GO:0070887  | 2745      | 4.70E-30   | 93                |
| GO:CC  | extracellular space                          | GO:0005615  | 2749      | 4.70E-30   | 92                |
| TF     | Factor: CPBP; motif: SNCCCN                  | TF:M01822   | 16885     | 6.80E-30   | 238               |
| TF     | Factor: Kid3; motif: CCACN; match class: 1   | TF:M01160_1 | 16941     | 1.30E-29   | 238               |
| TF     | Factor: PU.1; motif: AGGAAG                  | TF:M02031   | 15486     | 2.10E-29   | 227               |
| TF     | Factor: Elf-1; motif: AGGAAG                 | TF:M01266   | 15486     | 2.10E-29   | 227               |
| GO:BP  | regulation of biological process             | GO:0050789  | 10213     | 5.60E-29   | 181               |
| TF     | Factor: ZNF35; motif: SSAKA                  | TF:M07479   | 16059     | 1.50E-28   | 230               |
| GO:MF  | molecular_function                           | GO:0003674  | 16562     | 5.10E-28   | 232               |
| TF     | Factor: GKLf; motif: CCTCCYN                 | TF:M01835   | 13756     | 6.60E-28   | 211               |
| GO:CC  | cellular anatomical entity                   | GO:0110165  | 16869     | 1.30E-27   | 233               |
| GO:BP  | biological_process                           | GO:0008150  | 16323     | 1.80E-27   | 230               |
| GO:CC  | cellular_component                           | GO:0005575  | 16974     | 4.00E-27   | 233               |
| GO:BP  | response to stress                           | GO:0006950  | 3345      | 6.10E-27   | 98                |
| GO:BP  | response to organic substance                | GO:0010033  | 2758      | 6.40E-27   | 89                |
| GO:BP  | cellular response to stimulus                | GO:0051716  | 6392      | 5.00E-26   | 136               |

|       |   |              |       |          |     |
|-------|---|--------------|-------|----------|-----|
| GO:MF | binding   | GO:0005488   | 15390 | 5.10E-26 | 220 |
| GO:BP | multicellular organismal process                | GO:0032501   | 6431  | 9.30E-26 | 136 |
| GO:BP | tissue development                              | GO:0009888   | 1688  | 1.10E-25 | 69  |
| TF    | Factor: CPBP; motif: SNCCCN; match class: 1     | TF:M01822_1  | 16464 | 2.50E-25 | 228 |
| TF    | Factor: ZNF684; motif: MAAGGGGTGGACTGT          | TF:M10550    | 13426 | 2.50E-25 | 204 |
| GO:MF | protein binding                                 | GO:0005515   | 13368 | 4.80E-25 | 202 |
| GO:CC | plasma membrane                                 | GO:0005886   | 4761  | 7.20E-25 | 113 |
| TF    | Factor: Lyl-1; motif: NCAKCTGYTNYCNN            | TF:M09977    | 11924 | 9.50E-25 | 190 |
| TF    | Factor: HSF4; motif: CTGCMRN                    | TF:M07322    | 14568 | 1.60E-24 | 212 |
| GO:BP | cellular response to organic substance          | GO:0071310   | 2188  | 3.30E-24 | 76  |
| TF    | Factor: TR4; motif: ACCCCGS                     | TF:M04934    | 15997 | 8.10E-24 | 222 |
| MIRNA | MIRNA root                                      | MIRNA:000000 | 13878 | 8.10E-24 | 204 |
| GO:BP | cellular process                                | GO:0009987   | 15441 | 1.30E-23 | 217 |
| TF    | Factor: Smad2; motif: AGACAN                    | TF:M03580    | 13070 | 1.30E-23 | 198 |
| TF    | Factor: Elf-1; motif: AGGAAG; match class: 1    | TF:M01266_1  | 11933 | 1.40E-23 | 188 |
| TF    | Factor: PU.1; motif: AGGAAG; match class: 1     | TF:M02031_1  | 11933 | 1.40E-23 | 188 |
| TF    | Factor: Pax-4; motif: DTTTTCCACCN               | TF:M04624    | 13570 | 1.80E-23 | 202 |
| GO:BP | regulation of cellular process                  | GO:0050794   | 9657  | 2.30E-23 | 166 |
| TF    | Factor: Pax-4; motif: NNNNNYACCCB               | TF:M00378    | 15748 | 3.60E-23 | 219 |
| GO:BP | anatomical structure development                | GO:0048856   | 5153  | 6.80E-23 | 116 |
| TF    | Factor: GKLf; motif: NNRGRRNGNSNNN              | TF:M07040    | 11567 | 1.30E-22 | 183 |
| GO:BP | animal organ development                        | GO:0048513   | 3102  | 1.50E-22 | 88  |
| TF    | Factor: THAP1; motif: YTGCCCNNA                 | TF:M07407    | 9580  | 1.80E-22 | 164 |
| TF    | Factor: myogenin; motif: CAGCTG                 | TF:M02101    | 11284 | 2.20E-22 | 180 |
| TF    | Factor: myogenin; motif: CAGCTG; match class: 1 | TF:M02101_1  | 11284 | 2.20E-22 | 180 |
| TF    | Factor: Sox-18; motif: CAAWGBB                  | TF:M03848    | 15043 | 2.50E-22 | 212 |

|       |  |            |       |          |     |
|-------|--|------------|-------|----------|-----|
| TF    | Factor: Sox-17; motif: TTGTYT                  | TF:M03803  | 13366 | 3.30E-22 | 198 |
| GO:BP | positive regulation of biological process      | GO:0048518 | 5512  | 4.40E-22 | 119 |
| TF    | Factor: ER71:E2A; motif: CASSTGNACCGAWRYN      | TF:M08568  | 15994 | 4.40E-22 | 219 |
| GO:BP | circulatory system development                 | GO:0072359 | 1015  | 5.20E-22 | 51  |
| GO:BP | signaling                                      | GO:0023052 | 5550  | 8.00E-22 | 119 |
| GO:BP | developmental process                          | GO:0032502 | 5648  | 1.00E-21 | 120 |
| TF    | Factor: ZBTB39; motif: CNCTGY                  | TF:M12689  | 13477 | 1.10E-21 | 198 |
| GO:BP | cell communication                             | GO:0007154 | 5601  | 6.70E-21 | 118 |
| TF    | Factor: Zbtb44; motif: CKGTGA                  | TF:M05405  | 11777 | 1.60E-20 | 181 |
| GO:BP | signal transduction                            | GO:0007165 | 5094  | 2.20E-20 | 111 |
| GO:CC | vesicle  | GO:0031982 | 3591  | 3.20E-20 | 90  |
| TF    | Factor: Erg; motif: NRRSAGGAAGNGG              | TF:M09907  | 10225 | 3.30E-20 | 166 |
| GO:BP | system development                             | GO:0048731 | 4335  | 4.10E-20 | 101 |
| TF    | Factor: T3R-beta; motif: NTGACCTYRNYRAGGTCAN   | TF:M11818  | 10182 | 6.60E-20 | 165 |
| GO:CC | external encapsulating structure               | GO:0030312 | 498   | 1.10E-19 | 35  |
| GO:BP | multicellular organism development             | GO:0007275 | 4634  | 1.20E-19 | 104 |
| GO:BP | regulation of multicellular organismal process | GO:0051239 | 2403  | 1.40E-19 | 73  |
| TF    | Factor: sin3A; motif: TGTCCNNGGTGCTG           | TF:M04756  | 12573 | 1.80E-19 | 186 |
| TF    | Factor: ING4; motif: CCACCA                    | TF:M01743  | 13898 | 2.80E-19 | 197 |
| TF    | Factor: CTF/NF1; motif: TTGGCN                 | TF:M02050  | 9395  | 3.30E-19 | 156 |
| GO:BP | anatomical structure morphogenesis             | GO:0009653 | 2447  | 3.90E-19 | 73  |
| GO:BP | cell adhesion                                  | GO:0007155 | 1388  | 4.60E-19 | 55  |
| GO:CC | collagen-containing extracellular matrix       | GO:0062023 | 383   | 4.70E-19 | 31  |
| GO:BP | cell surface receptor signaling pathway        | GO:0007166 | 2456  | 4.80E-19 | 73  |
| GO:BP | negative regulation of biological process      | GO:0048519 | 4967  | 5.30E-19 | 107 |
| GO:BP | biological adhesion                            | GO:0022610 | 1393  | 5.40E-19 | 55  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: Zic3; motif: NGGGKGGTC                               | TF:M00450   | 12380 | 8.40E-19 | 183 |
| GO:CC | extracellular matrix   | GO:0031012  | 497   | 1.00E-18 | 34  |
| REAC  | REACTOME root term   | REAC:000000 | 9607  | 1.60E-18 | 155 |
| GO:BP | anatomical structure formation involved in morphogenesis     | GO:0048646  | 1026  | 2.20E-18 | 47  |
| TF    | Factor: T3R-beta; motif: NTGACCTYRNYRAGGTCAN; match class: 1 | TF:M11818_1 | 9678  | 2.60E-18 | 157 |
| TF    | Factor: GEMIN3; motif: NCWGGRRRRGRGNGNG                      | TF:M09727   | 7710  | 2.90E-18 | 137 |
| GO:BP | blood vessel development                                     | GO:0001568  | 641   | 3.90E-18 | 38  |
| GO:BP | immune system process  | GO:0002376  | 2161  | 4.10E-18 | 67  |
| TF    | Factor: ZNF644; motif: TCCWGCCTCTSN                          | TF:M09737   | 6371  | 4.90E-18 | 122 |
| TF    | Factor: ZNF35; motif: SSAKA; match class: 1                  | TF:M07479_1 | 13256 | 5.40E-18 | 189 |
| TF    | Factor: PUR1; motif: GGGNCAGNN                               | TF:M01721   | 8254  | 6.30E-18 | 142 |
| TF    | Factor: SALL2; motif: GGGTGGG                                | TF:M04595   | 11697 | 7.40E-18 | 175 |
| TF    | Factor: LF-A1; motif: GGGSTCWR                               | TF:M00646   | 11261 | 7.70E-18 | 171 |
| GO:BP | positive regulation of cellular process                      | GO:0048522  | 5061  | 8.10E-18 | 106 |
| TF    | Factor: NF1C; motif: WGCCARR                                 | TF:M09763   | 9428  | 1.50E-17 | 153 |
| TF    | Factor: ETV4; motif: NCAGGAAGNN                              | TF:M12556   | 9336  | 1.70E-17 | 152 |
| GO:BP | vasculature development                                      | GO:0001944  | 671   | 1.90E-17 | 38  |
| TF    | Factor: Pax-4; motif: NNNNNYCACCCB; match class: 1           | TF:M00378_1 | 13163 | 2.10E-17 | 187 |
| KEGG  | KEGG root term   | KEGG:00000  | 7044  | 2.30E-17 | 125 |
| TF    | Factor: ETF; motif: CCCC GCCCYN                              | TF:M07039   | 14877 | 3.20E-17 | 201 |
| TF    | Factor: BEN; motif: CAGCGRNV                                 | TF:M01240   | 15004 | 3.30E-17 | 202 |
| TF    | Factor: TR4; motif: ACCCCGS; match class: 1                  | TF:M04934_1 | 13946 | 4.40E-17 | 193 |
| TF    | Factor: Erg; motif: NACCGATATCCGGTN                          | TF:M11393   | 12672 | 4.80E-17 | 182 |
| TF    | Factor: LRH-1; motif: TGACCTTGRNYCAAGGTCA                    | TF:M11830   | 6126  | 7.20E-17 | 117 |
| TF    | Factor: GKLf; motif: NNNRGGNGNGGSN                           | TF:M07289   | 13294 | 7.40E-17 | 187 |
| TF    | Factor: E2F-1:HES-7; motif: GGRCGTGSYNNWNGGCGCSM             | TF:M08525   | 15473 | 7.90E-17 | 205 |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: CSX; motif: NKRAAGWGS                   | TF:M10008         | 9182  | 9.00E-17 | 149 |
| GO:BP | animal organ morphogenesis                      | GO:0009887        | 931   | 1.00E-16 | 43  |
| TF    | Factor: RREB-1; motif: CCCCCAACMMCCCC           | TF:M00257         | 9419  | 1.30E-16 | 151 |
| GO:BP | response to external stimulus                   | GO:0009605        | 2310  | 1.40E-16 | 67  |
| TF    | Factor: NMYC; motif: CAYCTG                     | TF:M01808         | 10951 | 2.50E-16 | 165 |
| GO:BP | response to oxygen-containing compound          | GO:1901700        | 1480  | 2.60E-16 | 53  |
| TF    | Factor: PEA3; motif: NNCAGGAARNN                | TF:M09915         | 10849 | 2.60E-16 | 164 |
| REAC  | Immune System                                   | REAC:R-HSA-168256 | 1770  | 2.80E-16 | 57  |
| TF    | Factor: p300; motif: ACNTCCG                    | TF:M04826         | 15885 | 3.30E-16 | 207 |
| TF    | Factor: FOXO1A:ETV7; motif: NWMAACAGGAMNNCTCCNN | TF:M08304         | 12194 | 3.40E-16 | 176 |
| TF    | Factor: RXRA; motif: RRGTCATGACCYY              | TF:M04490         | 6522  | 3.80E-16 | 120 |
| TF    | Factor: egr-3; motif: GTGGGY                    | TF:M03818         | 11653 | 4.00E-16 | 171 |
| TF    | Factor: IRF-4; motif: AAGTTTC                   | TF:M04855         | 6624  | 4.40E-16 | 121 |
| TF    | Factor: LUMAN; motif: CYCAGCYCY                 | TF:M09729         | 9533  | 4.40E-16 | 151 |
| TF    | Factor: ZBTB39; motif: CNCTGY; match class: 1   | TF:M12689_1       | 8347  | 5.40E-16 | 139 |
| TF    | Factor: E2F4; motif: YCCCGCCNCNNSSNNSNN         | TF:M12599         | 15611 | 8.30E-16 | 204 |
| TF    | Factor: HSF4; motif: CTGCMRN; match class: 1    | TF:M07322_1       | 10436 | 8.90E-16 | 159 |
| TF    | Factor: IRF-4; motif: RGGAASWGR                 | TF:M04818         | 8202  | 9.60E-16 | 137 |
| TF    | Factor: c-Ets-2; motif: CTTCTG                  | TF:M01207         | 8932  | 1.40E-15 | 144 |
| TF    | Factor: Elk-1; motif: CTTCKG                    | TF:M07252         | 8932  | 1.40E-15 | 144 |
| GO:BP | regulation of developmental process             | GO:0050793        | 2221  | 1.60E-15 | 64  |
| TF    | Factor: NFATc2; motif: GGAAAA                   | TF:M03555         | 13979 | 1.60E-15 | 190 |
| TF    | Factor: NFATc3; motif: GGAAAA                   | TF:M01886         | 13979 | 1.60E-15 | 190 |
| TF    | Factor: NFATc2; motif: GGAAAA                   | TF:M01281         | 13979 | 1.60E-15 | 190 |
| TF    | Factor: LRH-1; motif: TCAAGGTCRYGACCTTGR        | TF:M11828         | 9272  | 2.10E-15 | 147 |
| GO:BP | regulation of cell death                        | GO:0010941        | 1440  | 2.30E-15 | 51  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: Sox-10; motif: CWTTGT                             | TF:M03138   | 11286 | 2.30E-15 | 166 |
| TF    | Factor: TCF-1; motif: CTTTGW                              | TF:M03857   | 11286 | 2.30E-15 | 166 |
| TF    | Factor: GKLf; motif: CCTCCYN; match class: 1              | TF:M01835_1 | 9081  | 2.40E-15 | 145 |
| TF    | Factor: Smad2; motif: AGACAN; match class: 1              | TF:M03580_1 | 7607  | 2.40E-15 | 130 |
| TF    | Factor: GATAD2A; motif: CCTKTG                            | TF:M09726   | 13089 | 2.50E-15 | 182 |
| TF    | Factor: Pax-5; motif: RRNGRNGCAN                          | TF:M03577   | 7727  | 3.20E-15 | 131 |
| TF    | Factor: ZXDA; motif: NAGGGTG                              | TF:M06203   | 6420  | 3.20E-15 | 117 |
| TF    | Factor: ZXDB; motif: NAGGGTG                              | TF:M06202   | 6420  | 3.20E-15 | 117 |
| TF    | Factor: ZNF273; motif: GAGAGGAGCTAC                       | TF:M10460   | 11221 | 3.60E-15 | 165 |
| TF    | Factor: Kaiso; motif: GCMGGGRGCRGS                        | TF:M03876   | 12564 | 3.80E-15 | 177 |
| TF    | Factor: NF1B; motif: CYTGGCNYNCWGCCAN                     | TF:M09762   | 4967  | 4.90E-15 | 100 |
| TF    | Factor: GR; motif: RGNACANKNTGTCY                         | TF:M09625   | 7867  | 5.20E-15 | 132 |
| TF    | Factor: NR1B1; motif: NRGGNCRTGACCTN                      | TF:M11796   | 9466  | 5.50E-15 | 148 |
| TF    | Factor: ZNFPT1; motif: YCNNCNCWGCCNY                      | TF:M12721   | 8164  | 5.60E-15 | 135 |
| TF    | Factor: Elk-1; motif: GGAAGN                              | TF:M03819   | 12382 | 5.80E-15 | 175 |
| TF    | Factor: Erg; motif: NACCGATATCCGGTN; match class: 1       | TF:M11393_1 | 12292 | 7.10E-15 | 174 |
| GO:CC | membrane  | GO:0016020  | 8518  | 8.50E-15 | 136 |
| GO:BP | cellular developmental process                            | GO:0048869  | 3759  | 1.10E-14 | 84  |
| GO:CC | organelle   | GO:0043226  | 13412 | 1.20E-14 | 181 |
| TF    | Factor: MAZ; motif: GGGMGGGSSGGGGGGGGGG                   | TF:M09636   | 14816 | 1.30E-14 | 195 |
| TF    | Factor: LRH-1; motif: TGACCTTGRNYCAAGGTCA; match class: 1 | TF:M11830_1 | 5296  | 1.40E-14 | 103 |
| TF    | Factor: CDP:SRF; motif: NCCWTAYAAGTGMNKRATCRATN           | TF:M08520   | 8843  | 1.40E-14 | 141 |
| TF    | Factor: PRDM16; motif: KGGTCATRACCM                       | TF:M05946   | 6003  | 1.50E-14 | 111 |
| TF    | Factor: Sox-9; motif: NNNNACAAARGNNSMN                    | TF:M07269   | 8565  | 1.70E-14 | 138 |
| GO:BP | cell death  | GO:0008219  | 1881  | 2.00E-14 | 57  |
| TF    | Factor: PARP; motif: TTTCYN                               | TF:M02027   | 14025 | 2.00E-14 | 188 |

|       |  |            |       |          |     |
|-------|--|------------|-------|----------|-----|
| GO:CC | extracellular exosome                                | GO:0070062 | 1901  | 2.20E-14 | 56  |
| TF    | Factor: AP-2gamma:Elk-1; motif: NGCCKNRGGSGRCGGAAGTG | TF:M08441  | 14756 | 2.20E-14 | 194 |
| TF    | Factor: FOXO1A:PDEF; motif: WNCCGGATGTTDN            | TF:M08486  | 9927  | 2.50E-14 | 151 |
| GO:BP | response to cytokine                                 | GO:0034097 | 833   | 2.70E-14 | 38  |
| GO:BP | inflammatory response                                | GO:0006954 | 651   | 2.70E-14 | 34  |
| TF    | Factor: LBP-1; motif: CAGCTGS                        | TF:M00644  | 7824  | 2.80E-14 | 130 |
| GO:BP | cellular response to cytokine stimulus               | GO:0071345 | 744   | 3.20E-14 | 36  |
| GO:BP | positive regulation of metabolic process             | GO:0009893 | 3369  | 3.50E-14 | 78  |
| GO:CC | extracellular vesicle                                | GO:1903561 | 1921  | 3.50E-14 | 56  |
| GO:CC | extracellular membrane-bounded organelle             | GO:0065010 | 1922  | 3.50E-14 | 56  |
| GO:CC | extracellular organelle                              | GO:0043230 | 1922  | 3.50E-14 | 56  |
| GO:CC | cytoplasm  | GO:0005737 | 11064 | 3.70E-14 | 159 |
| GO:BP | cell differentiation                                 | GO:0030154 | 3683  | 4.00E-14 | 82  |
| TF    | Factor: TFII-I; motif: NAGGAAGTGN                    | TF:M04636  | 11048 | 4.30E-14 | 161 |
| GO:BP | negative regulation of cellular process              | GO:0048523 | 4412  | 4.70E-14 | 91  |
| TF    | Factor: RORA; motif: CCYTGNCTN                       | TF:M12659  | 6920  | 4.70E-14 | 120 |
| TF    | Factor: NF-1C; motif: NYTGGCNNYNNGCCARN              | TF:M10002  | 5930  | 5.60E-14 | 109 |
| GO:BP | response to endogenous stimulus                      | GO:0009719 | 1439  | 5.70E-14 | 49  |
| GO:BP | localization   | GO:0051179 | 5792  | 5.80E-14 | 107 |
| TF    | Factor: ZNF586; motif: CAGGCCYRGAGG                  | TF:M10491  | 12307 | 6.30E-14 | 172 |
| TF    | Factor: PURBETA; motif: NCWGRGGCTGGGG                | TF:M12726  | 6869  | 7.70E-14 | 119 |
| TF    | Factor: Zic1; motif: KGGGTGGTC                       | TF:M00448  | 9729  | 7.70E-14 | 148 |
| GO:BP | epithelium development                               | GO:0060429 | 1015  | 9.10E-14 | 41  |
| GO:BP | cell activation                                      | GO:0001775 | 914   | 9.20E-14 | 39  |
| GO:BP | defense response                                     | GO:0006952 | 1343  | 9.70E-14 | 47  |
| TF    | Factor: GTF2IRD1-isoform2; motif: GGGATTRNR          | TF:M01229  | 13062 | 1.20E-13 | 178 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: VDR; motif: RRGGTCANNRGRKTC                       | TF:M09671   | 7096  | 1.20E-13 | 121 |
| TF    | Factor: NURR1:RXR-ALPHA; motif: NRGGTCRRTTGACCCYN         | TF:M08957   | 9681  | 1.30E-13 | 147 |
| TF    | Factor: Ikaros; motif: TGGGAGN                            | TF:M07260   | 11832 | 1.40E-13 | 167 |
| TF    | Factor: T3R-beta; motif: NRGGTCAAAGGTCRN                  | TF:M11814   | 12177 | 1.50E-13 | 170 |
| TF    | Factor: MafB; motif: GNTGAC                               | TF:M01227   | 10227 | 1.60E-13 | 152 |
| GO:BP | regulation of biological quality                          | GO:0065008  | 3465  | 1.70E-13 | 78  |
| GO:BP | positive regulation of macromolecule metabolic process    | GO:0010604  | 3089  | 1.70E-13 | 73  |
| GO:BP | regulation of programmed cell death                       | GO:0043067  | 1308  | 1.80E-13 | 46  |
| TF    | Factor: MAFB; motif: NTCAGCN                              | TF:M08888   | 8591  | 1.80E-13 | 136 |
| TF    | Factor: MAZ; motif: GGGMGGGGSSGGGGGGGGGGG; match class: 1 | TF:M09636_1 | 13118 | 1.90E-13 | 178 |
| GO:BP | tube morphogenesis  | GO:0035239  | 788   | 2.00E-13 | 36  |
| TF    | Factor: Sox-18; motif: CAAWGBB; match class: 1            | TF:M03848_1 | 10894 | 2.10E-13 | 158 |
| TF    | Factor: T3R-beta; motif: NRGGTCAAAGGTCAN                  | TF:M11816   | 10084 | 3.10E-13 | 150 |
| TF    | Factor: IRX-1; motif: NACRYNNNNNNNNRYGNN                  | TF:M11018   | 15325 | 3.30E-13 | 196 |
| TF    | Factor: E2F-3:TBR2; motif: ANGTGYKANGGCGCSTTNNCRNNT       | TF:M08207   | 15326 | 3.30E-13 | 196 |
| GO:BP | regulation of response to stimulus                        | GO:0048583  | 3512  | 3.60E-13 | 78  |
| TF    | Factor: PHB; motif: NCCCAGCCCCY                           | TF:M12725   | 8966  | 3.80E-13 | 139 |
| TF    | Factor: ZGPAT; motif: GRGGCWGNGGNG                        | TF:M09739   | 7490  | 4.00E-13 | 124 |
| GO:BP | regulation of apoptotic process                           | GO:0042981  | 1281  | 4.20E-13 | 45  |
| GO:CC | membrane-bounded organelle                                | GO:0043227  | 12679 | 4.20E-13 | 171 |
| GO:BP | cellular response to oxygen-containing compound           | GO:1901701  | 1062  | 4.30E-13 | 41  |
| GO:BP | cell migration  | GO:0016477  | 1339  | 4.30E-13 | 46  |
| GO:CC | secretory granule   | GO:0030141  | 760   | 4.40E-13 | 34  |
| GO:BP | wound healing   | GO:0042060  | 384   | 4.60E-13 | 26  |
| TF    | Factor: MEL1; motif: GATGAG                               | TF:M08793   | 10128 | 4.70E-13 | 150 |
| TF    | Factor: NKX2-2; motif: NNNCCACTCAANN                      | TF:M12456   | 8199  | 5.30E-13 | 131 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: HLTF; motif: AGSCARAAAGYRGSTGS                | TF:M04613   | 6765  | 5.70E-13 | 116 |
| TF    | Factor: MZF-1; motif: TGGGGAR                         | TF:M01733   | 10043 | 5.70E-13 | 149 |
| GO:BP | tube development                                      | GO:0035295  | 967   | 6.00E-13 | 39  |
| TF    | Factor: REST; motif: AAGGTGCT                         | TF:M04926   | 5504  | 6.20E-13 | 102 |
| GO:BP | response to wounding                                  | GO:0009611  | 505   | 6.40E-13 | 29  |
| TF    | Factor: DREF; motif: CTYYCWCTCCY                      | TF:M09725   | 6415  | 7.10E-13 | 112 |
| GO:CC | intracellular anatomical structure                    | GO:0005622  | 14269 | 7.90E-13 | 184 |
| GO:MF | extracellular matrix structural constituent           | GO:0005201  | 156   | 8.10E-13 | 18  |
| TF    | Factor: Pax-5; motif: BCNNNRNGCANBGNTGNRTAGCSGC HNB   | TF:M00143   | 10199 | 9.20E-13 | 150 |
| TF    | Factor: GR; motif: NNNNNNCNNTNTGTNCTNN                | TF:M00192   | 6349  | 9.60E-13 | 111 |
| TF    | Factor: PAX5; motif: RNGCGTGACCNN                     | TF:M09817   | 11285 | 1.00E-12 | 160 |
| TF    | Factor: BRN1; motif: HAATGCN                          | TF:M03813   | 11080 | 1.10E-12 | 158 |
| TF    | Factor: TWIST; motif: CACCTGG                         | TF:M03582   | 7309  | 1.20E-12 | 121 |
| TF    | Factor: CP2; motif: NNNNCCAGNCNN                      | TF:M07602   | 9815  | 1.30E-12 | 146 |
| GO:BP | blood vessel morphogenesis                            | GO:0048514  | 563   | 1.40E-12 | 30  |
| TF    | Factor: KLF; motif: GGGNGGGG                          | TF:M07461   | 7906  | 1.50E-12 | 127 |
| TF    | Factor: GABP-alpha; motif: AACCGGAAR                  | TF:M04748   | 14181 | 1.50E-12 | 185 |
| GO:BP | positive regulation of response to stimulus           | GO:0048584  | 1882  | 1.60E-12 | 54  |
| TF    | Factor: Fli-1; motif: NNRGGMAGGAAGRRRGR               | TF:M09920   | 8216  | 1.70E-12 | 130 |
| TF    | Factor: E2F-3; Prrxl1; motif: SGCGCTAATTNN            | TF:M08206   | 10480 | 1.70E-12 | 152 |
| GO:BP | extracellular matrix organization                     | GO:0030198  | 300   | 1.80E-12 | 23  |
| GO:BP | extracellular structure organization                  | GO:0043062  | 301   | 1.90E-12 | 23  |
| TF    | Factor: ZNF684; motif: MAAGGGTGGACTGT; match class: 1 | TF:M10550_1 | 8324  | 1.90E-12 | 131 |
| GO:BP | external encapsulating structure organization         | GO:0045229  | 302   | 2.10E-12 | 23  |
| TF    | Factor: RUNX2; motif: NRACCGCAAACCGCAN                | TF:M04106   | 12597 | 2.10E-12 | 171 |
| TF    | Factor: PEA3; motif: NNCAGGAARNN; match class: 1      | TF:M09915_1 | 4914  | 2.30E-12 | 94  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: MRF4; motif: CASCTGC                              | TF:M03831   | 7565  | 2.40E-12 | 123 |
| TF    | Factor: HTF4; motif: CASCTGB                              | TF:M02018   | 7565  | 2.40E-12 | 123 |
| TF    | Factor: TCF-7; motif: TCAAAG                              | TF:M00805   | 10201 | 2.50E-12 | 149 |
| TF    | Factor: TCF-3; motif: CTTTGA                              | TF:M03858   | 10201 | 2.50E-12 | 149 |
| TF    | Factor: AR; motif: ARGAAACANNNTGTNC                       | TF:M07204   | 4006  | 2.60E-12 | 83  |
| TF    | Factor: ERG; motif: ACCGGAWATCCGGT                        | TF:M03976   | 11502 | 2.60E-12 | 161 |
| TF    | Factor: ZNF37A; motif: CCYGGCTCCNTSCCMN                   | TF:M12354   | 10103 | 2.70E-12 | 148 |
| TF    | Factor: KLF15; motif: RCCMCRCCMCN                         | TF:M12160   | 11726 | 2.70E-12 | 163 |
| TF    | Factor: ER71:E2A; motif: CASSTGNACCGAWRYN; match class: 1 | TF:M08568_1 | 13552 | 2.80E-12 | 179 |
| TF    | Factor: NF-KAPPAB1; motif: NGGKRNTTYCCCN                  | TF:M08952   | 7005  | 2.80E-12 | 117 |
| TF    | Factor: Erg; motif: MCAGAAA                               | TF:M07284   | 9694  | 2.90E-12 | 144 |
| TF    | Factor: Pax-4; motif: DTTTCCACCN; match class: 1          | TF:M04624_1 | 8077  | 3.10E-12 | 128 |
| TF    | Factor: GEMIN3; motif: NCWGGRRRRGRGNGNG; match class: 1   | TF:M09727_1 | 2934  | 3.10E-12 | 69  |
| TF    | Factor: SMAD5; motif: GSGGCAGM                            | TF:M03846   | 7589  | 3.10E-12 | 123 |
| GO:BP | positive regulation of developmental process              | GO:0051094  | 1182  | 3.20E-12 | 42  |
| TF    | Factor: E2F-4; motif: SNGGGCGGAANN                        | TF:M09894   | 14891 | 3.60E-12 | 190 |
| TF    | Factor: Erm; motif: NRRSAGGAARNGRN                        | TF:M09916   | 5923  | 3.90E-12 | 105 |
| TF    | Factor: T3R-beta; motif: NTGACCTNRNYNAGGTGAN              | TF:M11820   | 4448  | 4.00E-12 | 88  |
| TF    | Factor: EHF; motif: BTTCCTGC                              | TF:M07251   | 5394  | 4.10E-12 | 99  |
| GO:BP | programmed cell death                                     | GO:0012501  | 1737  | 4.70E-12 | 51  |
| TF    | Factor: AP-2gamma; motif: GCCYNNNGS                       | TF:M00470   | 8826  | 5.00E-12 | 135 |
| TF    | Factor: Churchill; motif: CGGGNN                          | TF:M00986   | 13164 | 5.20E-12 | 175 |
| TF    | Factor: LUMAN; motif: CYCAGCYCY; match class: 1           | TF:M09729_1 | 4222  | 5.40E-12 | 85  |
| TF    | Factor: RelA-p65; motif: AASTCCC                          | TF:M04849   | 5419  | 5.60E-12 | 99  |
| TF    | Factor: E2F-3; HES-7; motif: NNSGCGCSNNNNNCRGCGYNN        | TF:M08526   | 15314 | 5.70E-12 | 193 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:CC | endomembrane system   | GO:0012505  | 4326  | 6.60E-12 | 84  |
| TF    | Factor: Sox-17; motif: TTGTYT; match class: 1                             | TF:M03803_1 | 7955  | 6.60E-12 | 126 |
| TF    | Factor: ZNF300; motif: SWGGGGGSN  | TF:M07486   | 11503 | 6.80E-12 | 160 |
| TF    | Factor: NF-E4; motif: GTGAGGS   | TF:M08826   | 10022 | 8.70E-12 | 146 |
| TF    | Factor: GCMA:PEA3; motif: ATRCGGGCGGAAGTR                                 | TF:M08313   | 13815 | 9.20E-12 | 180 |
| GO:BP | cellular response to endogenous stimulus                                  | GO:0071495  | 1220  | 9.40E-12 | 42  |
| TF    | Factor: ZNF777; motif: GTCCGYCCCGTCSAACAAT                                | TF:M08993   | 9617  | 9.80E-12 | 142 |
| GO:BP | biological process involved in interspecies interaction between organisms | GO:0044419  | 1282  | 1.10E-11 | 43  |
| GO:CC | intrinsic component of membrane   | GO:0031224  | 5051  | 1.10E-11 | 92  |
| TF    | Factor: Lyl-1; motif: NCAKCTGYTNYCNN; match class: 1                      | TF:M09977_1 | 6570  | 1.10E-11 | 111 |
| TF    | Factor: ZNF436; motif: TCCTCCAGGAAGCCY                                    | TF:M10477   | 12825 | 1.40E-11 | 171 |
| TF    | Factor: TCF-1; motif: ACATCGRGRGCTGW                                      | TF:M11603   | 14822 | 1.40E-11 | 188 |
| TF    | Factor: ZFP14; motif: SCNNYCCNGNNSCTSCNC                                  | TF:M12694   | 9765  | 1.50E-11 | 143 |
| TF    | Factor: ZNF592; motif: NSARNATGGAGKN                                      | TF:M09766   | 6223  | 1.50E-11 | 107 |
| GO:BP | positive regulation of multicellular organismal process                   | GO:0051240  | 1298  | 1.60E-11 | 43  |
| TF    | Factor: HDAC1; motif: KGCARGGTC   | TF:M07041   | 11165 | 1.60E-11 | 156 |
| TF    | Factor: c-Fos; motif: ACTCACCA  | TF:M04802   | 6417  | 1.60E-11 | 109 |
| GO:BP | negative regulation of multicellular organismal process                   | GO:0051241  | 913   | 1.80E-11 | 36  |
| GO:BP | locomotion  | GO:0040011  | 1669  | 1.80E-11 | 49  |
| GO:BP | immune response   | GO:0006955  | 1363  | 1.90E-11 | 44  |
| TF    | Factor: SRY; motif: TTGTTT  | TF:M03854   | 12068 | 1.90E-11 | 164 |
| TF    | Factor: FOXO1A; motif: AAACAA   | TF:M03823   | 12068 | 1.90E-11 | 164 |
| TF    | Factor: TORC2; motif: TGGGCTKKD   | TF:M07341   | 4235  | 2.00E-11 | 84  |
| TF    | Factor: NR3C1; motif: NRGWACAYNRTGTWCYN                                   | TF:M04476   | 6162  | 2.10E-11 | 106 |
| GO:BP | heart development   | GO:0007507  | 535   | 2.20E-11 | 28  |
| TF    | Factor: Kaiso; motif: TCTCGGAG  | TF:M04691   | 13571 | 2.20E-11 | 177 |

|       |  |                      |       |          |     |
|-------|--|----------------------|-------|----------|-----|
| TF    | Factor: Zic3; motif: NGGGKGGTC; match class: 1         | TF:M00450_1          | 7106  | 2.20E-11 | 116 |
| TF    | Factor: AP-2rep; motif: CAGTGGG                        | TF:M00468            | 6084  | 2.40E-11 | 105 |
| MIRNA | hsa-miR-335-5p   | MIRNA:hsa-miR-335-5p | 2271  | 2.50E-11 | 57  |
| GO:BP | response to other organism                             | GO:0051707           | 1142  | 2.60E-11 | 40  |
| GO:BP | response to external biotic stimulus                   | GO:0043207           | 1145  | 2.80E-11 | 40  |
| TF    | Factor: E2F-3; motif: NNITTTGGCGCCAAACT                | TF:M03962            | 9734  | 2.80E-11 | 142 |
| TF    | Factor: VDR:RXR-ALPHA; motif: NRRGTCANNNGGTTCCNN       | TF:M08980            | 9219  | 2.90E-11 | 137 |
| REAC  | Neutrophil degranulation                               | REAC:R-HSA-6798695   | 446   | 3.00E-11 | 25  |
| GO:BP | apoptotic process                                      | GO:0006915           | 1692  | 3.10E-11 | 49  |
| GO:BP | cell motility  | GO:0048870           | 1504  | 3.10E-11 | 46  |
| GO:BP | localization of cell                                   | GO:0051674           | 1504  | 3.10E-11 | 46  |
| TF    | Factor: Fli-1:Max; motif: NCCGGAACACGTGN               | TF:M08289            | 8814  | 3.10E-11 | 133 |
| TF    | Factor: E2F2; motif: AAAATGGCGCCATTTT                  | TF:M04517            | 8014  | 3.10E-11 | 125 |
| TF    | Factor: Fli-1:FIGLA; motif: NCCGGAARCASTGN             | TF:M08284            | 6950  | 3.20E-11 | 114 |
| TF    | Factor: HDAC1; motif: KGCARGGTC; match class: 1        | TF:M07041_1          | 5751  | 3.40E-11 | 101 |
| TF    | Factor: GKLf; motif: NNNRGGNGNGGSN; match class: 1     | TF:M07289_1          | 9758  | 3.50E-11 | 142 |
| TF    | Factor: myogenin; motif: CRCTGTBBNNTTTGGCACGSNGCCA RCH | TF:M00056            | 9551  | 3.60E-11 | 140 |
| TF    | Factor: GATAD2A; motif: CCTKTG; match class: 1         | TF:M09726_1          | 7641  | 3.80E-11 | 121 |
| TF    | Factor: ZNF462; motif: YYYCTSCWG                       | TF:M12707            | 8440  | 4.10E-11 | 129 |
| TF    | Factor: ZF5; motif: GSGGCGGS                           | TF:M10438            | 14973 | 4.50E-11 | 188 |
| TF    | Factor: Elk-1:PDEF; motif: NCMGGAMGGANATCCGGN          | TF:M08227            | 7470  | 4.80E-11 | 119 |
| GO:CC | integral component of membrane                         | GO:0016021           | 4917  | 5.00E-11 | 89  |
| GO:BP | system process   | GO:0003008           | 1781  | 5.20E-11 | 50  |
| TF    | Factor: GCMA; motif: RTGCGGNTN                         | TF:M11595            | 10870 | 5.30E-11 | 152 |
| TF    | Factor: Erg; motif: NRRSAGGAAGNGG; match class: 1      | TF:M09907_1          | 4480  | 5.50E-11 | 86  |

|       |   |                    |       |          |     |
|-------|---|--------------------|-------|----------|-----|
| TF    | Factor: T3R-beta; motif: NTGACCTNRNYNAGGTCCAN; match class: 1 | TF:M11820_1        | 4065  | 5.70E-11 | 81  |
| GO:BP | movement of cell or subcellular component                     | GO:0006928         | 1918  | 5.80E-11 | 52  |
| GO:CC | intracellular organelle                                       | GO:0043229         | 12728 | 6.00E-11 | 166 |
| TF    | Factor: AR; motif: RGGWACAYNGTGTWCYN                          | TF:M04453          | 6079  | 6.30E-11 | 104 |
| TF    | Factor: PUR1; motif: GGGNCAGNN; match class: 1                | TF:M01721_1        | 3127  | 7.20E-11 | 69  |
| GO:BP | angiogenesis  | GO:0001525         | 477   | 7.80E-11 | 26  |
| GO:BP | response to biotic stimulus                                   | GO:0009607         | 1182  | 7.80E-11 | 40  |
| TF    | Factor: RELA; motif: GGGRMTKYCCC                              | TF:M12657          | 5734  | 7.80E-11 | 100 |
| TF    | Factor: PU.1; motif: WGAGGAAG                                 | TF:M00658          | 3851  | 8.70E-11 | 78  |
| REAC  | Extracellular matrix organization                             | REAC:R-HSA-1474244 | 276   | 9.10E-11 | 20  |
| TF    | Factor: ZXDL; motif: NGGGGWS                                  | TF:M05775          | 6205  | 9.10E-11 | 105 |
| GO:CC | secretory vesicle   | GO:0099503         | 920   | 1.00E-10 | 34  |
| GO:BP | cell population proliferation                                 | GO:0008283         | 1750  | 1.10E-10 | 49  |
| TF    | Factor: MLLT10; motif: CYNCCNNGGGNGCTG                        | TF:M12636          | 8543  | 1.10E-10 | 129 |
| TF    | Factor: HOXA3; motif: NNNNRNTAATTARY                          | TF:M01337          | 13550 | 1.10E-10 | 175 |
| REAC  | Innate Immune System  | REAC:R-HSA-168249  | 914   | 1.20E-10 | 34  |
| TF    | Factor: Sox-10; motif: NACAAWG                                | TF:M02116          | 12073 | 1.20E-10 | 162 |
| TF    | Factor: SRY; motif: AACAAATNR                                 | TF:M08976          | 11740 | 1.20E-10 | 159 |
| TF    | Factor: HNRPUL1; motif: NCNCAGN                               | TF:M09746          | 12084 | 1.30E-10 | 162 |
| TF    | Factor: GATA-5; motif: TATCTN                                 | TF:M02006          | 7582  | 1.50E-10 | 119 |
| TF    | Factor: GCMA:FOXO1A; motif: GTMAATAMGGGTRN                    | TF:M08318          | 10029 | 1.50E-10 | 143 |
| GO:CC | integral component of plasma membrane                         | GO:0005887         | 1466  | 1.60E-10 | 43  |
| TF    | Factor: NR3C1; motif: NRGWACAYNRTGTWCYN; match class: 1       | TF:M04476_1        | 4480  | 1.60E-10 | 85  |
| TF    | Factor: ING4; motif: CCACCA; match class: 1                   | TF:M01743_1        | 8903  | 1.80E-10 | 132 |
| TF    | Factor: Elk-1:OC-2; motif: RCCGGAASCGATCGATNN                 | TF:M08223          | 11348 | 1.80E-10 | 155 |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: SREBP-1; motif: CACSCCA                     | TF:M00749         | 7520  | 2.00E-10 | 118 |
| GO:BP | regulation of multicellular organismal development  | GO:2000026        | 1218  | 2.10E-10 | 40  |
| GO:BP | negative regulation of cell death                   | GO:0060548        | 884   | 2.10E-10 | 34  |
| GO:CC | intrinsic component of plasma membrane              | GO:0031226        | 1541  | 2.10E-10 | 44  |
| TF    | Factor: Pet-1; motif: GCNGGAAGYG                    | TF:M09918         | 12251 | 2.10E-10 | 163 |
| TF    | Factor: TF3C-beta; motif: CCNGGAGGGCTTCTGGAGGAG     | TF:M04863         | 12366 | 2.10E-10 | 164 |
| TF    | Factor: Sox-10; motif: CWTTGTN                      | TF:M01131         | 7621  | 2.10E-10 | 119 |
| GO:BP | negative regulation of apoptotic process            | GO:0043066        | 783   | 2.30E-10 | 32  |
| TF    | Factor: ZNF614; motif: NCYCWGCCYYNNN                | TF:M09862         | 8627  | 2.30E-10 | 129 |
| TF    | Factor: ZF5; motif: GSGCGCGR                        | TF:M00716         | 14856 | 2.90E-10 | 185 |
| TF    | Factor: YB-1; motif: CCAMTCNGMR                     | TF:M03805         | 8857  | 2.90E-10 | 131 |
| TF    | Factor: NF-kappaB; motif: NGGGACTTTCCA              | TF:M00208         | 3300  | 3.00E-10 | 70  |
| TF    | Factor: AP-4; motif: RNCAGCTGC                      | TF:M00927         | 5587  | 3.10E-10 | 97  |
| GO:BP | regulation of metabolic process                     | GO:0019222        | 6103  | 3.70E-10 | 102 |
| GO:BP | epithelial cell differentiation                     | GO:0030855        | 555   | 3.70E-10 | 27  |
| GO:BP | negative regulation of programmed cell death        | GO:0043069        | 799   | 4.00E-10 | 32  |
| TF    | Factor: sin3A; motif: TGTCNNGGTGCTG; match class: 1 | TF:M04756_1       | 6912  | 4.00E-10 | 111 |
| TF    | Factor: CTF1; motif: TGGCASCNNGCCAA                 | TF:M01196         | 4131  | 4.10E-10 | 80  |
| TF    | Factor: ESE-1; motif: NTGTGCGGATGCN                 | TF:M11385         | 10801 | 4.40E-10 | 149 |
| TF    | Factor: NF-1B; motif: CTGGCASGV                     | TF:M07051         | 3030  | 5.60E-10 | 66  |
| TF    | Factor: E2F-3; motif: NTTTTGGCGCCAAAAN              | TF:M11526         | 6287  | 5.80E-10 | 104 |
| TF    | Factor: ZNF333; motif: ATAAT                        | TF:M01230         | 13185 | 5.90E-10 | 170 |
| TF    | Factor: RXR-alpha; motif: NNGNNRNNNARAGGTCCANN      | TF:M10055         | 5021  | 6.00E-10 | 90  |
| TF    | Factor: AP-4:Fl-1; motif: RSCGGAWRCAGSTGN           | TF:M08445         | 8339  | 6.60E-10 | 125 |
| TF    | Factor: CP2; motif: GCHCDAMCCAG                     | TF:M00072         | 7846  | 7.00E-10 | 120 |
| REAC  | Integrin cell surface interactions                  | REAC:R-HSA-216083 | 77    | 7.40E-10 | 12  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: PR; motif: NNNNNNGGNACRNNNTGTTCTNNNNN N | TF:M00954   | 4519  | 7.50E-10 | 84  |
| TF    | Factor: LKLF; motif: GGGGTGGKSN                 | TF:M07261   | 8865  | 7.70E-10 | 130 |
| TF    | Factor: MAZ; motif: GGGGAGGG                    | TF:M00649   | 8569  | 8.40E-10 | 127 |
| GO:BP | cell-cell adhesion                              | GO:0098609  | 828   | 1.00E-09 | 32  |
| GO:BP | tissue morphogenesis                            | GO:0048729  | 581   | 1.10E-09 | 27  |
| TF    | Factor: nerf; motif: YRNCAGGAAGYRGSTBDS         | TF:M00531   | 6635  | 1.10E-09 | 107 |
| GO:MF | signaling receptor binding                      | GO:0005102  | 1265  | 1.20E-09 | 39  |
| GO:BP | collagen fibril organization                    | GO:0030199  | 71    | 1.20E-09 | 12  |
| TF    | Factor: c-Maf; motif: NWNNTGCTGACKNNNNNNN       | TF:M01070   | 5525  | 1.20E-09 | 95  |
| TF    | Factor: NFE2L1; motif: NNNATGACTCAGCANW         | TF:M12499   | 8308  | 1.20E-09 | 124 |
| TF    | Factor: TEF-1; motif: GRRATG                    | TF:M00704   | 10603 | 1.20E-09 | 146 |
| TF    | Factor: SALL2; motif: GGGTGGG; match class: 1   | TF:M04595_1 | 6741  | 1.30E-09 | 108 |
| TF    | Factor: IRF-7; motif: AAGWGAA                   | TF:M01884   | 9133  | 1.30E-09 | 132 |
| TF    | Factor: AP-2gamma; motif: NTGSCCTGRGGSNN        | TF:M09591   | 7528  | 1.40E-09 | 116 |
| GO:BP | response to lipid                               | GO:0033993  | 787   | 1.50E-09 | 31  |
| TF    | Factor: CSX; motif: NKRAGWGS; match class: 1    | TF:M10008_1 | 3652  | 1.50E-09 | 73  |
| TF    | Factor: E2F3; motif: NNRGMKGGAR                 | TF:M12598   | 11508 | 1.60E-09 | 154 |
| TF    | Factor: ZNF342; motif: TRSTGGACRNT              | TF:M12075   | 5465  | 1.60E-09 | 94  |
| TF    | Factor: LRF; motif: RCGACCACNN                  | TF:M12230   | 7744  | 1.70E-09 | 118 |
| GO:CC | cytoplasmic vesicle                             | GO:0031410  | 2275  | 1.80E-09 | 53  |
| TF    | Factor: SMAD4; motif: GKSRKKGAGMCANCY           | TF:M00733   | 7655  | 1.80E-09 | 117 |
| GO:CC | intracellular vesicle                           | GO:0097708  | 2277  | 1.90E-09 | 53  |
| TF    | Factor: HNF-4alpha; motif: AGTCCAAR             | TF:M04903   | 5939  | 1.90E-09 | 99  |
| GO:BP | leukocyte activation                            | GO:0045321  | 795   | 2.00E-09 | 31  |
| GO:BP | response to bacterium                           | GO:0009617  | 504   | 2.00E-09 | 25  |
| TF    | Factor: GLI; motif: NGACCMCCCAN                 | TF:M07290   | 6316  | 2.00E-09 | 103 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: GKLf; motif: NNRRGRRNGNSNNN; match class: 1         | TF:M07040_1 | 7566  | 2.00E-09 | 116 |
| TF    | Factor: AP-4;Max; motif: NCAGCTGNNNNNNNNNCACGTGN            | TF:M08674   | 10025 | 2.10E-09 | 140 |
| TF    | Factor: GCMa;Erg; motif: ATGCGGGCGGAARKG                    | TF:M08487   | 12781 | 2.10E-09 | 165 |
| GO:BP | regulation of macromolecule metabolic process               | GO:0060255  | 5629  | 2.20E-09 | 95  |
| TF    | Factor: FXR;RXR-ALPHA; motif: NAGKTCATTGACCYN               | TF:M08954   | 5497  | 2.30E-09 | 94  |
| TF    | Factor: NMYC; motif: CAYCTG; match class: 1                 | TF:M01808_1 | 5049  | 2.30E-09 | 89  |
| TF    | Factor: LRF; motif: GGGGKYNNB                               | TF:M01100   | 6997  | 2.30E-09 | 110 |
| TF    | Factor: FOXO1A;Elk-1; motif: RWMAACAGGAAGTN                 | TF:M08299   | 6145  | 2.40E-09 | 101 |
| TF    | Factor: C-Jun; motif: TGACTC                                | TF:M03541   | 9625  | 2.50E-09 | 136 |
| GO:BP | negative regulation of developmental process                | GO:0051093  | 804   | 2.60E-09 | 31  |
| TF    | Factor: Zbtb44; motif: CKGTGA; match class: 1               | TF:M05405_1 | 5881  | 2.70E-09 | 98  |
| TF    | Factor: E2F-2; motif: GCGCGCGCNCS                           | TF:M11529   | 14928 | 2.80E-09 | 183 |
| TF    | Factor: E2F-3; motif: NTTTTGGCGCCAAAAN; match class: 1      | TF:M11526_1 | 5975  | 2.80E-09 | 99  |
| TF    | Factor: LRF; motif: NCGACCACCGN                             | TF:M12231   | 10281 | 2.90E-09 | 142 |
| TF    | Factor: E2F-3; motif: NNTTTTGGCGCCAAAAC; match class: 1     | TF:M03962_1 | 5799  | 3.00E-09 | 97  |
| TF    | Factor: PPARgamma;RXRalpha; motif: AAGTAGGTACACNGTGACCYACTT | TF:M00515   | 6738  | 3.10E-09 | 107 |
| TF    | Factor: SMAD3; motif: CAGACAS                               | TF:M07429   | 5352  | 3.30E-09 | 92  |
| GO:BP | positive regulation of signal transduction                  | GO:0009967  | 1394  | 3.40E-09 | 41  |
| TF    | Factor: TFII-I; motif: RGAGGKAGG                            | TF:M00706   | 5174  | 3.40E-09 | 90  |
| TF    | Factor: p300; motif: NNNGGGAGTNNNNS                         | TF:M00033   | 7624  | 3.40E-09 | 116 |
| TF    | Factor: AP-2alpha; motif: NNNGSCCTGRGGSN                    | TF:M04896   | 5266  | 3.50E-09 | 91  |
| GO:BP | cytokine-mediated signaling pathway                         | GO:0019221  | 430   | 3.60E-09 | 23  |
| GO:BP | regulation of cell communication                            | GO:0010646  | 3111  | 3.60E-09 | 65  |
| TF    | Factor: RelA-p65; motif: BCWGGGRANNK                        | TF:M04811   | 6469  | 3.60E-09 | 104 |
| TF    | Factor: ER-beta; motif: RGGTCASCNTGMCCY                     | TF:M09910   | 8635  | 3.70E-09 | 126 |
| TF    | Factor: BTEB3; motif: BNRNGGAGGNGT                          | TF:M01865   | 9056  | 4.00E-09 | 130 |



|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: p54NRB; motif: GRNNMGGATGRMNNCGGA           | TF:M07611   | 6106  | 4.10E-09 | 100 |
| TF    | Factor: SATB1; motif: NTTTTAT                       | TF:M03564   | 13565 | 4.20E-09 | 171 |
| TF    | Factor: c-Ets-2; motif: NACCGAAGYRCTTCCGGTN         | TF:M11417   | 12989 | 4.20E-09 | 166 |
| GO:BP | regulation of signaling                             | GO:0023051  | 3125  | 4.40E-09 | 65  |
| TF    | Factor: GR; motif: RGNACANMNTGTNCY                  | TF:M09941   | 4931  | 4.40E-09 | 87  |
| TF    | Factor: KLF4; motif: NNCCCCACCCNN                   | TF:M12489   | 5471  | 4.50E-09 | 93  |
| TF    | Factor: GLI4; motif: RGGCCTTGAATGCCANGCYMA          | TF:M10514   | 11095 | 4.60E-09 | 149 |
| TF    | Factor: SP2; motif: NNRCCAATSRGNRNSNGSN             | TF:M12668   | 10569 | 5.30E-09 | 144 |
| TF    | Factor: Sox-4; motif: AACAAA                        | TF:M03849   | 12223 | 5.30E-09 | 159 |
| TF    | Factor: VDR; motif: GGGKNARNRRGGWSA                 | TF:M00444   | 9297  | 5.30E-09 | 132 |
| GO:BP | regulation of signal transduction                   | GO:0009966  | 2751  | 5.50E-09 | 60  |
| TF    | Factor: TBX2; motif: NNNGTGTSNN                     | TF:M12026   | 6418  | 5.50E-09 | 103 |
| GO:BP | regulation of cell population proliferation         | GO:0042127  | 1482  | 5.80E-09 | 42  |
| TF    | Factor: TFAP2A; motif: NGCCYNNGGGCN                 | TF:M04148   | 9313  | 6.00E-09 | 132 |
| TF    | Factor: Fli-1; motif: NACCGAWWTCCGGTY               | TF:M11399   | 11690 | 6.40E-09 | 154 |
| TF    | Factor: ZNF586; motif: CAGGCCYRGAGG; match class: 1 | TF:M10491_1 | 6912  | 6.50E-09 | 108 |
| GO:CC | intracellular membrane-bounded organelle            | GO:0043231  | 11785 | 6.60E-09 | 152 |
| TF    | Factor: NFATc3; motif: GGAAAA; match class: 1       | TF:M01886_1 | 9439  | 7.20E-09 | 133 |
| TF    | Factor: NFATc2; motif: GGAAAA; match class: 1       | TF:M03555_1 | 9439  | 7.20E-09 | 133 |
| TF    | Factor: NFATc2; motif: GGAAAA; match class: 1       | TF:M01281_1 | 9439  | 7.20E-09 | 133 |
| TF    | Factor: NR1B2; motif: NTGACCY                       | TF:M02111   | 8513  | 7.40E-09 | 124 |
| TF    | Factor: ZF5; motif: NRNGNGCGCGCW                    | TF:M00333   | 13999 | 7.60E-09 | 174 |
| TF    | Factor: VDR, motif: RRTGNMICYTNNGTGAMCCNYNT         | TF:M00966   | 8419  | 7.90E-09 | 123 |
| TF    | Factor: AP-2gamma; motif: GCCYNCRGSN                | TF:M03811   | 8219  | 8.00E-09 | 121 |
| GO:BP | regulation of gene expression                       | GO:0010468  | 4415  | 8.20E-09 | 80  |
| TF    | Factor: ESE-1; motif: SATKGCGGATGCN                 | TF:M11381   | 13896 | 8.40E-09 | 173 |

|       |  |                    |       |          |     |
|-------|--|--------------------|-------|----------|-----|
| TF    | Factor: RORbeta; motif: TGACCYA                                    | TF:M01722          | 5168  | 8.40E-09 | 89  |
| TF    | Factor: ETF; motif: CCCC GCCCCYN; match class: 1                   | TF:M07039_1        | 12626 | 8.40E-09 | 162 |
| GO:BP | circulatory system process   | GO:0003013         | 539   | 8.50E-09 | 25  |
| GO:BP | homeostatic process  | GO:0042592         | 1631  | 8.60E-09 | 44  |
| GO:BP | positive regulation of cell communication                          | GO:0010647         | 1569  | 9.30E-09 | 43  |
| GO:BP | positive regulation of signaling                                   | GO:0023056         | 1573  | 1.00E-08 | 43  |
| TF    | Factor: CRX; motif: YTAATC   | TF:M01712          | 9480  | 1.00E-08 | 133 |
| TF    | Factor: E2F-3:TBR2; motif: ANGTGYKANGCGCSTTNNCRNNT; match class: 1 | TF:M08207_1        | 14160 | 1.00E-08 | 175 |
| GO:BP | response to molecule of bacterial origin                           | GO:0002237         | 292   | 1.10E-08 | 19  |
| TF    | Factor: PPARalpha:RXRalpha; motif: NNRGGTCATWGGGTSANG              | TF:M00518          | 8354  | 1.10E-08 | 122 |
| TF    | Factor: ETV4; motif: NCAGGAAGNN; match class: 1                    | TF:M12556_1        | 3399  | 1.10E-08 | 68  |
| REAC  | Interleukin-4 and Interleukin-13 signaling                         | REAC:R-HSA-6785807 | 97    | 1.20E-08 | 12  |
| TF    | Factor: CP2/LBP-1c/LSF; motif: GCTGGNTNGNNCYNG                     | TF:M00947          | 7463  | 1.20E-08 | 113 |
| TF    | Factor: Erg; motif: NACCGATATCCGGTN                                | TF:M11397          | 10892 | 1.20E-08 | 146 |
| TF    | Factor: GATA-3; motif: AGATAA                                      | TF:M01878          | 8472  | 1.20E-08 | 123 |
| TF    | Factor: ZNF273; motif: GAGAGAGCTAC; match class: 1                 | TF:M10460_1        | 5118  | 1.30E-08 | 88  |
| TF    | Factor: HOXA13; motif: ATAAMA                                      | TF:M01292          | 11353 | 1.40E-08 | 150 |
| TF    | Factor: ZFP14; motif: SCNNYCCNGNNSCTSCNC; match class: 1           | TF:M12694_1        | 4775  | 1.50E-08 | 84  |
| TF    | Factor: Elk-1; motif: GGAAGN; match class: 1                       | TF:M03819_1        | 6527  | 1.60E-08 | 103 |
| TF    | Factor: BEN; motif: CAGCGRNV; match class: 1                       | TF:M01240_1        | 12381 | 1.70E-08 | 159 |
| GO:BP | regulation of immune system process                                | GO:0002682         | 1217  | 1.80E-08 | 37  |
| REAC  | Binding and Uptake of Ligands by Scavenger Receptors               | REAC:R-HSA-2173782 | 41    | 1.80E-08 | 9   |
| TF    | Factor: c-Ets-2; motif: NACCGAAGYRCTTCCGGTN; match class: 1        | TF:M11417_1        | 12734 | 1.80E-08 | 162 |
| TF    | Factor: Cdx-1; motif: TTTATK                                       | TF:M02086          | 12282 | 1.90E-08 | 158 |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: c-Myb; motif: NNWGRCAGTTRN                         | TF:M09990   | 9243  | 1.90E-08 | 130 |
| TF    | Factor: PMX1; motif: TAATHA                                | TF:M03560   | 11838 | 1.90E-08 | 154 |
| TF    | Factor: CP2; motif: NNNNCCAGNCNN; match class: 1           | TF:M07602_1 | 4106  | 2.00E-08 | 76  |
| TF    | Factor: AREB6; motif: NNNYACCTGWVT                         | TF:M00412   | 3939  | 2.00E-08 | 74  |
| TF    | Factor: REST; motif: GGACAGCKC                             | TF:M04726   | 5256  | 2.10E-08 | 89  |
| TF    | Factor: myogenin; motif: RGCAGSTG                          | TF:M00712   | 6086  | 2.10E-08 | 98  |
| TF    | Factor: Tal-1; motif: CAGATGG                              | TF:M03804   | 4459  | 2.20E-08 | 80  |
| TF    | Factor: SZF1-1; motif: CCAGGGTAWCAGCNG                     | TF:M01109   | 3781  | 2.30E-08 | 72  |
| TF    | Factor: LF-A1; motif: GGGSTCWR; match class: 1             | TF:M00646_1 | 5629  | 2.30E-08 | 93  |
| GO:BP | negative regulation of nitrogen compound metabolic process | GO:0051172  | 2106  | 2.60E-08 | 50  |
| GO:BP | ossification   | GO:0001503  | 388   | 2.70E-08 | 21  |
| KEGG  | Cytokine-cytokine receptor interaction                     | KEGG:04060  | 213   | 2.80E-08 | 15  |
| TF    | Factor: GR; motif: RGWACATWAYGTWCY                         | TF:M11846   | 5101  | 2.80E-08 | 87  |
| GO:BP | transport  | GO:0006810  | 4269  | 3.00E-08 | 77  |
| TF    | Factor: NF-1C; motif: NTTGGCNNNTGCCARN                     | TF:M11728   | 2233  | 3.00E-08 | 52  |
| TF    | Factor: SMAD; motif: TGTCTGNNN                             | TF:M08897   | 3891  | 3.10E-08 | 73  |
| TF    | Factor: AP-2; motif: SNNCCNCAGGCN                          | TF:M00915   | 8995  | 3.10E-08 | 127 |
| TF    | Factor: VDR; motif: NRGGTCANNRGRGTCA                       | TF:M10106   | 6125  | 3.10E-08 | 98  |
| GO:BP | positive regulation of gene expression                     | GO:0010628  | 1001  | 3.20E-08 | 33  |
| TF    | Factor: Elk-1; motif: CTTCKG; match class: 1               | TF:M07252_1 | 3080  | 3.40E-08 | 63  |
| TF    | Factor: c-Ets-2; motif: CTTCTG; match class: 1             | TF:M01207_1 | 3080  | 3.40E-08 | 63  |
| TF    | Factor: NF-E2; motif: TGCTGAGTCAY                          | TF:M00037   | 5577  | 3.50E-08 | 92  |
| TF    | Factor: AR; motif: NGNACANNNTGTTTCYNN                      | TF:M09589   | 4327  | 3.50E-08 | 78  |
| TF    | Factor: E2F1; motif: GSGCGGGAAN                            | TF:M12597   | 13064 | 3.80E-08 | 164 |
| TF    | Factor: E2F4; motif: YCCGCCNCNNSNNSNN; match class: 1      | TF:M12599_1 | 14589 | 3.90E-08 | 177 |
| GO:BP | response to lipopolysaccharide                             | GO:0032496  | 277   | 4.10E-08 | 18  |

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|-------|--|--------------------|-------|----------|-----|
| GO:BP | negative regulation of response to stimulus                      | GO:0048585         | 1510  | 4.10E-08 | 41  |
| TF    | Factor: FOXO1A;Net; motif: RWMAACAGGAAGTN                        | TF:M08302          | 7909  | 4.20E-08 | 116 |
| TF    | Factor: PPARALPHA;RXR-ALPHA; motif: AWNTRGGTNAAGGTCAN            | TF:M08960          | 10094 | 4.50E-08 | 137 |
| TF    | Factor: MIF-1; motif: NNGTTGCWWGGYAAACNGS                        | TF:M00279          | 9883  | 4.60E-08 | 135 |
| TF    | Factor: Erm:E2A; motif: CASGTGNNNCGGAAGNN                        | TF:M08571          | 9890  | 4.80E-08 | 135 |
| GO:BP | muscle tissue development  | GO:0060537         | 359   | 5.00E-08 | 20  |
| TF    | Factor: c-Rel; motif: NRNRGGGRAATKCCA                            | TF:M10046          | 4101  | 5.00E-08 | 75  |
| TF    | Factor: GR; motif: NNNNNNGKACNNNTTCTNNNNN                        | TF:M00955          | 4102  | 5.10E-08 | 75  |
| TF    | Factor: E2F-1;HES-7; motif: GGRCGTGSYNNWNGGCGCSM; match class: 1 | TF:M08525_1        | 14157 | 5.10E-08 | 173 |
| TF    | Factor: LRH-1; motif: TCAAGGTCRYGACCTTGR; match class: 1         | TF:M11828_1        | 6856  | 5.60E-08 | 105 |
| TF    | Factor: ZNF692; motif: SYNGGCCASCCNC                             | TF:M09734          | 10664 | 5.70E-08 | 142 |
| TF    | Factor: Tbx5; motif: TNAGGTGTKV                                  | TF:M01020          | 9490  | 5.80E-08 | 131 |
| GO:BP | response to growth factor  | GO:0070848         | 640   | 5.90E-08 | 26  |
| GO:BP | establishment of localization                                    | GO:0051234         | 4416  | 6.00E-08 | 78  |
| REAC  | Cytokine Signaling in Immune system                              | REAC:R-HSA-1280215 | 634   | 6.00E-08 | 25  |
| GO:BP | regulation of cell differentiation                               | GO:0045595         | 1400  | 6.30E-08 | 39  |
| TF    | Factor: FXR;RXR-ALPHA; motif: NRGGTCANRGGKN                      | TF:M08955          | 8470  | 6.60E-08 | 121 |
| TF    | Factor: GR; motif: RGWACATWAYGTWCY                               | TF:M11847          | 4559  | 6.60E-08 | 80  |
| TF    | Factor: ESRRA; motif: CAAGGTCANNYSAAAGTCA                        | TF:M04458          | 9722  | 6.80E-08 | 133 |
| TF    | Factor: AP-2alpha; motif: NGCCYSNNGSN                            | TF:M01857          | 8679  | 6.80E-08 | 123 |
| TF    | Factor: AP-4;ER81; motif: RSCGGAAGCAGSTGNN                       | TF:M08443          | 9517  | 7.10E-08 | 131 |
| TF    | Factor: ZNF432; motif: NCAGNRCCNSRGRGAGC                         | TF:M12704          | 9203  | 7.10E-08 | 128 |
| GO:BP | embryo development   | GO:0009790         | 976   | 7.50E-08 | 32  |
| TF    | Factor: AML1; motif: TGTGGT                                      | TF:M00751          | 10268 | 7.50E-08 | 138 |
| TF    | Factor: AML1a; motif: TGTGGT                                     | TF:M00271          | 10268 | 7.50E-08 | 138 |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: AML1; motif: TGTGGT                         | TF:M02084         | 10268 | 7.50E-08 | 138 |
| GO:BP | positive regulation of cellular metabolic process   | GO:0031325        | 2936  | 7.80E-08 | 60  |
| TF    | Factor: GR; motif: RGRACATTNTGTYC                   | TF:M04750         | 4487  | 7.90E-08 | 79  |
| GO:BP | regulation of localization                          | GO:0032879        | 2549  | 8.00E-08 | 55  |
| TF    | Factor: Elk-1; Pax-5; motif: ACCGGAACYACGCWTSANYG   | TF:M08225         | 12715 | 8.00E-08 | 160 |
| TF    | Factor: DATF1; motif: SNGGRRGCWGNNGG                | TF:M09724         | 7588  | 8.20E-08 | 112 |
| GO:BP | skeletal system development                         | GO:0001501        | 457   | 8.40E-08 | 22  |
| GO:BP | regulation of cellular metabolic process            | GO:0031323        | 5347  | 8.60E-08 | 88  |
| TF    | Factor: THAP1; motif: YTGCCCNNA; match class: 1     | TF:M07407_1       | 3639  | 8.60E-08 | 69  |
| TF    | Factor: GR; motif: RGWACATWATGTWCY; match class: 1  | TF:M11847_1       | 3311  | 8.70E-08 | 65  |
| TF    | Factor: STAT5A; motif: TTCCNRGAANNNNNTTCCNNGRR      | TF:M00460         | 6618  | 8.90E-08 | 102 |
| GO:BP | negative regulation of cellular metabolic process   | GO:0031324        | 2256  | 9.10E-08 | 51  |
| TF    | Factor: TFAP2A; motif: NGCCYNNGGGCN; match class: 1 | TF:M04148_1       | 8927  | 9.50E-08 | 125 |
| TF    | Factor: Smad4; motif: NCAGACAN                      | TF:M07368         | 3322  | 1.00E-07 | 65  |
| GO:BP | regulation of angiogenesis                          | GO:0045765        | 256   | 1.10E-07 | 17  |
| GO:CC | blood microparticle                                 | GO:0072562        | 94    | 1.10E-07 | 11  |
| TF    | Factor: Sohlh2; motif: NNCACGTGNN                   | TF:M11075         | 10531 | 1.10E-07 | 140 |
| TF    | Factor: Fli-1; motif: NACCGGATATCCGGTN              | TF:M11401         | 10861 | 1.10E-07 | 143 |
| TF    | Factor: DPF2; motif: NYCACYTCCYCNYYCY               | TF:M09760         | 7424  | 1.10E-07 | 110 |
| TF    | Factor: PEA3; motif: ACWTCK                         | TF:M00655         | 8027  | 1.10E-07 | 116 |
| TF    | Factor: pax-6; motif: NYACGCNYSANYGMNCN             | TF:M11882         | 14157 | 1.10E-07 | 172 |
| GO:BP | negative regulation of molecular function           | GO:0044092        | 935   | 1.20E-07 | 31  |
| GO:BP | response to organonitrogen compound                 | GO:0010243        | 937   | 1.20E-07 | 31  |
| REAC  | Signaling by Interleukins                           | REAC:R-HSA-449147 | 411   | 1.20E-07 | 20  |
| TF    | Factor: rfx3; SREBP-2; motif: ATGGYAACRTCACGTGAY    | TF:M08412         | 9163  | 1.20E-07 | 127 |
| GO:BP | regulation of vasculature development               | GO:1901342        | 260   | 1.30E-07 | 17  |

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|-------|--|-------------|-------|----------|-----|
| KEGG  | Staphylococcus aureus infection                        | KEGG:05150  | 60    | 1.30E-07 | 9   |
| TF    | Factor: CTCF; motif: ACCAGGKGGC                        | TF:M04727   | 5802  | 1.30E-07 | 93  |
| TF    | Factor: C/EBP; motif: NTTRCNNAANN                      | TF:M00912   | 4188  | 1.40E-07 | 75  |
| GO:BP | apoptotic signaling pathway                            | GO:0097190  | 566   | 1.50E-07 | 24  |
| GO:BP | cellular response to growth factor stimulus            | GO:0071363  | 616   | 1.50E-07 | 25  |
| TF    | Factor: CDX-2; motif: TTTATN                           | TF:M02087   | 8261  | 1.50E-07 | 118 |
| TF    | Factor: TFAP2C; motif: NGCCNNRGGCA                     | TF:M04152   | 7062  | 1.50E-07 | 106 |
| TF    | Factor: HES-5; motif: NCACACKY                         | TF:M11069   | 9505  | 1.50E-07 | 130 |
| TF    | Factor: DEC1; motif: NCNCACRTGNSC                      | TF:M08870   | 6965  | 1.50E-07 | 105 |
| TF    | Factor: Spic; motif: NGNGGAASN                         | TF:M02077   | 7359  | 1.50E-07 | 109 |
| TF    | Factor: E2F-1; motif: NGGGCGGARV                       | TF:M07206   | 13501 | 1.50E-07 | 166 |
| GO:BP | mesenchyme development                                 | GO:0060485  | 263   | 1.60E-07 | 17  |
| TF    | Factor: TIEG1; motif: GSGGKGN                          | TF:M08905   | 4638  | 1.60E-07 | 80  |
| TF    | Factor: GLI; motif: NTGGGTGGTN                         | TF:M07292   | 5098  | 1.80E-07 | 85  |
| TF    | Factor: NRL; motif: NNNNTGCTGAC                        | TF:M04224   | 3869  | 1.80E-07 | 71  |
| TF    | Factor: CPBP; motif: GNNRGGHGGGNNGGRN                  | TF:M09973   | 10173 | 1.80E-07 | 136 |
| GO:BP | muscle structure development                           | GO:0061061  | 573   | 1.90E-07 | 24  |
| GO:BP | regulation of body fluid levels                        | GO:0050878  | 345   | 1.90E-07 | 19  |
| TF    | Factor: ZNF549; motif: NTGCTKYCMW                      | TF:M12355   | 5656  | 1.90E-07 | 91  |
| TF    | Factor: AP2; motif: GCCYSGGSN                          | TF:M08867   | 9433  | 1.90E-07 | 129 |
| TF    | Factor: Spz1; motif: DNNGRGGGWNNNN                     | TF:M00446   | 7790  | 1.90E-07 | 113 |
| TF    | Factor: Fli-1; motif: NACCGGATATCCGGTN; match class: 1 | TF:M11401_1 | 10722 | 1.90E-07 | 141 |
| GO:BP | response to nitrogen compound                          | GO:1901698  | 1015  | 2.00E-07 | 32  |
| TF    | Factor: ER-alpha; motif: AGGTCASMTGACCY                | TF:M09909   | 5943  | 2.00E-07 | 94  |
| TF    | Factor: E2F-3; FOXO6; motif: NAATGACACGCGCCMC          | TF:M08209   | 12393 | 2.00E-07 | 156 |
| GO:MF | structural molecule activity                           | GO:0005198  | 657   | 2.20E-07 | 25  |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| GO:BP | negative regulation of metabolic process            | GO:0009892        | 2853  | 2.20E-07 | 58  |
| TF    | Factor: ZABC1; motif: ATTCNCAC                      | TF:M01306         | 8006  | 2.20E-07 | 115 |
| TF    | Factor: Hey2; motif: NNCACGYGNN                     | TF:M11052         | 11397 | 2.20E-07 | 147 |
| TF    | Factor: Zic1; motif: KGGGTGGTC; match class: 1      | TF:M00448_1       | 3888  | 2.20E-07 | 71  |
| TF    | Factor: HSF2; motif: NGAANNWTCK                     | TF:M00147         | 4941  | 2.20E-07 | 83  |
| TF    | Factor: E2F2; motif: NNITTTGGCGCCAAAWN              | TF:M03959         | 7017  | 2.30E-07 | 105 |
| GO:BP | regulation of cell migration                        | GO:0030334        | 847   | 2.40E-07 | 29  |
| TF    | Factor: HNRPUL1; motif: NCNCAGN; match class: 1     | TF:M09746_1       | 6727  | 2.40E-07 | 102 |
| TF    | Factor: Six-2; motif: NNGTAWCRNN                    | TF:M11032         | 9253  | 2.40E-07 | 127 |
| TF    | Factor: CTCF; motif: CANNWRRTGGCAG                  | TF:M04745         | 7022  | 2.40E-07 | 105 |
| TF    | Factor: Erg; motif: NACCGATATCCGGTN; match class: 1 | TF:M11397_1       | 10645 | 2.40E-07 | 140 |
| GO:BP | cellular response to organonitrogen compound        | GO:0071417        | 582   | 2.60E-07 | 24  |
| TF    | Factor: DLX2; motif: AMSMCTGACKG                    | TF:M08873         | 6450  | 2.60E-07 | 99  |
| GO:BP | regulation of cell adhesion                         | GO:0030155        | 687   | 2.70E-07 | 26  |
| GO:CC | contractile fiber                                   | GO:0043292        | 229   | 2.80E-07 | 15  |
| GO:BP | cellular response to nitrogen compound              | GO:1901699        | 636   | 2.90E-07 | 25  |
| GO:BP | connective tissue development                       | GO:0061448        | 236   | 2.90E-07 | 16  |
| TF    | Factor: AP-2; motif: MKCCSCNGGCG                    | TF:M00189         | 10020 | 2.90E-07 | 134 |
| TF    | Factor: MAZ; motif: GGGGGAGGGGNGRGRRRGNRG           | TF:M09984         | 8861  | 2.90E-07 | 123 |
| GO:BP | regulation of cellular component movement           | GO:0051270        | 972   | 3.00E-07 | 31  |
| TF    | Factor: C/EBPbeta; motif: TKNNGCAANN                | TF:M01896         | 3827  | 3.00E-07 | 70  |
| TF    | Factor: DB1; motif: GGRRRRGRRGGAGGGGNGRRR           | TF:M10107         | 5428  | 3.00E-07 | 88  |
| TF    | Factor: Sox-4; motif: NYCTTTGTYYYYN                 | TF:M10069         | 6179  | 3.10E-07 | 96  |
| TF    | Factor: NR1H4; motif: NNAATGACCNN                   | TF:M09777         | 3246  | 3.10E-07 | 63  |
| REAC  | Signal Transduction                                 | REAC:R-HSA-162582 | 2365  | 3.20E-07 | 50  |
| TF    | Factor: STAT1; motif: NTTCCNGGA                     | TF:M04721         | 6860  | 3.20E-07 | 103 |

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|-------|--|--------------------|-------|----------|-----|
| TF    | Factor: JUNB:C-JUN; motif: KRTGACGTCATN                      | TF:M08945          | 8056  | 3.30E-07 | 115 |
| TF    | Factor: Tax/CREB; motif: RTGACGCATAYCCCC                     | TF:M00115          | 8263  | 3.40E-07 | 117 |
| REAC  | Assembly of collagen fibrils and other multimeric structures | REAC:R-HSA-2022090 | 56    | 3.50E-07 | 9   |
| TF    | Factor: Sall1; motif: NGGTCCCKRGKRA                          | TF:M05467          | 3757  | 3.50E-07 | 69  |
| TF    | Factor: AR; motif: AGAACANNNTGTTCT; match class: 1           | TF:M08907_1        | 1804  | 3.50E-07 | 44  |
| TF    | Factor: ZNF511; motif: GGRRRGRGGCWGNG                        | TF:M09738          | 9835  | 3.50E-07 | 132 |
| GO:BP | regulation of primary metabolic process                      | GO:0080090         | 5129  | 3.70E-07 | 84  |
| GO:BP | blood coagulation  | GO:0007596         | 205   | 3.70E-07 | 15  |
| TF    | Factor: Sox-2; motif: NNCCTTTGTNYYN                          | TF:M10067          | 5172  | 3.70E-07 | 85  |
| TF    | Factor: AP-2gamma; motif: GCCYNNNGGS; match class: 1         | TF:M00470_1        | 5364  | 4.00E-07 | 87  |
| TF    | Factor: IRF-2; motif: NAANYGAAASYR                           | TF:M08775          | 7180  | 4.00E-07 | 106 |
| REAC  | Collagen degradation   | REAC:R-HSA-1442490 | 57    | 4.10E-07 | 9   |
| TF    | Factor: VDR; motif: GRGTTTCATYGRGTTCA                        | TF:M04498          | 4463  | 4.10E-07 | 77  |
| TF    | Factor: NF-kappaB; motif: GGGGATYCCC                         | TF:M00051          | 5840  | 4.40E-07 | 92  |
| TF    | Factor: AP-2gamma:Max; motif: NNCCYNRGGSNNNNCACGTGN          | TF:M08664          | 2105  | 4.40E-07 | 48  |
| TF    | Factor: ER71:Pax-5; motif: ACCGGAACYACGCWTSANTG              | TF:M08266          | 13080 | 4.40E-07 | 161 |
| KEGG  | Malaria  | KEGG:05144         | 48    | 4.50E-07 | 8   |
| GO:BP | coagulation  | GO:0050817         | 208   | 4.60E-07 | 15  |
| TF    | Factor: NURR1; motif: YRRCCTT                                | TF:M01269          | 5012  | 4.60E-07 | 83  |
| TF    | Factor: c-Rel; motif: NGGGAATYTCCN                           | TF:M03545          | 4836  | 4.80E-07 | 81  |
| GO:BP | regulation of nitrogen compound metabolic process            | GO:0051171         | 4981  | 5.20E-07 | 82  |
| TF    | Factor: FOXM1; motif: TRTTTATNN                              | TF:M08883          | 5673  | 5.30E-07 | 90  |
| TF    | Factor: ZBRK1; motif: NGNNNGGTNAWAAAARRGCNG                  | TF:M10468          | 9361  | 5.30E-07 | 127 |
| GO:BP | positive regulation of immune system process                 | GO:0002684         | 764   | 5.40E-07 | 27  |
| GO:BP | hemostasis   | GO:0007599         | 211   | 5.60E-07 | 15  |

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|-------|--|-------------|-------|----------|-----|
| TF    | Factor: DBP; motif: TTRCATAANN                             | TF:M07038   | 4582  | 5.60E-07 | 78  |
| TF    | Factor: BTEB2; motif: WGGGTGKGGCNGGN                       | TF:M09972   | 8433  | 5.70E-07 | 118 |
| TF    | Factor: RUNX3; motif: NRACCGCAAACCGCAN                     | TF:M04109   | 8951  | 5.70E-07 | 123 |
| TF    | Factor: NF-1; motif: NNTTGGCNNNNNCCNNN                     | TF:M00193   | 4407  | 5.70E-07 | 76  |
| TF    | Factor: MTF-1; motif: NTTTTGCACACGGCNYN                    | TF:M12279   | 5776  | 5.80E-07 | 91  |
| TF    | Factor: NF-kappaB; motif: AGGGGAWTCCCCT                    | TF:M04054   | 2656  | 5.90E-07 | 55  |
| TF    | Factor: AP-2alphaA; motif: ANMGCCTNAGGCKNT                 | TF:M01047   | 7728  | 6.00E-07 | 111 |
| TF    | Factor: AP-2alphaA; motif: ANMGCCTNAGGCKNT; match class: 1 | TF:M01047_1 | 7728  | 6.00E-07 | 111 |
| TF    | Factor: PURBETA; motif: NCWGRGGCTGGGG; match class: 1      | TF:M12726_1 | 2201  | 6.20E-07 | 49  |
| TF    | Factor: SREBP-1; motif: CACSCCA; match class: 1            | TF:M00749_1 | 2428  | 6.20E-07 | 52  |
| TF    | Factor: HSF2; motif: NGAANNWTCK; match class: 1            | TF:M00147_1 | 3725  | 6.50E-07 | 68  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT                            | TF:M11206   | 6263  | 6.50E-07 | 96  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1            | TF:M11206_1 | 6263  | 6.50E-07 | 96  |
| GO:BP | leukocyte migration  | GO:0050900  | 329   | 6.70E-07 | 18  |
| GO:BP | cellular response to lipid                                 | GO:0071396  | 511   | 7.00E-07 | 22  |
| TF    | Factor: TEF-3;Elk-1; motif: RMATWCCGGAWGT                  | TF:M08418   | 10468 | 7.00E-07 | 137 |
| TF    | Factor: c-Ets-1; motif: RCAGGAAGTGNNNS                     | TF:M00339   | 5893  | 7.10E-07 | 92  |
| TF    | Factor: Elf5; motif: CSMGGAARNN                            | TF:M02057   | 9296  | 7.20E-07 | 126 |
| GO:BP | enzyme linked receptor protein signaling pathway           | GO:0007167  | 889   | 7.30E-07 | 29  |
| TF    | Factor: RelA-p65; motif: GGGANTTCCNN                       | TF:M03563   | 4079  | 7.30E-07 | 72  |
| GO:BP | renal system development                                   | GO:0072001  | 291   | 7.70E-07 | 17  |
| TF    | Factor: Fli-1; motif: RCAGGAAGTGR                          | TF:M07089   | 4264  | 8.20E-07 | 74  |
| GO:BP | response to toxic substance                                | GO:0009636  | 217   | 8.30E-07 | 15  |
| GO:CC | collagen trimer  | GO:0005581  | 87    | 8.30E-07 | 10  |
| TF    | Factor: CP2; motif: NTGNCTGGNN                             | TF:M03868   | 4006  | 8.50E-07 | 71  |
| TF    | Factor: HSF1; motif: TCYAGAANN TTC                         | TF:M07259   | 4006  | 8.50E-07 | 71  |

|       |   |                      |       |          |     |
|-------|---|----------------------|-------|----------|-----|
| TF    | Factor: AP-4;Max; motif: NCAGCTGNNNNNNNCAGTGN; match class: 1           | TF:M08674_1          | 4802  | 8.50E-07 | 80  |
| GO:MF | extracellular matrix structural constituent conferring tensile strength | GO:0030020           | 40    | 8.70E-07 | 8   |
| TF    | Factor: CP2; motif: NRRRCCGGCYNRARCCGGNN                                | TF:M12590            | 10284 | 8.90E-07 | 135 |
| GO:BP | positive regulation of cell differentiation                             | GO:0045597           | 782   | 9.00E-07 | 27  |
| TF    | Factor: NR1B1; motif: NRRGTCANNRGGTCAN                                  | TF:M11795            | 6883  | 9.00E-07 | 102 |
| REAC  | Collagen chain trimerization  | REAC:R-HSA-8948216   | 43    | 9.10E-07 | 8   |
| TF    | Factor: ZNF300; motif: SWGGGGGSN; match class: 1                        | TF:M07486_1          | 6786  | 9.10E-07 | 101 |
| GO:BP | regulation of cell motility   | GO:2000145           | 898   | 9.20E-07 | 29  |
| TF    | Factor: ZNF436; motif: TCCTCCAGGAAGCCY; match class: 1                  | TF:M10477_1          | 7782  | 9.20E-07 | 111 |
| REAC  | Collagen formation  | REAC:R-HSA-1474290   | 85    | 9.30E-07 | 10  |
| MIRNA | hsa-miR-26b-5p  | MIRNA:hsa-miR-26b-5p | 1739  | 9.60E-07 | 41  |
| TF    | Factor: AR; motif: AGAACANNNTGTTCT                                      | TF:M08907            | 1863  | 9.70E-07 | 44  |
| TF    | Factor: GR; motif: AGAACAN  | TF:M07355            | 4913  | 1.00E-06 | 81  |
| GO:BP | striated muscle tissue development                                      | GO:0014706           | 340   | 1.10E-06 | 18  |
| TF    | Factor: FOXO1A;ETV7; motif: NWMAACAGGAMNNCTCCNN; match class: 1         | TF:M08304_1          | 6512  | 1.10E-06 | 98  |
| TF    | Factor: E2F-4; motif: GCGGGAAANA  | TF:M02090            | 11183 | 1.10E-06 | 143 |
| TF    | Factor: Nrf2; motif: NNTGACTCAGCAN                                      | TF:M07265            | 4114  | 1.10E-06 | 72  |
| GO:BP | sensory organ development   | GO:0007423           | 525   | 1.20E-06 | 22  |
| TF    | Factor: E2F-3;T-bet; motif: AGGTGTNANGCGCST                             | TF:M08529            | 10334 | 1.30E-06 | 135 |
| TF    | Factor: HNF4A; motif: NNCAAAGTCCANN                                     | TF:M12503            | 2555  | 1.30E-06 | 53  |
| TF    | Factor: ER-beta; motif: NRRGTCANKSTGACCTNN                              | TF:M09610            | 5122  | 1.30E-06 | 83  |
| GO:MF | protein-containing complex binding                                      | GO:0044877           | 1204  | 1.40E-06 | 33  |
| GO:BP | muscle organ development  | GO:0007517           | 303   | 1.40E-06 | 17  |
| TF    | Factor: SRY; motif: TTGTTT; match class: 1                              | TF:M03854_1          | 7628  | 1.40E-06 | 109 |
| TF    | Factor: FOXO1A; motif: AAACAA; match class: 1                           | TF:M03823_1          | 7628  | 1.40E-06 | 109 |

|       |   |                    |       |          |     |
|-------|---|--------------------|-------|----------|-----|
| TF    | Factor: NR1B1; motif: NRGGNCRGTGACCTN; match class: 1 | TF:M11796_1        | 4315  | 1.40E-06 | 74  |
| TF    | Factor: c-Ets-1; motif: GGAGTTG                       | TF:M04822          | 4763  | 1.40E-06 | 79  |
| TF    | Factor: ERF:FOXO1A; motif: RTMACACAGGAARNS            | TF:M08241          | 6745  | 1.50E-06 | 100 |
| TF    | Factor: LHX3; motif: ATTAAW                           | TF:M02097          | 10034 | 1.50E-06 | 132 |
| TF    | Factor: MAZ; motif: NKGGGAGGGGRGGR                    | TF:M02023          | 6650  | 1.50E-06 | 99  |
| TF    | Factor: c-Ets-2; motif: NNNRGAARNRRR                  | TF:M09912          | 4412  | 1.50E-06 | 75  |
| TF    | Factor: FLI1; motif: ACCGAAATCCGGT                    | TF:M03989          | 9505  | 1.50E-06 | 127 |
| GO:BP | chronic inflammatory response                         | GO:0002544         | 14    | 1.60E-06 | 6   |
| REAC  | Collagen biosynthesis and modifying enzymes           | REAC:R-HSA-1650814 | 66    | 1.60E-06 | 9   |
| TF    | Factor: C/EBPalpha; motif: NGWVTKNKGYAAKNSAYA         | TF:M00201          | 3296  | 1.60E-06 | 62  |
| TF    | Factor: HMG1Y; motif: NNKKNAWTTTNYTNN                 | TF:M01010          | 6852  | 1.60E-06 | 101 |
| TF    | Factor: MOV0-B; motif: GNGGGGG                        | TF:M01104          | 9727  | 1.60E-06 | 129 |
| GO:BP | metabolic process                                     | GO:0008152         | 11098 | 1.70E-06 | 141 |
| TF    | Factor: Ik-3; motif: TNYTGGAATACC                     | TF:M00088          | 5052  | 1.70E-06 | 82  |
| TF    | Factor: ER-alpha; motif: NAGGTCACSGYGACCTN            | TF:M11844          | 4779  | 1.70E-06 | 79  |
| TF    | Factor: MAZ; motif: CCCTCCCYCYN                       | TF:M07297          | 2734  | 1.70E-06 | 55  |
| TF    | Factor: JunB; motif: GATGACGTCAYC                     | TF:M11273          | 7663  | 1.80E-06 | 109 |
| TF    | Factor: ZBTB44; motif: MACWGCAGS                      | TF:M12352          | 5619  | 1.80E-06 | 88  |
| KEGG  | TNF signaling pathway                                 | KEGG:04668         | 108   | 1.90E-06 | 10  |
| TF    | Factor: TWIST1; motif: NNNCCAGATGTNN                  | TF:M09790          | 2428  | 1.90E-06 | 51  |
| TF    | Factor: AR; motif: RGGWACAYNGTGTWCYN; match class: 1  | TF:M04453_1        | 3232  | 2.00E-06 | 61  |
| GO:MF | collagen binding                                      | GO:0005518         | 64    | 2.10E-06 | 9   |
| TF    | Factor: Elk-1:HOXA3; motif: ACCGGWAATKRNNNTNWCNNATTAN | TF:M08220          | 10624 | 2.10E-06 | 137 |
| TF    | Factor: FOXO1A:Elf-1; motif: NAGAAAACCGAANM           | TF:M08295          | 10193 | 2.10E-06 | 133 |
| GO:BP | regulation of inflammatory response                   | GO:0050727         | 313   | 2.30E-06 | 17  |

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|-------|--|--------------------|-------|----------|-----|
| GO:CC | Z disc   | GO:0030018         | 125   | 2.30E-06 | 11  |
| TF    | Factor: AP2; motif: GCCYGSAGGSN; match class: 1                      | TF:M08867_1        | 4993  | 2.30E-06 | 81  |
| GO:BP | regulation of molecular function                                     | GO:0065009         | 2797  | 2.40E-06 | 55  |
| GO:BP | regulation of locomotion   | GO:0040012         | 937   | 2.40E-06 | 29  |
| TF    | Factor: SP1; motif: GGGGYGGGNS                                       | TF:M01303          | 7502  | 2.40E-06 | 107 |
| TF    | Factor: MTF-1; motif: NTTTTGCACACGGCENN                              | TF:M12280          | 6032  | 2.50E-06 | 92  |
| TF    | Factor: rfx3:SRF; motif: TRGCAACNNNNCCNWTANGGN                       | TF:M08623          | 12775 | 2.50E-06 | 156 |
| TF    | Factor: AP-2gamma:Elk-1; motif: NGCCKNRGGSGRCGGAAGTG; match class: 1 | TF:M08441_1        | 11870 | 2.50E-06 | 148 |
| TF    | Factor: VDR; motif: GGGKNARNRRGGWSA; match class: 1                  | TF:M00444_1        | 4198  | 2.60E-06 | 72  |
| TF    | Factor: Sp3; motif: ASMCTTGGGSRGGG                                   | TF:M00665          | 7012  | 2.60E-06 | 102 |
| TF    | Factor: AP-4; motif: WGARYCAGCTGYGNCNK                               | TF:M00005          | 4645  | 2.60E-06 | 77  |
| REAC  | ECM proteoglycans  | REAC:R-HSA-3000178 | 70    | 2.70E-06 | 9   |
| TF    | Factor: c-Rel; motif: SGGRNITTCC                                     | TF:M00053          | 3259  | 2.70E-06 | 61  |
| TF    | Factor: BTEB3; motif: CCNNSCCNSCCCKCCCC                              | TF:M09826          | 10774 | 2.80E-06 | 138 |
| TF    | Factor: TIEG1; motif: NCCNSNCCCCGCCCC                                | TF:M12351          | 11551 | 2.80E-06 | 145 |
| TF    | Factor: MEL1; motif: GARGAT  | TF:M08794          | 9275  | 2.90E-06 | 124 |
| TF    | Factor: NF-1A; motif: NGCCARN  | TF:M03554          | 4210  | 2.90E-06 | 72  |
| GO:BP | response to inorganic substance                                      | GO:0010035         | 502   | 3.00E-06 | 21  |
| KEGG  | Amoebiasis   | KEGG:05146         | 85    | 3.00E-06 | 9   |
| GO:BP | intracellular signal transduction                                    | GO:0035556         | 2497  | 3.10E-06 | 51  |
| GO:BP | blood circulation  | GO:0008015         | 455   | 3.20E-06 | 20  |
| GO:BP | negative regulation of cell population proliferation                 | GO:0008285         | 660   | 3.20E-06 | 24  |
| TF    | Factor: CKROX; motif: SCCCTCCCC                                      | TF:M01175          | 6740  | 3.20E-06 | 99  |
| TF    | Factor: AR; motif: GGAACGGWACATGTTCT                                 | TF:M08190          | 6740  | 3.20E-06 | 99  |
| TF    | Factor: TEF-1; motif: ACATTCCWSNN                                    | TF:M07340          | 3273  | 3.20E-06 | 61  |

|       |   |                    |       |          |     |
|-------|---|--------------------|-------|----------|-----|
| TF    | Factor: IRF-4; motif: NAANGRGGAASTGAAASN                      | TF:M09959          | 2865  | 3.30E-06 | 56  |
| TF    | Factor: KLF15; motif: NCCMCGCCMCN                             | TF:M12158          | 9935  | 3.30E-06 | 130 |
| TF    | Factor: Elk-1; SREBP-2; motif: RTCACGTGACCGGAAGN              | TF:M08229          | 8564  | 3.30E-06 | 117 |
| GO:BP | negative regulation of macromolecule metabolic process        | GO:0010605         | 2662  | 3.40E-06 | 53  |
| GO:BP | odontogenesis   | GO:0042476         | 109   | 3.40E-06 | 11  |
| TF    | Factor: six-4; motif: ANNNATGACACNNNNN                        | TF:M01374          | 5406  | 3.40E-06 | 85  |
| TF    | Factor: MAFA; motif: TCAGCAN                                  | TF:M01709          | 5314  | 3.40E-06 | 84  |
| GO:BP | positive regulation of nitrogen compound metabolic process    | GO:0051173         | 2747  | 3.60E-06 | 54  |
| TF    | Factor: ZNFPT1; motif: YCNNCNCWGCCNY; match class: 1          | TF:M12721_1        | 2874  | 3.70E-06 | 56  |
| TF    | Factor: NFATc1; motif: TTTCCWN                                | TF:M01718          | 5045  | 3.70E-06 | 81  |
| TF    | Factor: IRX-1; motif: NACRYNNNNNNNRYGNN; match class: 1       | TF:M11018_1        | 14591 | 3.90E-06 | 171 |
| TF    | Factor: TEF; motif: YACATTCCWSNG                              | TF:M01305          | 3207  | 3.90E-06 | 60  |
| GO:BP | urogenital system development                                 | GO:0001655         | 325   | 4.10E-06 | 17  |
| KEGG  | Viral protein interaction with cytokine and cytokine receptor | KEGG:04061         | 63    | 4.10E-06 | 8   |
| TF    | Factor: NF-1C; motif: NYYTGCCWNNNNKCCMN                       | TF:M09640          | 2406  | 4.10E-06 | 50  |
| TF    | Factor: KLF; motif: GGGNGGGG; match class: 1                  | TF:M07461_1        | 3129  | 4.10E-06 | 59  |
| REAC  | Degradation of the extracellular matrix                       | REAC:R-HSA-1474228 | 128   | 4.20E-06 | 11  |
| GO:CC | complex of collagen trimers                                   | GO:0098644         | 21    | 4.30E-06 | 6   |
| GO:CC | sarcomere   | GO:0030017         | 201   | 4.30E-06 | 13  |
| TF    | Factor: AP-4; Dlx-3; motif: NCAGCTGNNNNNGTAAATKR              | TF:M08671          | 3638  | 4.40E-06 | 65  |
| TF    | Factor: ROX; motif: GNNNCASGTGGS                              | TF:M09764          | 5157  | 4.40E-06 | 82  |
| GO:MF | immune receptor activity                                      | GO:0140375         | 122   | 4.50E-06 | 11  |
| TF    | Factor: YB-1; motif: NNNNCCAATNN                              | TF:M03862          | 7885  | 4.50E-06 | 110 |
| TF    | Factor: ZNF37A; motif: CCYYGGCTCCNTSCCMN; match class: 1      | TF:M12354_1        | 5347  | 4.60E-06 | 84  |
| TF    | Factor: ERF; SREBP-2; motif: NSCGGAARTCACGTGAT                | TF:M08453          | 8820  | 4.70E-06 | 119 |

|       |  |                       |       |          |     |
|-------|--|-----------------------|-------|----------|-----|
| TF    | Factor: GR; motif: CNNNNTGTYCTNN                       | TF:M01836             | 4890  | 4.80E-06 | 79  |
| GO:BP | vascular process in circulatory system                 | GO:0003018            | 247   | 4.90E-06 | 15  |
| TF    | Factor: SMAD4; motif: GKSRRKCCAGMCANCY; match class: 1 | TF:M00733_1           | 2421  | 5.00E-06 | 50  |
| TF    | Factor: Thap1; motif: SCGCCATSTTKGNTNMGGGCARNN         | TF:M04723             | 10537 | 5.10E-06 | 135 |
| TF    | Factor: Sox-9; motif: RNACAAAGGVN                      | TF:M01284             | 5079  | 5.10E-06 | 81  |
| TF    | Factor: SMAD3; motif: CAGACAS; match class: 1          | TF:M07429_1           | 1137  | 5.30E-06 | 32  |
| TF    | Factor: MaFA; motif: TCTGCTGASCNN                      | TF:M07325             | 4356  | 5.30E-06 | 73  |
| GO:BP | organic substance metabolic process                    | GO:0071704            | 10615 | 5.40E-06 | 135 |
| TF    | Factor: P50; motif: GGRRANTCCCN                        | TF:M03557             | 4359  | 5.40E-06 | 73  |
| TF    | Factor: SREBP-2; motif: NNGYCACNNSMN                   | TF:M01177             | 7910  | 5.40E-06 | 110 |
| TF    | Factor: Oct-2; motif: ATTTGCA                          | TF:M04715             | 5273  | 5.50E-06 | 83  |
| TF    | Factor: TWIST1; motif: NNNCCAGATGTNN                   | TF:M12577             | 2350  | 5.50E-06 | 49  |
| TF    | Factor: TEF-1; motif: CRCATWCCN                        | TF:M12041             | 4007  | 5.50E-06 | 69  |
| TF    | Factor: MTF-1; motif: GTGTGCANMACTTTGCGCAC             | TF:M01242             | 3492  | 5.70E-06 | 63  |
| TF    | Factor: ATF-1; motif: CYYTGACGTCA                      | TF:M00691             | 4277  | 5.80E-06 | 72  |
| TF    | Factor: Pax-6; motif: CTGACCTGGAACCTM                  | TF:M00979             | 8330  | 5.90E-06 | 114 |
| TF    | Factor: NF-1; motif: TTGGCNN                           | TF:M07364             | 4189  | 5.90E-06 | 71  |
| TF    | Factor: Sox-4; motif: AACAAA; match class: 1           | TF:M03849_1           | 7618  | 6.00E-06 | 107 |
| GO:BP | cellular response to tumor necrosis factor             | GO:0071356            | 213   | 6.10E-06 | 14  |
| REAC  | Hemostasis   | REAC:R-HSA-109582     | 570   | 6.10E-06 | 21  |
| TF    | Factor: Erg; motif: NACCGGATATCCGGTN                   | TF:M11391             | 9170  | 6.10E-06 | 122 |
| MIRNA | hsa-miR-146a-5p  | MIRNA:hsa-miR-146a-5p | 194   | 6.10E-06 | 13  |
| GO:CC | secretory granule lumen                                | GO:0034774            | 289   | 6.50E-06 | 15  |
| TF    | Factor: LKLF; motif: CNCCACCCS                         | TF:M08819             | 5105  | 6.50E-06 | 81  |
| TF    | Factor: E2F-2; motif: GCGCGCGCNCS; match class: 1      | TF:M11529_1           | 13618 | 6.50E-06 | 162 |
| GO:CC | I band   | GO:0031674            | 138   | 6.60E-06 | 11  |

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|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: Fli-1; motif: NACCGAWWTCCGGTY; match class: 1 | TF:M11399_1       | 10467 | 6.60E-06 | 134 |
| TF    | Factor: ZXDL; motif: GSGSCNNGGGMRGCNCCGGGS            | TF:M12722         | 9932  | 6.80E-06 | 129 |
| GO:CC | endoplasmic reticulum lumen                           | GO:0005788        | 291   | 7.10E-06 | 15  |
| GO:CC | cytoplasmic vesicle lumen                             | GO:0060205        | 291   | 7.10E-06 | 15  |
| TF    | Factor: T-bet; motif: NNGNRGGTGTGRN                   | TF:M10089         | 5395  | 7.10E-06 | 84  |
| TF    | Factor: E2F-4; motif: NTTTTSCGCC                      | TF:M07380         | 12143 | 7.10E-06 | 149 |
| TF    | Factor: MAZ; motif: GGGMGGGGS                         | TF:M10432         | 8669  | 7.20E-06 | 117 |
| TF    | Factor: Pax-3; motif: TCGTCACRCTTHM                   | TF:M00360         | 10921 | 7.30E-06 | 138 |
| TF    | Factor: SRY; motif: AAACWAM                           | TF:M00148         | 7951  | 7.40E-06 | 110 |
| TF    | Factor: Miz-1; motif: NNRGGWGGGGAGGGGMRR              | TF:M10112         | 8054  | 7.40E-06 | 111 |
| GO:BP | embryonic morphogenesis                               | GO:0048598        | 530   | 7.70E-06 | 21  |
| GO:CC | vesicle lumen   | GO:0031983        | 293   | 7.70E-06 | 15  |
| GO:BP | positive regulation of angiogenesis                   | GO:0045766        | 148   | 7.80E-06 | 12  |
| GO:BP | positive regulation of vasculature development        | GO:1904018        | 148   | 7.80E-06 | 12  |
| GO:BP | artery morphogenesis                                  | GO:0048844        | 67    | 8.10E-06 | 9   |
| TF    | Factor: PR; motif: RGNACATTYGTNCTN                    | TF:M10042         | 2695  | 8.20E-06 | 53  |
| TF    | Factor: NFATc2; motif: NTTTTCCRTNNAYGGAAAN            | TF:M11984         | 9531  | 8.20E-06 | 125 |
| REAC  | Smooth Muscle Contraction                             | REAC:R-HSA-445355 | 37    | 8.30E-06 | 7   |
| TF    | Factor: FOXP1; motif: TNTGTTTMY                       | TF:M09933         | 4223  | 8.30E-06 | 71  |
| TF    | Factor: TEF-3:E2A; motif: NCAGSTGNGWATGYN             | TF:M08438         | 4948  | 8.30E-06 | 79  |
| TF    | Factor: AP-2; motif: GSCSCRCRGGCNRNRNN                | TF:M00800         | 8588  | 8.50E-06 | 116 |
| TF    | Factor: PARP; motif: TTTTCYN; match class: 1          | TF:M02027_1       | 10180 | 8.50E-06 | 131 |
| GO:BP | embryonic organ development                           | GO:0048568        | 387   | 8.70E-06 | 18  |
| GO:MF | growth factor binding                                 | GO:0019838        | 130   | 8.80E-06 | 11  |
| TF    | Factor: Hey1; motif: NGCRCGYGYN                       | TF:M11058         | 12064 | 8.80E-06 | 148 |
| TF    | Factor: E2F-3:FOX11; motif: NGACACCGCGCCAC            | TF:M08208         | 11509 | 9.10E-06 | 143 |

|       |  |                      |       |          |     |
|-------|--|----------------------|-------|----------|-----|
| TF    | Factor: C-JUN:FRA-2; motif: NRTGACGTMAT                    | TF:M08941            | 5804  | 9.30E-06 | 88  |
| TF    | Factor: Pasx-5; motif: GTCACGSTT                           | TF:M04765            | 9656  | 9.30E-06 | 126 |
| GO:BP | regulation of apoptotic signaling pathway                  | GO:2001233           | 344   | 9.60E-06 | 17  |
| TF    | Factor: pax-6; motif: NYACGCNTRSRYGCNRYN                   | TF:M11883            | 12304 | 9.60E-06 | 150 |
| GO:BP | artery development   | GO:0060840           | 93    | 1.00E-05 | 10  |
| GO:BP | regulation of response to stress                           | GO:0080134           | 1192  | 1.00E-05 | 32  |
| GO:CC | supramolecular polymer                                     | GO:0099081           | 834   | 1.00E-05 | 25  |
| GO:BP | regulation of anatomical structure morphogenesis           | GO:0022603           | 878   | 1.10E-05 | 27  |
| GO:BP | myeloid leukocyte migration                                | GO:0097529           | 186   | 1.10E-05 | 13  |
| REAC  | Non-integrin membrane-ECM interactions                     | REAC:R-HSA-3000171   | 58    | 1.10E-05 | 8   |
| GO:MF | platelet-derived growth factor binding                     | GO:0048407           | 11    | 1.20E-05 | 5   |
| KEGG  | AGE-RAGE signaling pathway in diabetic complications       | KEGG:04933           | 100   | 1.20E-05 | 9   |
| TF    | Factor: SMAD3; motif: TGCTGTCT                             | TF:M00701            | 3555  | 1.20E-05 | 63  |
| TF    | Factor: pax-6; motif: NYACGCNTSANYGCNRYN                   | TF:M11881            | 11996 | 1.20E-05 | 147 |
| TF    | Factor: NFATc2; motif: NTTTTCCRTNNAYGGAAAN; match class: 1 | TF:M11984_1          | 9477  | 1.20E-05 | 124 |
| TF    | Factor: NF1C; motif: WGCCARR; match class: 1               | TF:M09763_1          | 3644  | 1.20E-05 | 64  |
| TF    | Factor: C/EBPdelta; motif: TTGCNNMAN                       | TF:M03571            | 3137  | 1.20E-05 | 58  |
| MIRNA | hsa-miR-124-3p   | MIRNA:hsa-miR-124-3p | 1393  | 1.20E-05 | 34  |
| GO:CC | myofibril  | GO:0030016           | 220   | 1.30E-05 | 13  |
| TF    | Factor: AP4; motif: NMNCAGCTGGN                            | TF:M12580            | 5085  | 1.30E-05 | 80  |
| TF    | Factor: DRRS; motif: GNNGGGWGGG                            | TF:M10056            | 4356  | 1.30E-05 | 72  |
| TF    | Factor: C/EBPalpha; motif: NRTTGTGCAAYNN                   | TF:M09596            | 4356  | 1.30E-05 | 72  |
| TF    | Factor: MafB; motif: GNTGAC; match class: 1                | TF:M01227_1          | 4179  | 1.30E-05 | 70  |
| TF    | Factor: Sp1; motif: GGGGCGGGGT                             | TF:M00008            | 9493  | 1.30E-05 | 124 |
| TF    | Factor: rax; motif: NNCRTTAN                               | TF:M10948            | 10354 | 1.30E-05 | 132 |



|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | cellular homeostasis  | GO:0019725  | 828   | 1.40E-05 | 26  |
| TF    | Factor: SREBP-1; motif: RTCRCGTGAY                                  | TF:M11081   | 9930  | 1.40E-05 | 128 |
| TF    | Factor: STAT3; motif: NNTTCCRGGGAANNNNN                             | TF:M01595   | 6729  | 1.40E-05 | 97  |
| TF    | Factor: Smad3; motif: NGNCAGACASNNN                                 | TF:M01888   | 3489  | 1.40E-05 | 62  |
| TF    | Factor: GR; motif: GGTACAANNTGTYCTK                                 | TF:M00205   | 5664  | 1.40E-05 | 86  |
| GO:BP | response to hormone   | GO:0009725  | 774   | 1.50E-05 | 25  |
| TF    | Factor: IRF-7; motif: AAGWGAA; match class: 1                       | TF:M01884_1 | 3752  | 1.50E-05 | 65  |
| TF    | Factor: SATB2; motif: GSCGCTGTCCNNGGTGCTGN                          | TF:M12660   | 5015  | 1.50E-05 | 79  |
| TF    | Factor: BCL-11A; motif: NAAAGAGGAAGTGARAN                           | TF:M09595   | 3159  | 1.60E-05 | 58  |
| TF    | Factor: Egr-1; motif: NGCGTGCGY                                     | TF:M04950   | 10165 | 1.60E-05 | 130 |
| TF    | Factor: E2F-3; HES-7; motif: NNNSGCGCSNNNNCRCCGYGNN; match class: 1 | TF:M08526_1 | 14003 | 1.60E-05 | 164 |
| TF    | Factor: Lhx2; motif: WATTAN   | TF:M07047   | 9102  | 1.60E-05 | 120 |
| GO:BP | cellular ion homeostasis  | GO:0006873  | 609   | 1.70E-05 | 22  |
| TF    | Factor: Fli-1; motif: NNRGGMAGGAAGRRRGR; match class: 1             | TF:M09920_1 | 2997  | 1.70E-05 | 56  |
| TF    | Factor: c-Myc; motif: CACGTGGC                                      | TF:M03867   | 6456  | 1.70E-05 | 94  |
| TF    | Factor: RELB; motif: NNATTCCCNN                                     | TF:M09784   | 4657  | 1.70E-05 | 75  |
| TF    | Factor: p300; motif: CTGNCTYMAN                                     | TF:M07266   | 6955  | 1.70E-05 | 99  |
| GO:BP | regulation of response to external stimulus                         | GO:0032101  | 839   | 1.80E-05 | 26  |
| GO:BP | regulation of cellular protein metabolic process                    | GO:0032268  | 2160  | 1.80E-05 | 45  |
| TF    | Factor: p300; motif: ACNTCCG; match class: 1                        | TF:M04826_1 | 14020 | 1.80E-05 | 164 |
| TF    | Factor: C/EBP; motif: NNATTGCNNAANN                                 | TF:M00190   | 4665  | 1.80E-05 | 75  |
| TF    | Factor: NF-1C; motif: NTTGGCNNNTGCCARN                              | TF:M11729   | 1469  | 1.80E-05 | 36  |
| TF    | Factor: ZNF460; motif: NNACNCCCCCANN                                | TF:M12313   | 5505  | 1.90E-05 | 84  |
| TF    | Factor: E2F-3; motif: NNGGCGGGAAA                                   | TF:M09893   | 5600  | 1.90E-05 | 85  |
| TF    | Factor: ZNF614; motif: NCYCWGCCYYNNN; match class: 1                | TF:M09862_1 | 3950  | 1.90E-05 | 67  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: AR; motif: GGNACRNNRTGTWCT                   | TF:M01201   | 5602  | 1.90E-05 | 85  |
| TF    | Factor: CHD2; motif: TCTCGCGAG                       | TF:M04710   | 12870 | 1.90E-05 | 154 |
| TF    | Factor: E2F-3; motif: GGCGGGN                        | TF:M02089   | 12418 | 2.00E-05 | 150 |
| TF    | Factor: ZF5; motif: GSGCGCGR; match class: 1         | TF:M00716_1 | 13336 | 2.00E-05 | 158 |
| TF    | Factor: SUHW1; motif: TCTCTCCAGTRTGAATTCTCTGAT       | TF:M10541   | 6086  | 2.00E-05 | 90  |
| GO:BP | response to tumor necrosis factor                    | GO:0034612  | 235   | 2.10E-05 | 14  |
| TF    | Factor: LTF; motif: GKVACTTNC                        | TF:M01692   | 3701  | 2.20E-05 | 64  |
| TF    | Factor: egr-3; motif: GTGGGY; match class: 1         | TF:M03818_1 | 5816  | 2.30E-05 | 87  |
| TF    | Factor: TFAP2A; motif: YGCCNNRGGCN                   | TF:M04146   | 6009  | 2.30E-05 | 89  |
| TF    | Factor: Smad2; motif: TGTCTGNCWCCT                   | TF:M10059   | 5342  | 2.30E-05 | 82  |
| TF    | Factor: E2A; motif: CACCTGNY                         | TF:M00973   | 4692  | 2.30E-05 | 75  |
| TF    | Factor: RAR-gamma; motif: RGGTCANNNTGNCCNNNN         | TF:M10045   | 6400  | 2.30E-05 | 93  |
| TF    | Factor: Kaiso; motif: GCMGGGRGCRGS; match class: 1   | TF:M03876_1 | 8628  | 2.30E-05 | 115 |
| TF    | Factor: PBX2; motif: TGANTGACAGN                     | TF:M09736   | 4240  | 2.40E-05 | 70  |
| GO:BP | response to transforming growth factor beta          | GO:0071559  | 238   | 2.50E-05 | 14  |
| TF    | Factor: ZNF462; motif: YYYCTSCWG; match class: 1     | TF:M12707_1 | 3033  | 2.50E-05 | 56  |
| TF    | Factor: RUNX2; motif: WRACCGCANWAACCGCAN             | TF:M04107   | 11232 | 2.60E-05 | 139 |
| TF    | Factor: ZXDL; motif: NGGGWS; match class: 1          | TF:M05775_1 | 1561  | 2.60E-05 | 37  |
| GO:CC | anchoring junction                                   | GO:0070161  | 815   | 2.70E-05 | 24  |
| TF    | Factor: RBPJK; motif: NSNSTGGGAAN                    | TF:M10085   | 3038  | 2.70E-05 | 56  |
| TF    | Factor: ZNF592; motif: NSARNATGGAGKN; match class: 1 | TF:M09766_1 | 1421  | 2.70E-05 | 35  |
| TF    | Factor: Sp1; motif: GGNDGGRGGCGGGG                   | TF:M04953   | 8128  | 2.70E-05 | 110 |
| TF    | Factor: E2F-1; motif: NTTTTGGCGCCAWWWW               | TF:M11533   | 12131 | 2.70E-05 | 147 |
| TF    | Factor: ITF-2; motif: NGCAGSTGKS                     | TF:M09962   | 4254  | 2.70E-05 | 70  |
| TF    | Factor: HEB; motif: RCCWGCTG                         | TF:M00698   | 2470  | 2.70E-05 | 49  |
| TF    | Factor: SRY; motif: AACAAATANCATTGTT                 | TF:M04555   | 5745  | 2.80E-05 | 86  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | cellular chemical homeostasis                         | GO:0055082  | 741   | 2.90E-05 | 24  |
| GO:BP | epithelial cell proliferation                         | GO:0050673  | 371   | 2.90E-05 | 17  |
| TF    | Factor: ZNF148; motif: NNCCCTCCCC                     | TF:M12464   | 6431  | 3.00E-05 | 93  |
| GO:BP | intrinsic apoptotic signaling pathway                 | GO:0097193  | 283   | 3.10E-05 | 15  |
| TF    | Factor: SATB1; motif: NTTTTAT; match class: 1         | TF:M03564_1 | 10054 | 3.10E-05 | 128 |
| TF    | Factor: Gscl; motif: NTAATCCN                         | TF:M10924   | 5762  | 3.20E-05 | 86  |
| TF    | Factor: BRCA1:USF2; motif: KTNNGTTG                   | TF:M01082   | 6054  | 3.30E-05 | 89  |
| TF    | Factor: TEF-3:C/EBPbeta; motif: RTTGCGYAYNNNNNGGAATGY | TF:M08626   | 5958  | 3.30E-05 | 88  |
| TF    | Factor: GATA-1; motif: SNNGATNNNN                     | TF:M00075   | 6252  | 3.40E-05 | 91  |
| TF    | Factor: ZIC4; motif: NNCCNCCCRYNGYGN                  | TF:M12227   | 10284 | 3.40E-05 | 130 |
| TF    | Factor: ipf1; motif: TGATTGATK                        | TF:M10031   | 7448  | 3.50E-05 | 103 |
| TF    | Factor: HES-7; motif: GNCACGYGNN                      | TF:M11066   | 10511 | 3.60E-05 | 132 |
| TF    | Factor: C/EBPbeta; motif: RTTGCGCAA                   | TF:M04690   | 3752  | 3.70E-05 | 64  |
| TF    | Factor: Erg; motif: MCAGGAAA; match class: 1          | TF:M07284_1 | 3752  | 3.70E-05 | 64  |
| TF    | Factor: Egr-2; motif: CCCMCNCN                        | TF:M02092   | 4289  | 3.80E-05 | 70  |
| TF    | Factor: Erm:C/EBPdelta; motif: RSCGAWRTTGCGYAY        | TF:M08458   | 8491  | 3.80E-05 | 113 |
| TF    | Factor: BTEB4; motif: NCCACGCCCM                      | TF:M12186   | 8491  | 3.80E-05 | 113 |
| GO:CC | secretory granule membrane                            | GO:0030667  | 287   | 4.10E-05 | 14  |
| KEGG  | PI3K-Akt signaling pathway                            | KEGG:04151  | 319   | 4.10E-05 | 14  |
| TF    | Factor: PLAG1; motif: CCCCCKWNNNGGSCCC                | TF:M01973   | 5790  | 4.10E-05 | 86  |
| TF    | Factor: HOXA3; motif: NNNNRNTAATTARY; match class: 1  | TF:M01337_1 | 10095 | 4.10E-05 | 128 |
| TF    | Factor: AP-2beta; motif: NSCCNNNGGSN                  | TF:M11478   | 9237  | 4.10E-05 | 120 |
| GO:BP | cellular metal ion homeostasis                        | GO:0006875  | 531   | 4.20E-05 | 20  |
| TF    | Factor: C/EBPalpha; motif: NNNTTNNNGCAANN             | TF:M01866   | 4299  | 4.20E-05 | 70  |
| TF    | Factor: ZEB1; motif: CAGGTGN                          | TF:M04831   | 6971  | 4.20E-05 | 98  |
| TF    | Factor: TFIIB; motif: YTNTMTGMSN                      | TF:M08904   | 5698  | 4.20E-05 | 85  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: AP-4; motif: YCAGCTGNKN                           | TF:M10097   | 5226  | 4.30E-05 | 80  |
| TF    | Factor: MZF-1; motif: TGGGGAR; match class: 1             | TF:M01733_1 | 4394  | 4.30E-05 | 71  |
| TF    | Factor: Sp1; motif: NGGGGCGGGN                            | TF:M07395   | 10215 | 4.40E-05 | 129 |
| TF    | Factor: TEAD1; motif: NNACATTCCAGNN                       | TF:M12500   | 5045  | 4.60E-05 | 78  |
| GO:BP | regulation of cellular biosynthetic process               | GO:0031326  | 3648  | 4.70E-05 | 62  |
| TF    | Factor: XBP-1; motif: WNNGMCACGTC                         | TF:M01770   | 9900  | 4.70E-05 | 126 |
| TF    | Factor: AP-2; motif: NNGCCTK                              | TF:M01859   | 6687  | 4.70E-05 | 95  |
| TF    | Factor: NFATc1; motif: TTTTCCATGGAAAN                     | TF:M04053   | 7187  | 4.70E-05 | 100 |
| TF    | Factor: RARG; motif: RAGGTCAASYARAGGTCA                   | TF:M04485   | 4222  | 4.70E-05 | 69  |
| GO:BP | negative regulation of apoptotic signaling pathway        | GO:2001234  | 211   | 4.80E-05 | 13  |
| GO:BP | regulation of cytokine production                         | GO:0001817  | 646   | 4.90E-05 | 22  |
| TF    | Factor: Nfe2l1; motif: TGYNNAGTCATT                       | TF:M07390   | 5626  | 5.10E-05 | 84  |
| GO:BP | negative regulation of cellular protein metabolic process | GO:0032269  | 885   | 5.20E-05 | 26  |
| TF    | Factor: Tbx3; motif: NRAGGTGNNAR                          | TF:M10090   | 4322  | 5.20E-05 | 70  |
| GO:BP | chemical homeostasis                                      | GO:0048878  | 1078  | 5.30E-05 | 29  |
| GO:BP | positive regulation of cell death                         | GO:0010942  | 539   | 5.40E-05 | 20  |
| TF    | Factor: Flt-1:E2A; motif: NCCGAWRCASCTGN                  | TF:M08472   | 7411  | 5.50E-05 | 102 |
| TF    | Factor: ZNF383; motif: SSNGGGMGGNSNGGS                    | TF:M12703   | 8544  | 5.50E-05 | 113 |
| TF    | Factor: E2F-4; motif: SNGGGCGGAANN; match class: 1        | TF:M09894_1 | 13166 | 5.50E-05 | 155 |
| TF    | Factor: RXRALPHA; motif: CNNTGRCCTYNN                     | TF:M09833   | 4604  | 5.60E-05 | 73  |
| TF    | Factor: MLR1; motif: NTGNMCYYTGNNCYN                      | TF:M12637   | 3795  | 5.70E-05 | 64  |
| TF    | Factor: ZF5; motif: GGSGCGGS; match class: 1              | TF:M10438_1 | 13986 | 5.70E-05 | 162 |
| GO:BP | lymphocyte activation                                     | GO:0046649  | 652   | 5.80E-05 | 22  |
| GO:BP | cytokine production                                       | GO:0001816  | 652   | 5.80E-05 | 22  |
| GO:BP | cellular cation homeostasis                               | GO:0030003  | 596   | 5.80E-05 | 21  |
| GO:BP | chordate embryonic development                            | GO:0043009  | 596   | 5.80E-05 | 21  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: Erm; motif: NRRSAGGAARNGRN; match class: 1 | TF:M09916_1 | 1466  | 5.80E-05 | 35  |
| GO:BP | cell chemotaxis                                    | GO:0060326  | 255   | 6.00E-05 | 14  |
| GO:BP | morphogenesis of an epithelium                     | GO:0002009  | 490   | 6.00E-05 | 19  |
| TF    | Factor: CREB1; motif: NNNSSGGCGCSSNNNNRTGACGTCA C  | TF:M12591   | 12377 | 6.00E-05 | 148 |
| TF    | Factor: Pax-6; motif: TTTCACGCWGTGANTGMNYN         | TF:M04065   | 9085  | 6.10E-05 | 118 |
| TF    | Factor: BTEB2; motif: RGGNGKGGN                    | TF:M07277   | 8145  | 6.20E-05 | 109 |
| TF    | Factor: Nrf-2; motif: NTGCTGAGTCAKN                | TF:M00821   | 3984  | 6.30E-05 | 66  |
| TF    | Factor: KLF15; motif: RCCMCRCCCMCN; match class: 1 | TF:M12160_1 | 7532  | 6.30E-05 | 103 |
| GO:MF | cytokine binding                                   | GO:0019955  | 124   | 6.50E-05 | 10  |
| TF    | Factor: IRF-8; motif: NYGAAACYGAAACTN              | TF:M11684   | 3986  | 6.50E-05 | 66  |
| TF    | Factor: E2F-2; motif: NWTGCGCCAWWNN                | TF:M11530   | 13542 | 6.50E-05 | 158 |
| TF    | Factor: IRF-8; motif: AGTTTCW                      | TF:M01665   | 3988  | 6.60E-05 | 66  |
| TF    | Factor: LRF; motif: NRRGGKCKY                      | TF:M10115   | 6932  | 6.60E-05 | 97  |
| TF    | Factor: SPI1; motif: AGGAAGT                       | TF:M02278   | 5850  | 6.60E-05 | 86  |
| TF    | Factor: Fli-1; motif: MGGAAGT                      | TF:M07382   | 5850  | 6.60E-05 | 86  |
| TF    | Factor: PEA3; motif: AGGAAGT                       | TF:M03579   | 5850  | 6.60E-05 | 86  |
| TF    | Factor: C-ets-1; motif: AGGAAGN                    | TF:M01870   | 5850  | 6.60E-05 | 86  |
| GO:BP | response to peptide                                | GO:1901652  | 442   | 6.70E-05 | 18  |
| TF    | Factor: Six-2; motif: NCGTATCRNN                   | TF:M11031   | 7846  | 6.70E-05 | 106 |
| GO:MF | molecular transducer activity                      | GO:0060089  | 1139  | 6.80E-05 | 29  |
| GO:MF | signaling receptor activity                        | GO:0038023  | 1139  | 6.80E-05 | 29  |
| TF    | Factor: SRY; motif: TCAATAMCATTGA                  | TF:M04557   | 8365  | 6.80E-05 | 111 |
| TF    | Factor: SREBP-2; motif: NTCACCYNNNN                | TF:M03852   | 7238  | 6.80E-05 | 100 |
| TF    | Factor: Ikaros; motif: TGGGAGN; match class: 1     | TF:M07260_1 | 6245  | 6.90E-05 | 90  |
| GO:BP | muscle system process                              | GO:0003012  | 394   | 7.00E-05 | 17  |
| GO:BP | immune system development                          | GO:0002520  | 899   | 7.00E-05 | 26  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: AP-2beta; motif: GCNNNGGSCNGVGGGN                  | TF:M01858   | 7042  | 7.10E-05 | 98  |
| TF    | Factor: MafA; motif: GGTCAGCAGH                            | TF:M03796   | 2710  | 7.20E-05 | 51  |
| GO:BP | positive regulation of cell migration                      | GO:0030335  | 496   | 7.30E-05 | 19  |
| TF    | Factor: E2F-1; motif: NNNNGGCGGGAARN                       | TF:M09892   | 12641 | 7.40E-05 | 150 |
| TF    | Factor: E2F-3; motif: NTTTTGGCGCCAAAAN                     | TF:M11527   | 6161  | 7.70E-05 | 89  |
| TF    | Factor: ZNF333; motif: ATAAT; match class: 1               | TF:M01230_1 | 9656  | 7.80E-05 | 123 |
| TF    | Factor: RXR:RAR; motif: RGKTCANNNRGAGGTCA                  | TF:M02272   | 5486  | 7.80E-05 | 82  |
| GO:BP | negative regulation of catalytic activity                  | GO:0043086  | 607   | 7.90E-05 | 21  |
| KEGG  | Protein digestion and absorption                           | KEGG:04974  | 92    | 8.00E-05 | 8   |
| TF    | Factor: Spz1; motif: DNNGGRGGWVNNNN; match class: 1        | TF:M00446_1 | 2638  | 8.10E-05 | 50  |
| GO:BP | ion homeostasis  | GO:0050801  | 723   | 8.20E-05 | 23  |
| GO:BP | transforming growth factor beta receptor signaling pathway | GO:0007179  | 183   | 8.40E-05 | 12  |
| TF    | Factor: c-Jun; motif: NATGACGTCAYN                         | TF:M11266   | 7368  | 8.40E-05 | 101 |
| TF    | Factor: CEBPD; motif: NNTGACAAAYNN                         | TF:M12567   | 1780  | 8.40E-05 | 39  |
| GO:BP | regulation of biosynthetic process                         | GO:0009889  | 3706  | 8.50E-05 | 62  |
| GO:BP | hematopoietic or lymphoid organ development                | GO:0048534  | 846   | 8.60E-05 | 25  |
| TF    | Factor: BRN1; motif: HAATGCN; match class: 1               | TF:M03813_1 | 5787  | 8.70E-05 | 85  |
| TF    | Factor: Erm; motif: RSAGGAAGGAAGTN                         | TF:M11423   | 4288  | 8.80E-05 | 69  |
| TF    | Factor: HELIOS; motif: RNARRRGGAASTGARAN                   | TF:M09745   | 2894  | 9.00E-05 | 53  |
| TF    | Factor: IRF-4; motif: NYGAAASYGAAACYN                      | TF:M11686   | 2895  | 9.10E-05 | 53  |
| GO:BP | negative regulation of signal transduction                 | GO:0009968  | 1173  | 9.20E-05 | 30  |
| TF    | Factor: pax-6; motif: NYACGCWTSANYGMNCN                    | TF:M11880   | 11884 | 9.20E-05 | 143 |
| TF    | Factor: p53; motif: RGRCWWGYCYNGRCWWGYYY                   | TF:M01652   | 7281  | 9.30E-05 | 100 |
| TF    | Factor: ARP-1; motif: TGARCCYTTGAMCCCW                     | TF:M00155   | 4662  | 9.40E-05 | 73  |
| TF    | Factor: MIBP1; motif: WNWCCCCAGCTR                         | TF:M03878   | 2488  | 9.40E-05 | 48  |
| TF    | Factor: Oct-1; motif: MKVATTTGCATATT                       | TF:M00161   | 2408  | 9.50E-05 | 47  |

|       |   |                    |       |          |     |
|-------|---|--------------------|-------|----------|-----|
| TF    | Factor: Sox-10; motif: NACAAWG; match class: 1                      | TF:M02116_1        | 6582  | 9.50E-05 | 93  |
| GO:BP | embryo development ending in birth or egg hatching                  | GO:0009792         | 614   | 9.60E-05 | 21  |
| TF    | Factor: CTF/NF1; motif: TTGGCN; match class: 1                      | TF:M02050_1        | 3413  | 9.90E-05 | 59  |
| TF    | Factor: FOXP3; motif: NNNVAAACANWD                                  | TF:M07419          | 5230  | 9.90E-05 | 79  |
| TF    | Factor: HMX2; motif: SCACTTANC                                      | TF:M10646          | 6195  | 1.00E-04 | 89  |
| GO:MF | interleukin-1 receptor activity                                     | GO:0004908         | 7     | 1.10E-04 | 4   |
| TF    | Factor: E2F; motif: TTTSGCGS  | TF:M00426          | 11014 | 1.10E-04 | 135 |
| TF    | Factor: TCF-1; motif: ACATCGRGRCCGTGW                               | TF:M11601          | 13629 | 1.10E-04 | 158 |
| TF    | Factor: E2F-1; motif: WWTGGCGCCAAA                                  | TF:M04515          | 12480 | 1.10E-04 | 148 |
| GO:BP | response to oxidative stress  | GO:0006979         | 409   | 1.20E-04 | 17  |
| GO:BP | mesangial cell development  | GO:0072143         | 6     | 1.20E-04 | 4   |
| REAC  | Scavenging by Class A Receptors                                     | REAC:R-HSA-3000480 | 18    | 1.20E-04 | 5   |
| TF    | Factor: Pax-8; motif: NCNNTNNTGCRTGANNNN                            | TF:M00328          | 8029  | 1.20E-04 | 107 |
| TF    | Factor: FXR; motif: NRGGKANTGRCCNNNNNGG                             | TF:M10014          | 5159  | 1.20E-04 | 78  |
| TF    | Factor: Oct-2; motif: NYATGCAAATN                                   | TF:M10034          | 5065  | 1.20E-04 | 77  |
| TF    | Factor: ZBTB49; motif: NGSCGCTGTCCNNGGTGCTGAN                       | TF:M12692          | 1957  | 1.20E-04 | 41  |
| REAC  | Erythrocytes take up oxygen and release carbon dioxide              | REAC:R-HSA-1247673 | 8     | 1.30E-04 | 4   |
| TF    | Factor: E2F-1:Elk-1; motif: SGGCSNNAMCGGAAGT                        | TF:M08205          | 13426 | 1.30E-04 | 156 |
| TF    | Factor: Pax-5; motif: BCNNNRNGCANBGNTGNRTAGCSGC HNB; match class: 1 | TF:M00143_1        | 4608  | 1.30E-04 | 72  |
| TF    | Factor: PPARGAMMA; motif: NWNTRGGTYANN                              | TF:M08961          | 4518  | 1.30E-04 | 71  |
| GO:BP | positive regulation of cell motility                                | GO:2000147         | 516   | 1.40E-04 | 19  |
| GO:BP | muscle contraction  | GO:0006936         | 317   | 1.40E-04 | 15  |
| GO:BP | regulation of protein metabolic process                             | GO:0051246         | 2316  | 1.40E-04 | 45  |
| GO:CC | supramolecular fiber  | GO:0099512         | 826   | 1.40E-04 | 23  |
| TF    | Factor: NF-1B; motif: KCCAGANWN                                     | TF:M08825          | 4990  | 1.40E-04 | 76  |

|       |   |                      |      |          |     |
|-------|---|----------------------|------|----------|-----|
| TF    | Factor: RelB:p50; motif: RGAAANTCCCYNNHGC                       | TF:M03882            | 3891 | 1.40E-04 | 64  |
| TF    | Factor: E2F-2; motif: NTTTTGGCGCCAWWWW                          | TF:M11528            | 9539 | 1.40E-04 | 121 |
| GO:BP | cellular response to transforming growth factor beta stimulus   | GO:0071560           | 232  | 1.50E-04 | 13  |
| GO:BP | leukocyte chemotaxis  | GO:0030595           | 193  | 1.50E-04 | 12  |
| GO:BP | granulocyte migration   | GO:0097530           | 123  | 1.50E-04 | 10  |
| GO:BP | epithelial cell differentiation involved in kidney development  | GO:0035850           | 45   | 1.50E-04 | 7   |
| KEGG  | Complement and coagulation cascades                             | KEGG:04610           | 70   | 1.50E-04 | 7   |
| TF    | Factor: Sp2; motif: GGGGCGGGG                                   | TF:M10435            | 7447 | 1.50E-04 | 101 |
| TF    | Factor: TF3C-beta; motif: CCNGGAGGGCTTCTGGAGGAG; match class: 1 | TF:M04863_1          | 7966 | 1.50E-04 | 106 |
| TF    | Factor: Fli-1:HOXB13; motif: NNCGGAARYNRTWAA                    | TF:M08471            | 4441 | 1.50E-04 | 70  |
| TF    | Factor: NF-1; motif: NTGGNNNNNNGCCAANN                          | TF:M00806            | 3720 | 1.50E-04 | 62  |
| TF    | Factor: PU.1; motif: NRAAAGAGGAAGTGARA                          | TF:M09659            | 2208 | 1.50E-04 | 44  |
| TF    | Factor: AP-2gamma; motif: NSCCYNNRGSN                           | TF:M11482            | 6252 | 1.50E-04 | 89  |
| TF    | Factor: ehf; motif: NRANNAGGAARNRRNNN                           | TF:M09604            | 1976 | 1.60E-04 | 41  |
| TF    | Factor: HOXB5; motif: GTCATTAN                                  | TF:M10701            | 4817 | 1.60E-04 | 74  |
| TF    | Factor: PEA3; motif: NTCGTAAATGCA                               | TF:M11431            | 9024 | 1.60E-04 | 116 |
| TF    | Factor: AR; motif: NNNGNRRGNACANNGTGTTCTNNNNN N                 | TF:M00953            | 1978 | 1.60E-04 | 41  |
| TF    | Factor: Olf-1; motif: NNCDABTCCCYAGRGARBKGN                     | TF:M00261            | 3203 | 1.60E-04 | 56  |
| TF    | Factor: MAZ; motif: GGGGAGGG; match class: 1                    | TF:M00649_1          | 3905 | 1.60E-04 | 64  |
| TF    | Factor: SREBP-1; motif: KATCACCCAC                              | TF:M00221            | 6557 | 1.60E-04 | 92  |
| MIRNA | hsa-miR-29a-3p  | MIRNA:hsa-miR-29a-3p | 256  | 1.60E-04 | 13  |
| TF    | Factor: C/EBPgamma:Elf-1; motif: TKRCGHAATWSCGGAAGT             | TF:M08676            | 7465 | 1.70E-04 | 101 |
| TF    | Factor: NF-KAPPAB1; motif: NGGKRNTTYCCCN; match class: 1        | TF:M08952_1          | 3120 | 1.70E-04 | 55  |
| TF    | Factor: TFII-I; motif: RGAGGKAGG; match class: 1                | TF:M00706_1          | 1461 | 1.70E-04 | 34  |
| TF    | Factor: ESR1; motif: NNNNMAGGTACCCCTGACCY                       | TF:M02261            | 4090 | 1.70E-04 | 66  |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| TF    | Factor: AP-2gamma; motif: GCCYNCRGSN; match class: 1    | TF:M03811_1        | 3646 | 1.80E-04 | 61  |
| TF    | Factor: POU2F1; motif: ATTTGCATN                        | TF:M07058          | 2707 | 1.80E-04 | 50  |
| GO:MF | integrin binding  | GO:0005178         | 139  | 1.90E-04 | 10  |
| GO:BP | regulation of intrinsic apoptotic signaling pathway     | GO:2001242         | 160  | 1.90E-04 | 11  |
| GO:BP | negative regulation of protein metabolic process        | GO:0051248         | 947  | 1.90E-04 | 26  |
| TF    | Factor: CTF1; motif: TGGCASCNNGCCAA; match class: 1     | TF:M01196_1        | 1324 | 1.90E-04 | 32  |
| TF    | Factor: ER-beta; motif: RGGTCASCNTGMCCY; match class: 1 | TF:M09910_1        | 3740 | 1.90E-04 | 62  |
| TF    | Factor: C/EBPbeta; motif: RTTGCGCAA; match class: 1     | TF:M04690_1        | 3216 | 1.90E-04 | 56  |
| TF    | Factor: Gli2; motif: GACCACCCANG                        | TF:M01703          | 3303 | 1.90E-04 | 57  |
| TF    | Factor: Sp1; motif: NGGGGGCGGGCCNGGGGGGGG               | TF:M10071          | 8206 | 1.90E-04 | 108 |
| TF    | Factor: znf136; motif: CAAGAATWCTATAYCCAG               | TF:M10535          | 6878 | 1.90E-04 | 95  |
| GO:BP | epithelial cell apoptotic process                       | GO:1904019         | 96   | 2.00E-04 | 9   |
| GO:BP | positive regulation of cellular component movement      | GO:0051272         | 529  | 2.00E-04 | 19  |
| GO:BP | positive regulation of locomotion                       | GO:0040017         | 530  | 2.00E-04 | 19  |
| REAC  | Signaling by Receptor Tyrosine Kinases                  | REAC:R-HSA-9006934 | 472  | 2.00E-04 | 17  |
| TF    | Factor: TEF-1; motif: GRRATG; match class: 1            | TF:M00704_1        | 4564 | 2.00E-04 | 71  |
| GO:BP | kidney development                                      | GO:0001822         | 282  | 2.10E-04 | 14  |
| GO:BP | pattern specification process                           | GO:0007389         | 376  | 2.10E-04 | 16  |
| TF    | Factor: Lhx8; motif: TGATTG                             | TF:M07476          | 7600 | 2.10E-04 | 102 |
| TF    | Factor: Freac-7; motif: WNNANATAAAAYANNNN               | TF:M00293          | 3753 | 2.10E-04 | 62  |
| TF    | Factor: C/EBPalpha; motif: NRTTGTGCAAYN                 | TF:M09880          | 2890 | 2.20E-04 | 52  |
| TF    | Factor: Dlx-5; motif: AATTAN                            | TF:M03546          | 9177 | 2.20E-04 | 117 |
| TF    | Factor: DRI1; motif: AATTAA                             | TF:M01654          | 9177 | 2.20E-04 | 117 |
| TF    | Factor: AP-2; motif: SNNCCNCAGGCN; match class: 1       | TF:M00915_1        | 4390 | 2.20E-04 | 69  |
| TF    | Factor: AHR; motif: CACGCN                              | TF:M01855          | 7712 | 2.20E-04 | 103 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: nerf; motif: YRNCAGGAAGYRGSTBDS; match class: 1 | TF:M00531_1 | 1624  | 2.30E-04 | 36  |
| TF    | Factor: CRX; motif: YTAATC; match class: 1              | TF:M01712_1 | 4120  | 2.30E-04 | 66  |
| TF    | Factor: AR; motif: AGWACATNWTGTCT                       | TF:M00447   | 3496  | 2.30E-04 | 59  |
| TF    | Factor: C-FOS; motif: NNNKATGACGTCATNNN                 | TF:M08947   | 5921  | 2.50E-04 | 85  |
| TF    | Factor: HOXA7; motif: GYMATTAN                          | TF:M10690   | 8983  | 2.50E-04 | 115 |
| TF    | Factor: TCF-1; motif: ACATCGRGRGCTGW; match class: 1    | TF:M11603_1 | 12396 | 2.50E-04 | 146 |
| TF    | Factor: HOXD4; motif: NNYMATTANN                        | TF:M08774   | 3332  | 2.50E-04 | 57  |
| GO:BP | neutrophil migration                                    | GO:1990266  | 99    | 2.60E-04 | 9   |
| TF    | Factor: Sox-10; motif: CWTTGT; match class: 1           | TF:M03138_1 | 5442  | 2.60E-04 | 80  |
| TF    | Factor: TCF-1; motif: CTTTGW; match class: 1            | TF:M03857_1 | 5442  | 2.60E-04 | 80  |
| TF    | Factor: C/EBPgamma; motif: YTBATTTCARAAW                | TF:M00622   | 5635  | 2.60E-04 | 82  |
| TF    | Factor: Elf-1; motif: RNWMBAGGAART                      | TF:M00746   | 2905  | 2.60E-04 | 52  |
| TF    | Factor: E2F-1; motif: TTTGGCGCCAAA                      | TF:M04516   | 10723 | 2.60E-04 | 131 |
| TF    | Factor: LRF; motif: NGNAGNGGGTYN                        | TF:M04617   | 5639  | 2.60E-04 | 82  |
| GO:CC | non-membrane-bounded organelle                          | GO:0043228  | 4977  | 2.70E-04 | 72  |
| GO:CC | intracellular non-membrane-bounded organelle            | GO:0043232  | 4977  | 2.70E-04 | 72  |
| TF    | Factor: MAF; motif: GCTGAGTCAN                          | TF:M07296   | 4877  | 2.70E-04 | 74  |
| TF    | Factor: BTEB1; motif: GGGGGCGGGCNGSGGGNGS               | TF:M09723   | 9530  | 2.70E-04 | 120 |
| TF    | Factor: FOXM1; motif: NAGASTGATTA                       | TF:M04611   | 7843  | 2.70E-04 | 104 |
| TF    | Factor: AR; motif: GNCCNNNTGTTCTN                       | TF:M01996   | 2495  | 2.70E-04 | 47  |
| GO:BP | regulation of cell activation                           | GO:0050865  | 541   | 2.80E-04 | 19  |
| GO:BP | granulocyte chemotaxis                                  | GO:0071621  | 100   | 2.80E-04 | 9   |
| TF    | Factor: RBPJK; motif: SYGTGRGAANN                       | TF:M09665   | 3871  | 2.80E-04 | 63  |
| TF    | Factor: B-ATF; motif: NNATGACACN                        | TF:M11300   | 7440  | 2.80E-04 | 100 |
| TF    | Factor: Rarb; motif: AGGTCANNYARAGTCA                   | TF:M08035   | 4979  | 2.80E-04 | 75  |
| GO:BP | mesangial cell differentiation                          | GO:0072007  | 7     | 2.90E-04 | 4   |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| KEGG  | IL-17 signaling pathway                                | KEGG:04657  | 77    | 2.90E-04 | 7   |
| TF    | Factor: NKX25; motif: NNANCCACTTRAAWTT                 | TF:M01414   | 8271  | 2.90E-04 | 108 |
| TF    | Factor: RREB-1; motif: CCCCAAACMMCCCC; match class: 1  | TF:M00257_1 | 4057  | 2.90E-04 | 65  |
| TF    | Factor: NF-kappaB; motif: GGGAMTTYCC                   | TF:M00054   | 2179  | 2.90E-04 | 43  |
| GO:BP | regulation of epithelial cell apoptotic process        | GO:1904035  | 73    | 3.00E-04 | 8   |
| TF    | Factor: LBX2; motif: CTNRANSTAATTA                     | TF:M04383   | 6738  | 3.00E-04 | 93  |
| TF    | Factor: AR; motif: NGNACANNNTGTTYNN; match class: 1    | TF:M09589_1 | 945   | 3.00E-04 | 26  |
| GO:BP | metal ion homeostasis                                  | GO:0055065  | 601   | 3.10E-04 | 20  |
| GO:BP | defense response to other organism                     | GO:0098542  | 842   | 3.10E-04 | 24  |
| TF    | Factor: E2F-3; motif: NTTTTGGCGCCAAAAN; match class: 1 | TF:M11527_1 | 5953  | 3.10E-04 | 85  |
| GO:BP | organonitrogen compound metabolic process              | GO:1901564  | 5820  | 3.20E-04 | 83  |
| GO:BP | nephron development                                    | GO:0072006  | 133   | 3.20E-04 | 10  |
| TF    | Factor: Tbx3; motif: NAGGTGTSAN                        | TF:M12024   | 3800  | 3.30E-04 | 62  |
| TF    | Factor: NKX2-2; motif: NNNCCACTCAANN; match class: 1   | TF:M12456_1 | 2512  | 3.30E-04 | 47  |
| GO:BP | supramolecular fiber organization                      | GO:0097435  | 722   | 3.40E-04 | 22  |
| TF    | Factor: GKLF; motif: GCCMCRCCNNN                       | TF:M01588   | 8294  | 3.40E-04 | 108 |
| TF    | Factor: RXRA; motif: RRGTCATGACCYY; match class: 1     | TF:M04490_1 | 3016  | 3.40E-04 | 53  |
| TF    | Factor: E2F-2; motif: NWTTCGGCGCCAWWNN; match class: 1 | TF:M11530_1 | 12570 | 3.50E-04 | 147 |
| TF    | Factor: TGIF; motif: TGACAGS                           | TF:M10101   | 4444  | 3.50E-04 | 69  |
| TF    | Factor: ZNF394; motif: NRARWRGAANNAMWGNAAK             | TF:M10147   | 4537  | 3.50E-04 | 70  |
| TF    | Factor: GLI; motif: NGACCMCCCAN; match class: 1        | TF:M07290_1 | 1730  | 3.60E-04 | 37  |
| TF    | Factor: EGR3; motif: NCMCRCCCACTNMN                    | TF:M08877   | 5486  | 3.60E-04 | 80  |
| TF    | Factor: WT1; motif: NNGGGNGGGSGN                       | TF:M07436   | 6072  | 3.70E-04 | 86  |
| TF    | Factor: CTCF; motif: NNYGCCCYCTRSTGGN                  | TF:M09744   | 3458  | 3.70E-04 | 58  |
| TF    | Factor: AP-4; motif: NCAGCTGYNGNCN                     | TF:M01860   | 5298  | 3.70E-04 | 78  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: PPARalpha; motif: NWSTRGGNSAAAGTCA                 | TF:M10037   | 5298  | 3.70E-04 | 78  |
| GO:BP | mesenchyme morphogenesis                                   | GO:0072132  | 51    | 3.80E-04 | 7   |
| TF    | Factor: EVX1; motif: NTCATTAN                              | TF:M10864   | 4360  | 3.80E-04 | 68  |
| TF    | Factor: SNA; motif: NNRGCAGGTGCNNNN                        | TF:M10528   | 3905  | 3.80E-04 | 63  |
| TF    | Factor: T3R-beta; motif: NRGGTCAAAGGTCRN; match class: 1   | TF:M11814_1 | 6374  | 3.80E-04 | 89  |
| TF    | Factor: Pax-3; motif: NNNNNNCGTCACGSTYNNNNN                | TF:M00327   | 11907 | 3.80E-04 | 141 |
| GO:MF | cytokine receptor activity                                 | GO:0004896  | 85    | 3.90E-04 | 8   |
| GO:BP | cellular divalent inorganic cation homeostasis             | GO:0072503  | 444   | 3.90E-04 | 17  |
| TF    | Factor: ZXDA; motif: NGGGGTC                               | TF:M06190   | 5303  | 3.90E-04 | 78  |
| TF    | Factor: ZXDB; motif: NGGGGTC                               | TF:M06191   | 5303  | 3.90E-04 | 78  |
| KEGG  | ECM-receptor interaction                                   | KEGG:04512  | 81    | 4.00E-04 | 7   |
| TF    | Factor: ER-beta; motif: NRGGTCANKSTGACCTNN; match class: 1 | TF:M09610_1 | 1369  | 4.00E-04 | 32  |
| TF    | Factor: NF-E4; motif: GTGAGGS; match class: 1              | TF:M08826_1 | 4182  | 4.00E-04 | 66  |
| TF    | Factor: Oct-1; motif: TATGCAATN                            | TF:M00342   | 2446  | 4.00E-04 | 46  |
| TF    | Factor: ZNF563; motif: NGNNTCMTNCCNGGCAGCTGY               | TF:M10158   | 5212  | 4.00E-04 | 77  |
| TF    | Factor: HEY1; motif: NYYYATCTNN                            | TF:M12614   | 4742  | 4.10E-04 | 72  |
| TF    | Factor: EAR2; motif: YGNNTTTGNCCTK                         | TF:M01728   | 5407  | 4.10E-04 | 79  |
| GO:BP | cation homeostasis   | GO:0055080  | 671   | 4.20E-04 | 21  |
| TF    | Factor: C/EBPbeta; motif: NNTTKCNMAN                       | TF:M07315   | 2449  | 4.20E-04 | 46  |
| TF    | Factor: Elk-1; motif: ANSCGGACGGATDTCGGNT                  | TF:M08214   | 7191  | 4.20E-04 | 97  |
| GO:BP | macromolecule metabolic process                            | GO:0043170  | 9254  | 4.30E-04 | 116 |
| GO:BP | positive regulation of cellular biosynthetic process       | GO:0031328  | 1776  | 4.30E-04 | 37  |
| KEGG  | African trypanosomiasis                                    | KEGG:05143  | 31    | 4.30E-04 | 5   |
| TF    | Factor: C/EBPalpha; motif: NNNNNTTKCNNAAN                  | TF:M07037   | 2783  | 4.30E-04 | 50  |
| GO:MF | cell adhesion molecule binding                             | GO:0050839  | 535   | 4.40E-04 | 18  |
| GO:MF | molecular function regulator                               | GO:0098772  | 1692  | 4.40E-04 | 35  |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| GO:BP | T cell activation   | GO:0042110         | 448  | 4.40E-04 | 17  |
| GO:BP | response to abiotic stimulus  | GO:0009628         | 1055 | 4.40E-04 | 27  |
| REAC  | Interleukin-10 signaling  | REAC:R-HSA-6783783 | 41   | 4.40E-04 | 6   |
| TF    | Factor: Pax-2; motif: NNNNGTCANGNRTKANNNN                                 | TF:M00098          | 6494 | 4.40E-04 | 90  |
| TF    | Factor: LXR; motif: NTGACCKNNAGTRACCYNN                                   | TF:M03795          | 5609 | 4.40E-04 | 81  |
| TF    | Factor: SF-1; motif: NYYCAAGGYCA  | TF:M10084          | 3390 | 4.50E-04 | 57  |
| TF    | Factor: MAFB; motif: NTCAGCN; match class: 1                              | TF:M08888_1        | 2789 | 4.60E-04 | 50  |
| TF    | Factor: AP-2beta; motif: NSCCYNRGGSN                                      | TF:M11477          | 7511 | 4.60E-04 | 100 |
| TF    | Factor: NF1B; motif: CYTGGCYNWCWCCAN; match class: 1                      | TF:M09762_1        | 1309 | 4.70E-04 | 31  |
| TF    | Factor: P53; motif: NNNGRCATGCCAGRCATGYCY                                 | TF:M12647          | 5044 | 4.80E-04 | 75  |
| TF    | Factor: PPARgamma:RXRalpha; motif: AAGTAGGTACNGTGACCYACTT; match class: 1 | TF:M00515_1        | 3841 | 4.80E-04 | 62  |
| TF    | Factor: Sp1; motif: RGGGMGGRGSNGGGG                                       | TF:M10529          | 6507 | 4.80E-04 | 90  |
| TF    | Factor: Octamer; motif: TNATTTGCATN                                       | TF:M00795          | 3752 | 4.90E-04 | 61  |
| TF    | Factor: Fra-1; motif: NATGAWTCAYN   | TF:M11286          | 2546 | 4.90E-04 | 47  |
| TF    | Factor: MafG; motif: CMATGACTCAGCAGA                                      | TF:M07048          | 5916 | 4.90E-04 | 84  |
| KEGG  | Proteoglycans in cancer   | KEGG:05205         | 197  | 5.00E-04 | 10  |
| TF    | Factor: E2F3; motif: NNRGMKGGAR; match class: 1                           | TF:M12598_1        | 6610 | 5.00E-04 | 91  |
| TF    | Factor: c-MAF; motif: CNNNCTCAGCA   | TF:M03816          | 4956 | 5.10E-04 | 74  |
| TF    | Factor: WT1; motif: NGCGGGGGGTSMMCYN                                      | TF:M05327          | 5338 | 5.10E-04 | 78  |
| TF    | Factor: RelA-p65; motif: GGGRRNTTCCM                                      | TF:M09668          | 3228 | 5.10E-04 | 55  |
| TF    | Factor: Sp1; motif: NGGGGCGGGGYN  | TF:M00196          | 9855 | 5.20E-04 | 122 |
| TF    | Factor: SAP-1a; motif: CWTCKGT  | TF:M03844          | 2306 | 5.20E-04 | 44  |
| TF    | Factor: ER71; motif: CWTCTGT  | TF:M07282          | 2306 | 5.20E-04 | 44  |
| GO:BP | regulation of immune response   | GO:0050776         | 741  | 5.30E-04 | 22  |
| GO:BP | negative regulation of cell communication                                 | GO:0010648         | 1273 | 5.30E-04 | 30  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: IRF-4; motif: AAGTTTC; match class: 1           | TF:M04855_1 | 1681 | 5.30E-04 | 36  |
| TF    | Factor: Six-1; motif: CTCARRTWCN                        | TF:M07466   | 2887 | 5.30E-04 | 51  |
| TF    | Factor: JunD; motif: NRTGACGTCATS                       | TF:M11270   | 7948 | 5.30E-04 | 104 |
| TF    | Factor: GCMA:C/EBPbeta; motif: ATGCGGGTNNRTTGGCAAY      | TF:M08575   | 5928 | 5.40E-04 | 84  |
| GO:BP | inorganic ion homeostasis                               | GO:0098771  | 682  | 5.50E-04 | 21  |
| GO:BP | negative regulation of signaling                        | GO:0023057  | 1275 | 5.50E-04 | 30  |
| GO:BP | neutrophil chemotaxis                                   | GO:0030593  | 79   | 5.60E-04 | 8   |
| GO:BP | cell differentiation involved in kidney development     | GO:0061005  | 54   | 5.60E-04 | 7   |
| TF    | Factor: ER-beta; motif: ANNSTGACCYRGNN                  | TF:M03821   | 5542 | 5.60E-04 | 80  |
| TF    | Factor: HFH8; motif: NNNTGTTTATNTR                      | TF:M00294   | 2978 | 5.60E-04 | 52  |
| TF    | Factor: AP-2alpha; motif: NSCCNCRGGSN                   | TF:M07348   | 7543 | 5.60E-04 | 100 |
| TF    | Factor: RARA; motif: AGGCANNYAAAGGTCA                   | TF:M08019   | 4689 | 5.80E-04 | 71  |
| TF    | Factor: Sp1; motif: GGGGCGGGGC                          | TF:M00931   | 9875 | 5.80E-04 | 122 |
| GO:MF | identical protein binding                               | GO:0042802  | 1948 | 5.90E-04 | 38  |
| GO:BP | cartilage development                                   | GO:0051216  | 179  | 5.90E-04 | 11  |
| GO:BP | regulation of DNA-binding transcription factor activity | GO:0051090  | 406  | 6.00E-04 | 16  |
| GO:BP | immune effector process                                 | GO:0002252  | 513  | 6.10E-04 | 18  |
| GO:CC | fibrillar collagen trimer                               | GO:0005583  | 12   | 6.20E-04 | 4   |
| GO:CC | banded collagen fibril                                  | GO:0098643  | 12   | 6.20E-04 | 4   |
| TF    | Factor: COUP-TF1; motif: RAGGTCANTGACCTY                | TF:M11745   | 5556 | 6.20E-04 | 80  |
| GO:CC | ficolin-1-rich granule                                  | GO:0101002  | 175  | 6.30E-04 | 10  |
| TF    | Factor: Nkx2-3; motif: NNCGTTRWS                        | TF:M10638   | 9672 | 6.30E-04 | 120 |
| TF    | Factor: IRF-8; motif: NYGAAASYGAAACYN                   | TF:M11682   | 3251 | 6.50E-04 | 55  |
| GO:BP | positive regulation of biosynthetic process             | GO:0009891  | 1807 | 6.60E-04 | 37  |
| TF    | Factor: En-2; motif: NTCRTTARN                          | TF:M10858   | 7670 | 6.60E-04 | 101 |
| GO:BP | divalent inorganic cation homeostasis                   | GO:0072507  | 462  | 6.70E-04 | 17  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| GO:BP | hemopoiesis  | GO:0030097  | 815  | 6.80E-04 | 23  |
| TF    | Factor: POU3F2; motif: NTATGCWAATKAG                   | TF:M11909   | 4151 | 6.80E-04 | 65  |
| TF    | Factor: SMAD; motif: TNGNCAGACWN                       | TF:M00974   | 3788 | 6.80E-04 | 61  |
| TF    | Factor: AP-2gamma; motif: NNNNWGCCYNCRGSCN             | TF:M07349   | 2998 | 6.90E-04 | 52  |
| TF    | Factor: TR4; motif: NCCCTGACCYB                        | TF:M08906   | 3971 | 6.90E-04 | 63  |
| TF    | Factor: TWIST; motif: CACCTGG; match class: 1          | TF:M03582_1 | 2249 | 7.00E-04 | 43  |
| TF    | Factor: GR; motif: RGNACANMNTGTNCY; match class: 1     | TF:M09941_1 | 1701 | 7.00E-04 | 36  |
| KEGG  | Relaxin signaling pathway                              | KEGG:04926  | 123  | 7.10E-04 | 8   |
| TF    | Factor: Churchill; motif: CGGGNN; match class: 1       | TF:M00986_1 | 9909 | 7.10E-04 | 122 |
| TF    | Factor: SMAD5; motif: GSGGCAGM; match class: 1         | TF:M03846_1 | 2251 | 7.20E-04 | 43  |
| TF    | Factor: HES-5; motif: NCACACKY; match class: 1         | TF:M11069_1 | 3616 | 7.30E-04 | 59  |
| TF    | Factor: NFATc1; motif: NTTTCRTNNAYGGAAAN               | TF:M11979   | 7686 | 7.30E-04 | 101 |
| GO:BP | regulation of epithelial cell proliferation            | GO:0050678  | 313  | 7.40E-04 | 14  |
| TF    | Factor: NF-1C; motif: NYTGGCNNYNGCCARN; match class: 1 | TF:M10002_1 | 1481 | 7.40E-04 | 33  |
| TF    | Factor: RUNX3; motif: NRACCGCANWAACCRGAN               | TF:M04110   | 8526 | 7.50E-04 | 109 |
| TF    | Factor: STAT3; motif: NNYTTCCMRGAA                     | TF:M10081   | 3093 | 7.60E-04 | 53  |
| GO:BP | cellular response to chemical stress                   | GO:0062197  | 314  | 7.70E-04 | 14  |
| TF    | Factor: PR; motif: NNNNNNRGNACNNKNTGTTCTNNNNN          | TF:M00957   | 3356 | 7.70E-04 | 56  |
| TF    | Factor: NF-kappaB; motif: NGGGANTTYCCMNNNN             | TF:M00774   | 1632 | 7.70E-04 | 35  |
| GO:BP | muscle cell proliferation                              | GO:0033002  | 184  | 7.80E-04 | 11  |
| TF    | Factor: TBP; motif: NGNNTATAAAA                        | TF:M03581   | 5782 | 7.80E-04 | 82  |
| TF    | Factor: E2F-1; motif: NTTSGCGG                         | TF:M00430   | 7491 | 7.90E-04 | 99  |
| TF    | Factor: RelA-p65; motif: AAATCCCCT                     | TF:M04814   | 3986 | 7.90E-04 | 63  |
| TF    | Factor: TCF-3; motif: CTTTGA; match class: 1           | TF:M03858_1 | 4541 | 8.00E-04 | 69  |
| TF    | Factor: TCF-7; motif: TCAAAG; match class: 1           | TF:M00805_1 | 4541 | 8.00E-04 | 69  |

|       |  |                    |       |          |     |
|-------|--|--------------------|-------|----------|-----|
| TF    | Factor: Egr; motif: GTGGSGCRRS   | TF:M00807          | 4079  | 8.00E-04 | 64  |
| TF    | Factor: Sp1; motif: CCCC GCCCN   | TF:M00933          | 9282  | 8.10E-04 | 116 |
| TF    | Factor: Erm:E2A; motif: CASGTGNNNCGGAAGNN; match class: 1                | TF:M08571_1        | 3898  | 8.10E-04 | 62  |
| GO:BP | regulation of heart contraction  | GO:0008016         | 185   | 8.20E-04 | 11  |
| TF    | Factor: C/EBP; motif: NNNTKNNGNAAN                                       | TF:M00770          | 4639  | 8.30E-04 | 70  |
| TF    | Factor: NF-kappaB; motif: NGGGGAMTTTCCNN                                 | TF:M00194          | 2103  | 8.30E-04 | 41  |
| TF    | Factor: E2F-4; motif: NNTTCCCGCCNN                                       | TF:M04823          | 11934 | 8.30E-04 | 140 |
| REAC  | Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell | REAC:R-HSA-198933  | 101   | 8.40E-04 | 8   |
| TF    | Factor: AP-2beta; motif: NSCCNNNGGSN; match class: 1                     | TF:M11478_1        | 7500  | 8.40E-04 | 99  |
| TF    | Factor: Sox-6; motif: NARACAAAARN  | TF:M03888          | 2932  | 8.50E-04 | 51  |
| TF    | Factor: ctf; motif: YGGCCACCAGRKGGCRSYN                                  | TF:M09890          | 7814  | 8.60E-04 | 102 |
| GO:MF | anion transmembrane transporter activity                                 | GO:0008509         | 294   | 8.70E-04 | 13  |
| GO:BP | regulation of wound healing  | GO:0061041         | 114   | 8.70E-04 | 9   |
| REAC  | Syndecan interactions  | REAC:R-HSA-3000170 | 26    | 8.70E-04 | 5   |
| TF    | Factor: GCMa; motif: RTGCGGGTN; match class: 1                           | TF:M11595_1        | 5310  | 8.70E-04 | 77  |
| TF    | Factor: ATF3; motif: CBCTGACGTCANCS                                      | TF:M00513          | 5504  | 8.70E-04 | 79  |
| REAC  | Erythrocytes take up carbon dioxide and release oxygen                   | REAC:R-HSA-1237044 | 12    | 8.80E-04 | 4   |
| REAC  | O2/CO2 exchange in erythrocytes  | REAC:R-HSA-1480926 | 12    | 8.80E-04 | 4   |
| TF    | Factor: MEF-2C; motif: TATTTWT   | TF:M02025          | 10824 | 8.80E-04 | 130 |
| TF    | Factor: ZNF692; motif: SYNGGSCCCASCCNC; match class: 1                   | TF:M09734_1        | 5798  | 8.80E-04 | 82  |
| TF    | Factor: Sp3; motif: GGGCGGGGSNN  | TF:M07615          | 6593  | 8.90E-04 | 90  |
| TF    | Factor: SP1; motif: GGCCCCGCCCCCN  | TF:M12666          | 8342  | 8.90E-04 | 107 |
| GO:BP | regulation of macromolecule biosynthetic process                         | GO:0010556         | 3510  | 9.00E-04 | 57  |
| TF    | Factor: Pbx; motif: NKTGATTGACRKS  | TF:M01967          | 4369  | 9.00E-04 | 67  |



|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: CDP:SRF; motif: NCCWTAAYAAGGTMNKRATCRATN; match class: 1 | TF:M08520_1 | 3199 | 9.10E-04 | 54  |
| GO:BP | negative regulation of cell differentiation                      | GO:0045596  | 585  | 9.20E-04 | 19  |
| TF    | Factor: E2F-4; motif: TTTGGCGCCAAA                               | TF:M04519   | 4279 | 9.20E-04 | 66  |
| TF    | Factor: SP2; motif: GNNGGGGCGGGGSN                               | TF:M03807   | 8142 | 9.50E-04 | 105 |
| TF    | Factor: STAT3; motif: TTCYGGGAAN                                 | TF:M07065   | 4283 | 9.50E-04 | 66  |
| TF    | Factor: NR1B1:RXR-ALPHA; motif: RRGGTCANNNNNRGGTCA               | TF:M08964   | 6106 | 9.60E-04 | 85  |
| TF    | Factor: RELA; motif: GGGRMTKYCCC; match class: 1                 | TF:M12657_1 | 1353 | 9.70E-04 | 31  |
| GO:MF | transmembrane signaling receptor activity                        | GO:0004888  | 947  | 1.00E-03 | 24  |
| GO:BP | cellular response to organic cyclic compound                     | GO:0071407  | 531  | 1.00E-03 | 18  |
| GO:BP | heart morphogenesis  | GO:0003007  | 230  | 1.00E-03 | 12  |
| GO:BP | skeletal system morphogenesis                                    | GO:0048705  | 189  | 1.00E-03 | 11  |
| GO:BP | pericyte cell differentiation                                    | GO:1904238  | 9    | 1.00E-03 | 4   |
| GO:BP | glomerulus development   | GO:0032835  | 59   | 1.00E-03 | 7   |
| TF    | Factor: COUP-TF1; motif: GRGGKSARAGGTCAGNG                       | TF:M09886   | 4855 | 1.00E-03 | 72  |
| TF    | Factor: E2F-1; motif: NNNNGGCGGGAARN; match class: 1             | TF:M09892_1 | 8790 | 1.00E-03 | 111 |
| TF    | Factor: NURR1:RXR-ALPHA; motif: NRGGTCRRTTGACCYN; match class: 1 | TF:M08957_1 | 4480 | 1.00E-03 | 68  |
| TF    | Factor: AP-2alpha; motif: NGCCYSNNGSN; match class: 1            | TF:M01857_1 | 4480 | 1.00E-03 | 68  |
| TF    | Factor: Sp1; motif: NNGGGGCGGGGNN                                | TF:M00932   | 9977 | 1.10E-03 | 122 |
| TF    | Factor: CTCF; motif: ACCAGGKGGC; match class: 1                  | TF:M04727_1 | 1359 | 1.10E-03 | 31  |
| TF    | Factor: C/EBPbeta; motif: NKNTTGCNYAAYNN                         | TF:M00117   | 3480 | 1.10E-03 | 57  |
| TF    | Factor: NFATc1; motif: NTTTCCRTNNAAYGAAAN; match class: 1        | TF:M11979_1 | 7539 | 1.10E-03 | 99  |
| TF    | Factor: CPBP; motif: GNNRGGGHGGGGNNGGGRN; match class: 1         | TF:M09973_1 | 6323 | 1.10E-03 | 87  |
| TF    | Factor: POU2F1; motif: ATGCAATN                                  | TF:M07059   | 1361 | 1.10E-03 | 31  |
| TF    | Factor: GATA-1; motif: NTGNNNNNNNSAGATAAGR                       | TF:M09621   | 4581 | 1.10E-03 | 69  |
| TF    | Factor: Pax-6; motif: NNNNTTCACGCWTGANTKNNN                      | TF:M00097   | 9552 | 1.10E-03 | 118 |

|       |  |                   |       |          |     |
|-------|--|-------------------|-------|----------|-----|
| TF    | Factor: Erg; motif: NACCGGATATCCGGTN; match class: 1           | TF:M11391_1       | 8275  | 1.10E-03 | 106 |
| GO:BP | cardiac chamber development                                    | GO:0003205        | 153   | 1.20E-03 | 10  |
| GO:BP | chemotaxis   | GO:0006935        | 538   | 1.20E-03 | 18  |
| GO:BP | cochlea morphogenesis  | GO:0090103        | 21    | 1.20E-03 | 5   |
| GO:CC | cell surface   | GO:0009986        | 741   | 1.20E-03 | 20  |
| KEGG  | Fluid shear stress and atherosclerosis                         | KEGG:05418        | 132   | 1.20E-03 | 8   |
| TF    | Factor: CP2/LBP-1c/LSF; motif: GCTGGNTNGNNCYNG; match class: 1 | TF:M00947_1       | 2373  | 1.20E-03 | 44  |
| TF    | Factor: HIC1; motif: NNNGGKTCGCCSNNNNNN                        | TF:M01073         | 3847  | 1.20E-03 | 61  |
| TF    | Factor: Pax-5; motif: NGTCACGCWTSANTGMNY                       | TF:M04064         | 9027  | 1.20E-03 | 113 |
| TF    | Factor: E2F; motif: TTTTCGCGC                                  | TF:M00425         | 10329 | 1.20E-03 | 125 |
| TF    | Factor: CLOCK; motif: NNCAYGYGYN                               | TF:M11046         | 2134  | 1.20E-03 | 41  |
| TF    | Factor: IRF-4; motif: GAAARTA                                  | TF:M01883         | 6944  | 1.20E-03 | 93  |
| TF    | Factor: Dlx-5; motif: NTCRTTAN                                 | TF:M10612         | 6843  | 1.20E-03 | 92  |
| TF    | Factor: Dlx-7; motif: NTCRTTAN                                 | TF:M10603         | 6843  | 1.20E-03 | 92  |
| TF    | Factor: TIEG1; motif: NCCNSNCCCCGCCCC; match class: 1          | TF:M12351_1       | 7871  | 1.20E-03 | 102 |
| GO:BP | ureteric bud development                                       | GO:0001657        | 88    | 1.30E-03 | 8   |
| GO:BP | cellular response to peptide                                   | GO:1901653        | 329   | 1.30E-03 | 14  |
| GO:BP | taxis  | GO:0042330        | 542   | 1.30E-03 | 18  |
| GO:BP | regulation of RNA biosynthetic process                         | GO:2001141        | 3024  | 1.30E-03 | 51  |
| GO:CC | supramolecular complex   | GO:0099080        | 1157  | 1.30E-03 | 26  |
| REAC  | Muscle contraction   | REAC:R-HSA-397014 | 183   | 1.30E-03 | 10  |
| TF    | Factor: ETS1; motif: GCCGAWGTACTTCCGGN                         | TF:M03978         | 11000 | 1.30E-03 | 131 |
| TF    | Factor: pax-2; motif: NCGTCACGCNYSRNYGCNYN                     | TF:M11877         | 10450 | 1.30E-03 | 126 |
| TF    | Factor: KLF3; motif: NNNNNNGGGCGGGGCNNGN                       | TF:M09970         | 7465  | 1.30E-03 | 98  |
| GO:BP | cardiac muscle tissue development                              | GO:0048738        | 195   | 1.40E-03 | 11  |
| GO:BP | mesonephric tubule development                                 | GO:0072164        | 89    | 1.40E-03 | 8   |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| GO:BP | mesonephric epithelium development                                       | GO:0072163  | 89   | 1.40E-03 | 8   |
| GO:BP | regulation of proteolysis  | GO:0030162  | 662  | 1.40E-03 | 20  |
| GO:CC | endoplasmic reticulum  | GO:0005783  | 1854 | 1.40E-03 | 35  |
| GO:CC | tertiary granule   | GO:0070820  | 151  | 1.40E-03 | 9   |
| TF    | Factor: CEBPD; motif: RTTRCGCAAY   | TF:M04202   | 4325 | 1.40E-03 | 66  |
| TF    | Factor: IRF-2; motif: NGAAASYGAAAS                                       | TF:M11665   | 2063 | 1.40E-03 | 40  |
| TF    | Factor: Iκ-2; motif: NNNTGGGAWNNC  | TF:M00087   | 3067 | 1.40E-03 | 52  |
| GO:BP | transmembrane receptor protein serine/threonine kinase signaling pathway | GO:0007178  | 333  | 1.50E-03 | 14  |
| TF    | Factor: CTCF; motif: WGCGCCMYCTAGYGGYN                                   | TF:M03895   | 8633 | 1.50E-03 | 109 |
| TF    | Factor: STAT3; motif: NTTCCYGGAAAN                                       | TF:M09664   | 4899 | 1.50E-03 | 72  |
| TF    | Factor: AP-2alpha; motif: NGCCTSAGGCN; match class: 1                    | TF:M11480_1 | 5380 | 1.50E-03 | 77  |
| TF    | Factor: BCL-6; motif: NYGCTTTCKAGGAANN                                   | TF:M12341   | 5187 | 1.50E-03 | 75  |
| TF    | Factor: RUNX2; motif: NRACCGCAAACCGCAN; match class: 1                   | TF:M04106_1 | 7901 | 1.50E-03 | 102 |
| TF    | Factor: C/EBPdelta; motif: TKNNGCAATN                                    | TF:M07316   | 2731 | 1.50E-03 | 48  |
| TF    | Factor: Smad2; motif: TGTCTGNCWCCCT; match class: 1                      | TF:M10059_1 | 1029 | 1.50E-03 | 26  |
| TF    | Factor: TEF-1; motif: NRCATWCCN  | TF:M12042   | 4433 | 1.50E-03 | 67  |
| TF    | Factor: ZNF432; motif: NCAGNRCCNSRGRGAGC; match class: 1                 | TF:M12704_1 | 4435 | 1.60E-03 | 67  |
| TF    | Factor: PEBP2beta; motif: TGTGGTY  | TF:M03841   | 6476 | 1.60E-03 | 88  |
| TF    | Factor: PEA3; motif: ACAGGAAGGAAGTN                                      | TF:M11429   | 4815 | 1.60E-03 | 71  |
| TF    | Factor: GR; motif: RGNACANKNTGTNCY; match class: 1                       | TF:M09625_1 | 3523 | 1.60E-03 | 57  |
| TF    | Factor: ctf; motif: CCNCNAGRKGGCRSTN                                     | TF:M07249   | 6280 | 1.60E-03 | 86  |
| TF    | Factor: DBP; motif: TTWTGYAA   | TF:M01872   | 2158 | 1.60E-03 | 41  |
| TF    | Factor: TEF-3:Elf-1; motif: RGAATGCGGAAGTN                               | TF:M08415   | 8231 | 1.60E-03 | 105 |
| TF    | Factor: Smad4; motif: NCAGACAN; match class: 1                           | TF:M07368_1 | 423  | 1.60E-03 | 16  |
| GO:BP | detoxification   | GO:0098754  | 123  | 1.70E-03 | 9   |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| GO:BP | ion transport   | GO:0006811         | 1420 | 1.70E-03 | 31  |
| GO:BP | regulation of defense response                            | GO:0031347         | 551  | 1.70E-03 | 18  |
| GO:BP | reproductive structure development                        | GO:0048608         | 387  | 1.70E-03 | 15  |
| TF    | Factor: C/EBPbeta; motif: ATTGCGYAAT                      | TF:M07413          | 2826 | 1.70E-03 | 49  |
| TF    | Factor: TFAP2C; motif: NGCCCNRRGGCA; match class: 1       | TF:M04152_1        | 5107 | 1.70E-03 | 74  |
| TF    | Factor: GKLf; motif: NNCCMCRCCCN                          | TF:M12173          | 9407 | 1.70E-03 | 116 |
| TF    | Factor: HSF1; motif: GAANNITCTRGNAN                       | TF:M02017          | 3440 | 1.70E-03 | 56  |
| TF    | Factor: E2F-3; motif: GGCGGGN; match class: 1             | TF:M02089_1        | 9086 | 1.70E-03 | 113 |
| TF    | Factor: AP-2alpha; motif: NGCCTSAGGCN                     | TF:M11480          | 5694 | 1.70E-03 | 80  |
| TF    | Factor: Oct-2; motif: NTATGCWAATN                         | TF:M11896          | 4354 | 1.70E-03 | 66  |
| TF    | Factor: ER-alpha; motif: AGGTGANMNTGACC                   | TF:M04738          | 3712 | 1.70E-03 | 59  |
| TF    | Factor: TGIF; motif: TGACAGS; match class: 1              | TF:M10101_1        | 712  | 1.70E-03 | 21  |
| GO:BP | gene expression   | GO:0010467         | 6162 | 1.80E-03 | 84  |
| GO:BP | leukocyte cell-cell adhesion                              | GO:0007159         | 338  | 1.80E-03 | 14  |
| GO:BP | proteolysis   | GO:0006508         | 1576 | 1.80E-03 | 33  |
| REAC  | Scavenging of heme from plasma                            | REAC:R-HSA-2168880 | 14   | 1.80E-03 | 4   |
| TF    | Factor: POU2F1; motif: NNATTTGCATNN                       | TF:M03561          | 1770 | 1.80E-03 | 36  |
| TF    | Factor: BTEB3; motif: CCNNSCCNSCCCKKCCCKC; match class: 1 | TF:M09826_1        | 7207 | 1.80E-03 | 95  |
| TF    | Factor: GR; motif: RGWACATWAYGTWCY; match class: 1        | TF:M11846_1        | 3358 | 1.80E-03 | 55  |
| GO:BP | ear development   | GO:0043583         | 201  | 1.90E-03 | 11  |
| GO:BP | reproductive system development                           | GO:0061458         | 390  | 1.90E-03 | 15  |
| GO:BP | negative regulation of epithelial cell apoptotic process  | GO:1904036         | 41   | 1.90E-03 | 6   |
| TF    | Factor: PLAGL2; motif: AAGGACC                            | TF:M05548          | 3631 | 1.90E-03 | 58  |
| TF    | Factor: Pax-5; motif: GTYAYGCTTSRCTGVNYN                  | TF:M04754          | 4648 | 1.90E-03 | 69  |
| TF    | Factor: TBP; motif: MTATAAAARS                            | TF:M10088          | 3905 | 1.90E-03 | 61  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | mesonephros development   | GO:0001823  | 93    | 2.00E-03 | 8   |
| GO:BP | regulation of system process                                    | GO:0044057  | 500   | 2.00E-03 | 17  |
| GO:BP | glomerulus vasculature development                              | GO:0072012  | 23    | 2.00E-03 | 5   |
| TF    | Factor: Elk-1; Pax-9; motif: ACCGGAACYACGCWYSANTG               | TF:M08226   | 10969 | 2.00E-03 | 130 |
| TF    | Factor: Sp1; motif: NGGGGCGGGGYN; match class: 1                | TF:M00196_1 | 5813  | 2.00E-03 | 81  |
| TF    | Factor: SREBP-1; motif: RTCACCCAY                               | TF:M07405   | 5912  | 2.00E-03 | 82  |
| TF    | Factor: ZXDB; motif: NAGGGTG; match class: 1                    | TF:M06202_1 | 1701  | 2.00E-03 | 35  |
| TF    | Factor: ZXDA; motif: NAGGGTG; match class: 1                    | TF:M06203_1 | 1701  | 2.00E-03 | 35  |
| TF    | Factor: C/EBPbeta; motif: NATTGCRYAAYN                          | TF:M09597   | 2506  | 2.00E-03 | 45  |
| TF    | Factor: NR1B2; motif: RAGGTCATGACCTN                            | TF:M11803   | 2760  | 2.00E-03 | 48  |
| GO:BP | regulation of catalytic activity                                | GO:0050790  | 2138  | 2.10E-03 | 40  |
| TF    | Factor: TTF-1; motif: NTKGAGTGSN                                | TF:M10007   | 3916  | 2.10E-03 | 61  |
| TF    | Factor: c-Jun; motif: NATGACGTCAYN; match class: 1              | TF:M11266_1 | 5332  | 2.10E-03 | 76  |
| GO:BP | RNA biosynthetic process  | GO:0032774  | 3164  | 2.20E-03 | 52  |
| TF    | Factor: NR1B2; motif: NTGACCY; match class: 1                   | TF:M02111_1 | 2939  | 2.20E-03 | 50  |
| TF    | Factor: rfx3;SRF; motif: TRGCAACNNNNCCNWATANGGN; match class: 1 | TF:M08623_1 | 7240  | 2.20E-03 | 95  |
| GO:BP | regulation of nucleobase-containing compound metabolic process  | GO:0019219  | 3523  | 2.30E-03 | 56  |
| GO:BP | myeloid leukocyte activation                                    | GO:0002274  | 205   | 2.30E-03 | 11  |
| TF    | Factor: CTCF; motif: NNGCCASCAGRKGGCRSNN                        | TF:M01200   | 3651  | 2.30E-03 | 58  |
| TF    | Factor: HMGYI; motif: NGWWATTN                                  | TF:M01653   | 5150  | 2.30E-03 | 74  |
| TF    | Factor: Oct-2; motif: NNNATTATGCAW                              | TF:M11894   | 2946  | 2.30E-03 | 50  |
| GO:BP | leukocyte differentiation                                       | GO:0002521  | 507   | 2.40E-03 | 17  |
| TF    | Factor: MEL1; motif: GATGAG; match class: 1                     | TF:M08793_1 | 4116  | 2.40E-03 | 63  |
| TF    | Factor: FEZF1; motif: NYTGYCTTTTN                               | TF:M09919   | 2030  | 2.40E-03 | 39  |
| GO:BP | morphogenesis of a branching epithelium                         | GO:0061138  | 166   | 2.50E-03 | 10  |
| TF    | Factor: GATA-5; motif: TATCTN; match class: 1                   | TF:M02006_1 | 2441  | 2.50E-03 | 44  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: E2F-1; motif: TTTGGCGCCAAA; match class: 1     | TF:M04516_1 | 9692 | 2.50E-03 | 118 |
| TF    | Factor: PU.1; motif: NNNYYYACTTCCTCTTTY                | TF:M01172   | 3663 | 2.50E-03 | 58  |
| GO:BP | regulation of muscle system process                    | GO:0090257  | 208  | 2.60E-03 | 11  |
| TF    | Factor: KLF8; motif: NGGGGTGYGG                        | TF:M08818   | 1417 | 2.60E-03 | 31  |
| TF    | Factor: Foxc1; motif: TTVYTTTNW                        | TF:M07254   | 6449 | 2.60E-03 | 87  |
| TF    | Factor: ATF-3; motif: GATGAYGTCATN                     | TF:M11288   | 4312 | 2.60E-03 | 65  |
| TF    | Factor: PHB; motif: NCCCAGCCCCY; match class: 1        | TF:M12725_1 | 4127 | 2.60E-03 | 63  |
| GO:CC | platelet alpha granule lumen                           | GO:0031093  | 59   | 2.70E-03 | 6   |
| TF    | Factor: NFATc1; motif: TTTCCAYWRTGGAAA                 | TF:M04052   | 5658 | 2.70E-03 | 79  |
| TF    | Factor: Fra-1; motif: GRTGACGTCATC                     | TF:M11285   | 6557 | 2.70E-03 | 88  |
| TF    | Factor: T3R-beta; motif: NRRGGTCRTGACCYYN              | TF:M11817   | 4694 | 2.70E-03 | 69  |
| TF    | Factor: ER-alpha; motif: NAGGCANSNTGACCYN              | TF:M11845   | 3225 | 2.70E-03 | 53  |
| GO:BP | regulation of epithelial cell differentiation          | GO:0030856  | 131  | 2.80E-03 | 9   |
| TF    | Factor: AP-2gamma;Dlx-3; motif: NSCCYNNRGGCANNNNYAATTA | TF:M08660   | 3138 | 2.80E-03 | 52  |
| TF    | Factor: Sox-10; motif: MAANRRNNNCWTTGTT                | TF:M10065   | 5861 | 2.80E-03 | 81  |
| TF    | Factor: ZGPAT; motif: GRGGCWGNGGNG; match class: 1     | TF:M09739_1 | 2537 | 2.80E-03 | 45  |
| TF    | Factor: NF-kappaB; motif: GGGRATTTCC                   | TF:M00052   | 1650 | 2.80E-03 | 34  |
| GO:CC | focal adhesion   | GO:0005925  | 413  | 2.90E-03 | 14  |
| TF    | Factor: MZF-1; motif: KNGNKAGGGGNA                     | TF:M00084   | 5964 | 2.90E-03 | 82  |
| TF    | Factor: ER71;C/EBPdelta; motif: NCCGGAWRTTRCGYAAN      | TF:M08246   | 7178 | 2.90E-03 | 94  |
| TF    | Factor: BRN1; motif: NANNTATGCATAATNNA                 | TF:M01324   | 4046 | 2.90E-03 | 62  |
| TF    | Factor: CDX-2; motif: TTTATN; match class: 1           | TF:M02087_1 | 3954 | 2.90E-03 | 61  |
| GO:BP | regulation of transcription, DNA-templated             | GO:0006355  | 3018 | 3.00E-03 | 50  |
| GO:BP | regulation of nucleic acid-templated transcription     | GO:1903506  | 3019 | 3.00E-03 | 50  |
| TF    | Factor: IRF-8; motif: NCGAAACCGAAACYN                  | TF:M11683   | 4049 | 3.00E-03 | 62  |
| TF    | Factor: Smad1; motif: NGGCAGACN                        | TF:M03845   | 3958 | 3.00E-03 | 61  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: c-Myc; motif: NCCACGTGCNN  | TF:M09992   | 4899  | 3.00E-03 | 71  |
| GO:BP | cell adhesion mediated by integrin   | GO:0033627  | 69    | 3.10E-03 | 7   |
| GO:BP | regulation of RNA metabolic process  | GO:0051252  | 3290  | 3.10E-03 | 53  |
| TF    | Factor: Fli-1:C/EBPdelta; motif: NNCGGAWATTGCGCAAT                             | TF:M08469   | 5776  | 3.10E-03 | 80  |
| TF    | Factor: IRF-1; motif: TTCACTT  | TF:M00747   | 4332  | 3.10E-03 | 65  |
| TF    | Factor: CDP:T-bet; motif: NTCACACNYRATCRATM                                    | TF:M08203   | 5093  | 3.10E-03 | 73  |
| TF    | Factor: Cdx-2; motif: NRTCCTAANNNN   | TF:M10849   | 9841  | 3.10E-03 | 119 |
| TF    | Factor: Oct-2; motif: NNNATTTGCATRT  | TF:M07120   | 3962  | 3.10E-03 | 61  |
| GO:BP | kidney vasculature development   | GO:0061440  | 25    | 3.20E-03 | 5   |
| GO:BP | renal system vasculature development   | GO:0061437  | 25    | 3.20E-03 | 5   |
| GO:BP | response to steroid hormone  | GO:0048545  | 304   | 3.20E-03 | 13  |
| GO:BP | humoral immune response  | GO:0006959  | 171   | 3.20E-03 | 10  |
| TF    | Factor: TEAD4; motif: NRCATTCCWN   | TF:M04145   | 1213  | 3.20E-03 | 28  |
| GO:BP | response to organic cyclic compound  | GO:0014070  | 828   | 3.30E-03 | 22  |
| GO:BP | extrinsic apoptotic signaling pathway  | GO:0097191  | 213   | 3.30E-03 | 11  |
| TF    | Factor: C/EBPdelta; motif: NRTTGCGYAAAYN                                       | TF:M11321   | 4812  | 3.30E-03 | 70  |
| TF    | Factor: Sox-9; motif: NNNNNACAAARGNNSMN; match class: 1                        | TF:M07269_1 | 2893  | 3.30E-03 | 49  |
| TF    | Factor: sp4; motif: NNGNARGRGGCGGRGCNNRR                                       | TF:M10072   | 10068 | 3.30E-03 | 121 |
| TF    | Factor: Erg; motif: NACCGAWWTCCGGTN  | TF:M11395   | 7927  | 3.30E-03 | 101 |
| GO:BP | regulation of endothelial cell apoptotic process                               | GO:2000351  | 45    | 3.40E-03 | 6   |
| GO:BP | regulation of extrinsic apoptotic signaling pathway via death domain receptors | GO:1902041  | 45    | 3.40E-03 | 6   |
| TF    | Factor: SP2; motif: GGGCGGGAC  | TF:M01783   | 8669  | 3.40E-03 | 108 |
| TF    | Factor: LBP9; motif: ACYRGTNNNNACYRGT  | TF:M11492   | 6898  | 3.40E-03 | 91  |
| TF    | Factor: LHX4; motif: NNCRTTAN  | TF:M11005   | 9424  | 3.40E-03 | 115 |
| TF    | Factor: MEF-2D; motif: WAAATAR   | TF:M02026   | 6393  | 3.50E-03 | 86  |
| TF    | Factor: Pitx1; motif: NNNNRGGGATTAAMNNN  | TF:M01484   | 2900  | 3.50E-03 | 49  |

|       |   |                   |      |          |    |
|-------|---|-------------------|------|----------|----|
| GO:BP | cellular response to stress   | GO:0033554        | 1782 | 3.60E-03 | 35 |
| GO:CC | cell-substrate junction   | GO:0030055        | 421  | 3.60E-03 | 14 |
| KEGG  | Lipid and atherosclerosis   | KEGG:05417        | 199  | 3.60E-03 | 9  |
| REAC  | Cell surface interactions at the vascular wall  | REAC:R-HSA-202733 | 123  | 3.60E-03 | 8  |
| TF    | Factor: TFAP2A; motif: YGCCNNRGGCN; match class: 1                                      | TF:M04146_1       | 3522 | 3.60E-03 | 56 |
| TF    | Factor: GR; motif: GGTACAANNNTGTCTK; match class: 1                                     | TF:M00205_1       | 1220 | 3.60E-03 | 28 |
| TF    | Factor: FXR; motif: NAGGTCAWNKN   | TF:M08953         | 4074 | 3.70E-03 | 62 |
| TF    | Factor: MEIS1A:HOXA9; motif: TGACAGKTTTAYGA   | TF:M00420         | 4639 | 3.70E-03 | 68 |
| TF    | Factor: SREBP-1; motif: RTCRCGTGAY; match class: 1                                      | TF:M11081_1       | 7116 | 3.70E-03 | 93 |
| GO:BP | negative regulation of cell adhesion  | GO:0007162        | 261  | 3.80E-03 | 12 |
| GO:BP | positive regulation of intracellular signal transduction                                | GO:1902533        | 902  | 3.80E-03 | 23 |
| KEGG  | Rheumatoid arthritis  | KEGG:05323        | 78   | 3.80E-03 | 6  |
| TF    | Factor: AML3; motif: NWAACCACRAAAACCACRAN   | TF:M11999         | 5905 | 3.80E-03 | 81 |
| GO:BP | negative regulation of endothelial cell apoptotic process                               | GO:2000352        | 26   | 3.90E-03 | 5  |
| GO:BP | negative regulation of extrinsic apoptotic signaling pathway via death domain receptors | GO:1902042        | 26   | 3.90E-03 | 5  |
| GO:BP | mesenchymal cell differentiation  | GO:0048762        | 217  | 4.00E-03 | 11 |
| TF    | Factor: SP3; motif: NCCACGCCCMC   | TF:M03921         | 3536 | 4.00E-03 | 56 |
| GO:BP | heart contraction   | GO:0060047        | 218  | 4.10E-03 | 11 |
| GO:CC | cytoskeleton  | GO:0005856        | 2118 | 4.10E-03 | 37 |
| GO:CC | actin cytoskeleton  | GO:0015629        | 484  | 4.10E-03 | 15 |
| TF    | Factor: PARP; motif: YDRGAAAWAS   | TF:M01211         | 2156 | 4.10E-03 | 40 |
| TF    | Factor: Tbx20; motif: SGAGGTGTGAGGSGR   | TF:M07474         | 3181 | 4.10E-03 | 52 |
| TF    | Factor: C-JUN:FRA-2; motif: NNRTGAGTCAYN  | TF:M08940         | 3007 | 4.20E-03 | 50 |
| TF    | Factor: ESRRA; motif: AAGGTCATNCAAGGTCA   | TF:M04457         | 3008 | 4.30E-03 | 50 |
| TF    | Factor: TFII-I; motif: NAGGAAGTGN; match class: 1                                       | TF:M04636_1       | 4849 | 4.30E-03 | 70 |
| GO:BP | transcription, DNA-templated  | GO:0006351        | 3149 | 4.40E-03 | 51 |

|       |  |                      |       |          |     |
|-------|--|----------------------|-------|----------|-----|
| GO:BP | nucleic acid-templated transcription                 | GO:0097659           | 3150  | 4.40E-03 | 51  |
| TF    | Factor: ER-alpha; motif: TGACCCYN                    | TF:M03547            | 4003  | 4.40E-03 | 61  |
| GO:BP | odontogenesis of dentin-containing tooth             | GO:0042475           | 73    | 4.50E-03 | 7   |
| KEGG  | Estrogen signaling pathway                           | KEGG:04915           | 117   | 4.50E-03 | 7   |
| REAC  | Phase I - Functionalization of compounds             | REAC:R-HSA-211945    | 91    | 4.50E-03 | 7   |
| TF    | Factor: Pet-1; motif: GCNGGAAGYG; match class: 1     | TF:M09918_1          | 6634  | 4.50E-03 | 88  |
| TF    | Factor: HOXA7; motif: YCAATCT                        | TF:M01108            | 2497  | 4.50E-03 | 44  |
| GO:BP | cellular component organization                      | GO:0016043           | 6205  | 4.60E-03 | 83  |
| TF    | Factor: HOXA10; motif: NGTCGTAAAAN                   | TF:M10795            | 5936  | 4.70E-03 | 81  |
| TF    | Factor: NF-kappaB; motif: GGGGATYCCC; match class: 1 | TF:M00051_1          | 2586  | 4.70E-03 | 45  |
| TF    | Factor: SREBP-2; motif: RTGGGGTGAY                   | TF:M07406            | 5054  | 4.70E-03 | 72  |
| GO:BP | cellular response to oxidative stress                | GO:0034599           | 267   | 4.80E-03 | 12  |
| GO:BP | morphogenesis of a branching structure               | GO:0001763           | 179   | 4.80E-03 | 10  |
| TF    | Factor: ZF5; motif: NRNGNGCGCGCWN; match class: 1    | TF:M00333_1          | 11811 | 4.80E-03 | 136 |
| TF    | Factor: Smad4; motif: TGTCTGN                        | TF:M01889            | 4482  | 4.80E-03 | 66  |
| TF    | Factor: E2F-1; motif: WWTGGCGCCAAA; match class: 1   | TF:M04515_1          | 11473 | 4.80E-03 | 133 |
| TF    | Factor: FLI-1; motif: CMGGAWGTSAN                    | TF:M01208            | 5544  | 4.80E-03 | 77  |
| TF    | Factor: POU6F1; motif: NNNNATAATGAGSTNNN             | TF:M01462            | 4868  | 5.00E-03 | 70  |
| TF    | Factor: POU3F1; motif: RNYBCATTTGCATTWCAA            | TF:M03842            | 4299  | 5.00E-03 | 64  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT                      | TF:M11208            | 3562  | 5.10E-03 | 56  |
| MIRNA | hsa-miR-29b-3p                                       | MIRNA:hsa-miR-29b-3p | 249   | 5.10E-03 | 11  |
| TF    | Factor: NeuroD; motif: NNSCWGCTGNSY                  | TF:M01288            | 4210  | 5.20E-03 | 63  |
| TF    | Factor: MafB; motif: TGCTGASTNNN                     | TF:M09978            | 2768  | 5.20E-03 | 47  |
| GO:BP | positive regulation of RNA metabolic process         | GO:0051254           | 1577  | 5.30E-03 | 32  |
| GO:BP | cellular response to hormone stimulus                | GO:0032870           | 538   | 5.30E-03 | 17  |
| TF    | Factor: ER-alpha; motif: GNCNNNTGACCCYN              | TF:M07283            | 2597  | 5.30E-03 | 45  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: JunD; motif: NRTGAGTCAYN  | TF:M09964   | 4213  | 5.30E-03 | 63  |
| TF    | Factor: SP1; motif: NCCCCCKCCCC   | TF:M07226   | 7901  | 5.30E-03 | 100 |
| GO:MF | ion binding   | GO:0043167  | 5669  | 5.40E-03 | 76  |
| GO:BP | positive regulation of nucleobase-containing compound metabolic process | GO:0045935  | 1735  | 5.40E-03 | 34  |
| GO:BP | transmembrane transport   | GO:0055085  | 1426  | 5.40E-03 | 30  |
| GO:BP | positive regulation of programmed cell death                            | GO:0043068  | 481   | 5.50E-03 | 16  |
| GO:MF | NAD+ nucleotidase, cyclic ADP-ribose generating                         | GO:0061809  | 16    | 5.60E-03 | 4   |
| GO:MF | NAD(P)+ nucleosidase activity   | GO:0050135  | 16    | 5.60E-03 | 4   |
| GO:CC | hemoglobin complex  | GO:0005833  | 7     | 5.60E-03 | 3   |
| GO:CC | haptoglobin-hemoglobin complex  | GO:0031838  | 7     | 5.60E-03 | 3   |
| TF    | Factor: NF-1C; motif: TTGGCNN   | TF:M07300   | 5371  | 5.60E-03 | 75  |
| TF    | Factor: LRF; motif: NGKGGGTSNCN   | TF:M07387   | 4792  | 5.70E-03 | 69  |
| TF    | Factor: Oct3; motif: WTATGCGCATAW; match class: 1                       | TF:M11934_1 | 7810  | 5.80E-03 | 99  |
| TF    | Factor: LBP-1; motif: CAGCTGS; match class: 1                           | TF:M00644_1 | 3578  | 5.80E-03 | 56  |
| TF    | Factor: HoxA5; motif: RTCATTAN  | TF:M10704   | 4413  | 5.80E-03 | 65  |
| TF    | Factor: Pax-5; motif: RRMSWGANWYCTNRAGCGKRACRSRY NSM                    | TF:M00144   | 12083 | 6.00E-03 | 138 |
| GO:BP | heart process   | GO:0003015  | 227   | 6.10E-03 | 11  |
| TF    | Factor: CTCF; motif: NNRSYGCCMCCTGSTGGCCN                               | TF:M12593   | 8029  | 6.10E-03 | 101 |
| TF    | Factor: LKLF; motif: GGGGTGGKSN; match class: 1                         | TF:M07261_1 | 3767  | 6.10E-03 | 58  |
| TF    | Factor: Oct-2; motif: NNNTATGCAAAATNNNN                                 | TF:M01368   | 1947  | 6.10E-03 | 37  |
| GO:BP | regulation of response to wounding                                      | GO:1903034  | 144   | 6.20E-03 | 9   |
| GO:BP | ear morphogenesis   | GO:0042471  | 108   | 6.20E-03 | 8   |
| GO:BP | innate immune response  | GO:0045087  | 667   | 6.30E-03 | 19  |
| TF    | Factor: STAT2; motif: NRGAAANNNGAACTNA                                  | TF:M09733   | 2444  | 6.30E-03 | 43  |
| GO:BP | regulation of blood circulation   | GO:1903522  | 228   | 6.40E-03 | 11  |
| GO:BP | organic cyclic compound biosynthetic process                            | GO:1901362  | 3736  | 6.40E-03 | 57  |

|       |   |                   |      |          |     |
|-------|---|-------------------|------|----------|-----|
| GO:BP | endothelial cell apoptotic process                          | GO:0072577        | 50   | 6.40E-03 | 6   |
| TF    | Factor: OCT-x; motif: CTNATTTGCATAY                         | TF:M00210         | 3408 | 6.40E-03 | 54  |
| TF    | Factor: Pax-4; motif: SWAATWAN                              | TF:M04063         | 3957 | 6.40E-03 | 60  |
| GO:CC | cytoplasmic vesicle membrane                                | GO:0030659        | 1119 | 6.50E-03 | 24  |
| TF    | Factor: GTF2IRD1-isoform2; motif: GGGATTRNR; match class: 1 | TF:M01229_1       | 7936 | 6.50E-03 | 100 |
| GO:BP | regulation of intracellular signal transduction             | GO:1902531        | 1594 | 6.60E-03 | 32  |
| TF    | Factor: Sp1; motif: GGGGCGGGGC; match class: 1              | TF:M00931_1       | 5788 | 6.60E-03 | 79  |
| TF    | Factor: AP-1; motif: NTGASTCAG                              | TF:M00199         | 4054 | 6.60E-03 | 61  |
| TF    | Factor: FOSB;JUND; motif: NNTNACTNATN                       | TF:M08928         | 5006 | 6.70E-03 | 71  |
| TF    | Factor: FRA-2; motif: RTGANTCA                              | TF:M08914         | 3234 | 6.70E-03 | 52  |
| REAC  | Transport of small molecules                                | REAC:R-HSA-382551 | 679  | 6.80E-03 | 18  |
| TF    | Factor: P50; motif: GGRRANTCCNN; match class: 1             | TF:M03557_1       | 1188 | 6.80E-03 | 27  |
| TF    | Factor: Sox-9; motif: MACARWGNNNYCNTTNW                     | TF:M08838         | 3505 | 6.80E-03 | 55  |
| TF    | Factor: ATF-2; motif: RRTGANGTCAY                           | TF:M09867         | 3596 | 6.80E-03 | 56  |
| GO:MF | cation binding  | GO:0043169        | 4050 | 6.90E-03 | 59  |
| TF    | Factor: ESE-1; motif: NTGTGCGGATGCN; match class: 1         | TF:M11385_1       | 4913 | 6.90E-03 | 70  |
| TF    | Factor: AR; motif: GGTACANNRTGTTCT; match class: 1          | TF:M00481_1       | 1957 | 6.90E-03 | 37  |
| TF    | Factor: WT1; motif: RGGNGGGGAGGRGGNGGRG                     | TF:M10108         | 6095 | 6.90E-03 | 82  |
| TF    | Factor: E2F2; motif: AAAAATGGCGCCAAAWG                      | TF:M03958         | 9442 | 6.90E-03 | 114 |
| GO:BP | regulation of peptidase activity                            | GO:0052547        | 379  | 7.00E-03 | 14  |
| TF    | Factor: TAFII250; motif: RARRWGCGGMGGNGR                    | TF:M10086         | 8689 | 7.00E-03 | 107 |
| GO:MF | calcium ion binding   | GO:0005509        | 653  | 7.10E-03 | 18  |
| GO:BP | metanephros development                                     | GO:0001656        | 78   | 7.10E-03 | 7   |
| TF    | Factor: AP-2beta; motif: GCNNNGGSCNGVGGGN; match class: 1   | TF:M01858_1       | 3063 | 7.10E-03 | 50  |
| GO:BP | negative regulation of endopeptidase activity               | GO:0010951        | 187  | 7.20E-03 | 10  |
| TF    | Factor: FAC1; motif: NNNCAMAACACRNA                         | TF:M00456         | 6812 | 7.30E-03 | 89  |

|       |  |                       |       |          |     |
|-------|--|-----------------------|-------|----------|-----|
| TF    | Factor: PATZ; motif: GGGNGGGGGMKGRRNGGNRN                        | TF:M10026             | 7954  | 7.30E-03 | 100 |
| TF    | Factor: AR; motif: NNNNNNRGNACRNNGTGTTCTNNNNN N                  | TF:M00956             | 2207  | 7.30E-03 | 40  |
| TF    | Factor: AP-2beta; motif: NSCCYNRGGSN; match class: 1             | TF:M11477_1           | 6305  | 7.30E-03 | 84  |
| TF    | Factor: LXR-alpha; motif: NNRRGGTYACTNNAGNCA                     | TF:M10013             | 2716  | 7.30E-03 | 46  |
| GO:BP | positive regulation of macromolecule biosynthetic process        | GO:0010557            | 1682  | 7.40E-03 | 33  |
| TF    | Factor: RORA; motif: CCYTGNCCTN; match class: 1                  | TF:M12659_1           | 1963  | 7.40E-03 | 37  |
| TF    | Factor: GATA-1; motif: NTGNNNNNNNAGATAAGN                        | TF:M09936             | 3607  | 7.40E-03 | 56  |
| TF    | Factor: ipf1; motif: CATTAR                                      | TF:M01275             | 7333  | 7.50E-03 | 94  |
| TF    | Factor: p53; motif: GGACATGCCCGGGCATGTCY                         | TF:M00034             | 3977  | 7.50E-03 | 60  |
| TF    | Factor: FXR:RXR-ALPHA; motif: NAGKTCATTGACCYN; match class: 1    | TF:M08954_1           | 1884  | 7.50E-03 | 36  |
| MIRNA | hsa-miR-1238-3p  | MIRNA:hsa-miR-1238-3p | 128   | 7.50E-03 | 8   |
| GO:MF | metal ion binding  | GO:0046872            | 3968  | 7.60E-03 | 58  |
| GO:BP | cardiac chamber morphogenesis                                    | GO:0003206            | 111   | 7.60E-03 | 8   |
| GO:BP | biomineral tissue development                                    | GO:0031214            | 148   | 7.70E-03 | 9   |
| GO:BP | extrinsic apoptotic signaling pathway via death domain receptors | GO:0008625            | 79    | 7.70E-03 | 7   |
| GO:BP | regionalization  | GO:0003002            | 280   | 7.80E-03 | 12  |
| GO:BP | positive regulation of cell activation                           | GO:0050867            | 330   | 7.80E-03 | 13  |
| TF    | Factor: AP-2gamma; motif: NTGSCCTGRGGSNN; match class: 1         | TF:M09591_1           | 2550  | 7.80E-03 | 44  |
| TF    | Factor: Sp2; motif: TGGGCGCGCCCA                                 | TF:M06948             | 8390  | 7.80E-03 | 104 |
| GO:BP | response to reactive oxygen species                              | GO:0000302            | 189   | 7.90E-03 | 10  |
| TF    | Factor: TFAP4; motif: AWCAGCTGWT                                 | TF:M04192             | 4548  | 7.90E-03 | 66  |
| TF    | Factor: A-Myb:Elf-1; motif: NMCCGGAACCGTTA                       | TF:M08390             | 10013 | 7.90E-03 | 119 |
| GO:MF | haptoglobin binding  | GO:0031720            | 6     | 8.00E-03 | 3   |
| TF    | Factor: SP1; motif: GGGGYGGGNS; match class: 1                   | TF:M01303_1           | 3433  | 8.00E-03 | 54  |
| TF    | Factor: TCF-1; motif: NNNSWWCAAAGN                               | TF:M07433             | 4743  | 8.10E-03 | 68  |
| GO:BP | biomineralization  | GO:0110148            | 149   | 8.20E-03 | 9   |

|       |  |                   |      |          |     |
|-------|--|-------------------|------|----------|-----|
| TF    | Factor: Sp2; motif: NYSGCCCGCCCCCY                               | TF:M03567         | 7451 | 8.20E-03 | 95  |
| TF    | Factor: HOXA13; motif: ATAAMA; match class: 1                    | TF:M01292_1       | 6832 | 8.20E-03 | 89  |
| TF    | Factor: HSF1; motif: GAANNTTCTNGN                                | TF:M07459         | 2902 | 8.20E-03 | 48  |
| TF    | Factor: FPM315; motif: SRGGGAGGAGGN                              | TF:M01587         | 2990 | 8.20E-03 | 49  |
| TF    | Factor: AP-3; motif: TKGAAAKN                                    | TF:M04609         | 3528 | 8.30E-03 | 55  |
| TF    | Factor: VDR:RXR-ALPHA; motif: NRGGTCANNNGGTTCCNN; match class: 1 | TF:M08980_1       | 3529 | 8.30E-03 | 55  |
| GO:CC | vesicle membrane   | GO:0012506        | 1138 | 8.50E-03 | 24  |
| GO:CC | specific granule   | GO:0042581        | 145  | 8.50E-03 | 8   |
| TF    | Factor: ZNF511; motif: GGRRGRGGCWWGNG; match class: 1            | TF:M09738_1       | 4367 | 8.50E-03 | 64  |
| GO:BP | cardiac ventricle development                                    | GO:0003231        | 113  | 8.60E-03 | 8   |
| TF    | Factor: CTCF; motif: NNNNANASYGCCMYCTAGTGG                       | TF:M04689         | 4847 | 8.60E-03 | 69  |
| GO:BP | positive regulation of cell population proliferation             | GO:0008284        | 813  | 8.80E-03 | 21  |
| TF    | Factor: DEC1; motif: NGCACGTGAS                                  | TF:M09876         | 7777 | 8.80E-03 | 98  |
| TF    | Factor: Sox-15; motif: ACAAWGGG                                  | TF:M03847         | 1353 | 8.90E-03 | 29  |
| TF    | Factor: ER-beta; motif: GTCANASTGRCCYNR                          | TF:M01875         | 5536 | 8.90E-03 | 76  |
| GO:BP | regulation of leukocyte activation                               | GO:0002694        | 500  | 9.00E-03 | 16  |
| TF    | Factor: IRF; motif: NNGAAANTGAAANN                               | TF:M08887         | 1063 | 9.00E-03 | 25  |
| TF    | Factor: PPARgamma; motif: NWSTRGGKSARAGGKCA                      | TF:M10038         | 5836 | 9.10E-03 | 79  |
| TF    | Factor: AP-1; motif: NNNTGAGTCAKCN                               | TF:M00517         | 4189 | 9.20E-03 | 62  |
| TF    | Factor: STAT; motif: NNNNNTTCTKGGA                               | TF:M00777         | 4378 | 9.20E-03 | 64  |
| GO:BP | regulation of transport  | GO:0051049        | 1622 | 9.40E-03 | 32  |
| REAC  | SLC-mediated transmembrane transport                             | REAC:R-HSA-425407 | 229  | 9.40E-03 | 10  |
| TF    | Factor: AR; motif: GGTACANNRTGTTCT                               | TF:M00481         | 4286 | 9.40E-03 | 63  |
| TF    | Factor: CPBP; motif: NGGGCGG                                     | TF:M05444         | 8104 | 9.40E-03 | 101 |
| TF    | Factor: Sp6; motif: WGGGCGG                                      | TF:M05361         | 8104 | 9.40E-03 | 101 |
| TF    | Factor: Sp2; motif: WGGGCGG                                      | TF:M05332         | 8104 | 9.40E-03 | 101 |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: NR3C1; motif: RRGAAACATWMYGTYCTRN             | TF:M02219   | 5643 | 9.40E-03 | 77  |
| TF    | Factor: TFAP2C; motif: NGCCTNAGGCN                    | TF:M04154   | 3363 | 9.50E-03 | 53  |
| TF    | Factor: GLI2; motif: TGGGTGGTCNS                      | TF:M07291   | 2656 | 9.50E-03 | 45  |
| GO:BP | aorta morphogenesis                                   | GO:0035909  | 31   | 9.70E-03 | 5   |
| TF    | Factor: Tbx5; motif: NNAGGTGTNANN                     | TF:M01019   | 4960 | 9.70E-03 | 70  |
| TF    | Factor: Msx-1; motif: CNGTAWNTG                       | TF:M00394   | 7584 | 9.70E-03 | 96  |
| TF    | Factor: Oct3; motif: NNWTATGYWAATKANN                 | TF:M11935   | 2402 | 9.70E-03 | 42  |
| TF    | Factor: NFATc1; motif: TTTTCCATGGAAAN; match class: 1 | TF:M04053_1 | 4962 | 9.80E-03 | 70  |
| GO:BP | negative regulation of peptidase activity             | GO:0010466  | 194  | 9.90E-03 | 10  |
| GO:CC | membrane-enclosed lumen                               | GO:0031974  | 5613 | 9.90E-03 | 73  |
| GO:CC | intracellular organelle lumen                         | GO:0070013  | 5613 | 9.90E-03 | 73  |
| GO:CC | organelle lumen                                       | GO:0043233  | 5613 | 9.90E-03 | 73  |
| GO:CC | external side of plasma membrane                      | GO:0009897  | 291  | 9.90E-03 | 11  |
| TF    | Factor: c-Ets; motif: KRCAGGAARTRNKT                  | TF:M00340   | 4483 | 9.90E-03 | 65  |
| GO:BP | homotypic cell-cell adhesion                          | GO:0034109  | 82   | 1.00E-02 | 7   |
| GO:BP | tissue migration                                      | GO:0090130  | 287  | 1.00E-02 | 12  |
| GO:BP | glomerular mesangial cell development                 | GO:0072144  | 5    | 1.00E-02 | 3   |
| TF    | Factor: SNA; motif: NRCAGGTGCA                        | TF:M12258   | 2236 | 1.00E-02 | 40  |
| TF    | Factor: B-ATF; motif: NNAYGACACN; match class: 1      | TF:M11301_1 | 1669 | 1.00E-02 | 33  |
| TF    | Factor: TEF-3; motif: GNTATTTTT                       | TF:M07270   | 8541 | 1.00E-02 | 105 |
| TF    | Factor: Oct-1; motif: NNNNATGCAAATNAN                 | TF:M00195   | 3014 | 1.00E-02 | 49  |
| TF    | Factor: HFH2; motif: NNWAYRTAAACW                     | TF:M11555   | 3923 | 1.00E-02 | 59  |
| GO:MF | transition metal ion binding                          | GO:0046914  | 1017 | 1.10E-02 | 23  |
| GO:BP | nucleobase-containing compound biosynthetic process   | GO:0034654  | 3527 | 1.10E-02 | 54  |
| GO:BP | cellular response to cadmium ion                      | GO:0071276  | 32   | 1.10E-02 | 5   |
| TF    | Factor: Sp1; motif: GGGGCGGGGC                        | TF:M07063   | 6059 | 1.10E-02 | 81  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1          | TF:M11208_1 | 3285 | 1.10E-02 | 52  |
| TF    | Factor: NFATc2; motif: TTTTCCA                           | TF:M02265   | 6464 | 1.10E-02 | 85  |
| TF    | Factor: NFATc1; motif: NTTTTCCRTNNAYGGAAAN               | TF:M11981   | 5462 | 1.10E-02 | 75  |
| TF    | Factor: TFAP2A; motif: NNNNGCCYSAGGGCA                   | TF:M07231   | 4780 | 1.10E-02 | 68  |
| TF    | Factor: NKX2-5; motif: NNCACCTCAANN                      | TF:M12495   | 1914 | 1.10E-02 | 36  |
| TF    | Factor: HOXD4; motif: NYMATTAN                           | TF:M10712   | 3380 | 1.10E-02 | 53  |
| TF    | Factor: SMAD; motif: AGACNBCNN                           | TF:M00792   | 3290 | 1.10E-02 | 52  |
| TF    | Factor: ESE-1; motif: NWTRCGAWGCN                        | TF:M11382   | 9421 | 1.10E-02 | 113 |
| TF    | Factor: AR; motif: ARGAAACANNNTGTNC; match class: 1      | TF:M07204_1 | 736  | 1.10E-02 | 20  |
| TF    | Factor: gli3; motif: GACCACCCANG                         | TF:M01704   | 3113 | 1.10E-02 | 50  |
| TF    | Factor: POU2F1:PEA3; motif: ACCGGATATGCAN                | TF:M08402   | 6988 | 1.10E-02 | 90  |
| TF    | Factor: TFEA; motif: RGTCACGTGA                          | TF:M10100   | 5277 | 1.10E-02 | 73  |
| TF    | Factor: HOXD1; motif: NATYCAKCAN                         | TF:M12625   | 4694 | 1.10E-02 | 67  |
| TF    | Factor: SMAD3; motif: YGTCTAGACA                         | TF:M04026   | 5872 | 1.10E-02 | 79  |
| GO:BP | mononuclear cell differentiation                         | GO:1903131  | 397  | 1.20E-02 | 14  |
| GO:BP | negative regulation of hydrolase activity                | GO:0051346  | 293  | 1.20E-02 | 12  |
| TF    | Factor: Pbx; motif: GATTGATKGNS                          | TF:M00998   | 4313 | 1.20E-02 | 63  |
| TF    | Factor: NF-kappaB2; motif: NGGGGAANYACCN                 | TF:M11997   | 328  | 1.20E-02 | 13  |
| TF    | Factor: MLLT10; motif: CYNCCNNGGNGCTG; match class: 1    | TF:M12636_1 | 3206 | 1.20E-02 | 51  |
| TF    | Factor: Sp1; motif: GGGGCGGGGT; match class: 1           | TF:M00008_1 | 4794 | 1.20E-02 | 68  |
| TF    | Factor: MIF-1; motif: NNGTTGCWWGGYAACNGS; match class: 1 | TF:M00279_1 | 4699 | 1.20E-02 | 67  |
| TF    | Factor: NFATc1; motif: TTTCCAYWRTGGAAA; match class: 1   | TF:M04052_1 | 3299 | 1.20E-02 | 52  |
| TF    | Factor: AREB6; motif: VNRCACCTGKNC                       | TF:M00414   | 1527 | 1.20E-02 | 31  |
| TF    | Factor: FOSL1; motif: NNATGACTCATNN; match class: 1      | TF:M12518_1 | 1608 | 1.20E-02 | 32  |
| GO:BP | aorta development  | GO:0035904  | 56   | 1.30E-02 | 6   |
| GO:BP | ion transmembrane transport                              | GO:0034220  | 1045 | 1.30E-02 | 24  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: ZNF775; motif: RGRGAGAAGN   | TF:M12720   | 3038 | 1.30E-02 | 49  |
| TF    | Factor: MYB; motif: NAACNGNCN   | TF:M00913   | 4422 | 1.30E-02 | 64  |
| TF    | Factor: COUP-TF1; motif: RRGTCRNTGACCYY   | TF:M11741   | 3398 | 1.30E-02 | 53  |
| TF    | Factor: JunD; motif: NRTGASTCATN  | TF:M07104   | 2177 | 1.30E-02 | 39  |
| TF    | Factor: JUNB:C-JUN; motif: KRTGACGTGCATN; match class: 1  | TF:M08945_1 | 4907 | 1.30E-02 | 69  |
| TF    | Factor: CLOCK; motif: CNGNCACGTGNM  | TF:M09884   | 7117 | 1.30E-02 | 91  |
| TF    | Factor: IRF-4; motif: RGGGAASWGR; match class: 1  | TF:M04818_1 | 2691 | 1.30E-02 | 45  |
| TF    | Factor: AP-4; motif: YCAGCTGNKN; match class: 1   | TF:M10097_1 | 1307 | 1.30E-02 | 28  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT   | TF:M11210   | 3956 | 1.30E-02 | 59  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1   | TF:M11210_1 | 3956 | 1.30E-02 | 59  |
| TF    | Factor: IRF-4; motif: NCGAAACCGAACYN  | TF:M11687   | 3133 | 1.30E-02 | 50  |
| GO:MF | serine-type endopeptidase inhibitor activity  | GO:0004867  | 67   | 1.40E-02 | 6   |
| GO:BP | negative regulation of nucleobase-containing compound metabolic process   | GO:0045934  | 1341 | 1.40E-02 | 28  |
| GO:BP | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | GO:0002460  | 247  | 1.40E-02 | 11  |
| GO:BP | nitrogen compound metabolic process   | GO:0006807  | 9442 | 1.40E-02 | 112 |
| GO:BP | transmembrane receptor protein tyrosine kinase signaling pathway  | GO:0007169  | 579  | 1.40E-02 | 17  |
| KEGG  | NF-kappa B signaling pathway  | KEGG:04064  | 99   | 1.40E-02 | 6   |
| TF    | Factor: OVOL; motif: ANRTAACGG  | TF:M08894   | 7120 | 1.40E-02 | 91  |
| TF    | Factor: Isl2; motif: CTAATKR  | TF:M02079   | 4718 | 1.40E-02 | 67  |
| TF    | Factor: FOXO1A; motif: NNNYTGTTTNCN   | TF:M09931   | 5699 | 1.40E-02 | 77  |
| TF    | Factor: JunB; motif: GATGACGTCAYC; match class: 1   | TF:M11273_1 | 5600 | 1.40E-02 | 76  |
| TF    | Factor: FPM315; motif: GGAGGAGRRGRGRRGR   | TF:M07141   | 2017 | 1.40E-02 | 37  |
| TF    | Factor: ATF-3; motif: NATGATGCATN   | TF:M11290   | 5304 | 1.40E-02 | 73  |
| TF    | Factor: LRF; motif: GGGGKYNNB; match class: 1   | TF:M01100_1 | 2609 | 1.40E-02 | 44  |
| TF    | Factor: Oct-2; motif: NTGCATATGCAN  | TF:M11899   | 4532 | 1.40E-02 | 65  |



|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| GO:MF | enzyme inhibitor activity   | GO:0004857        | 327   | 1.50E-02 | 12  |
| GO:MF | inorganic anion transmembrane transporter activity                        | GO:0015103        | 138   | 1.50E-02 | 8   |
| GO:BP | sensory organ morphogenesis   | GO:0090596        | 250   | 1.50E-02 | 11  |
| GO:BP | negative regulation of cellular biosynthetic process                      | GO:0031327        | 1427  | 1.50E-02 | 29  |
| REAC  | Transport of bile salts and organic acids, metal ions and amine compounds | REAC:R-HSA-425366 | 75    | 1.50E-02 | 6   |
| TF    | Factor: Oct3; motif: WTATGCGCATAW   | TF:M11934         | 8394  | 1.50E-02 | 103 |
| TF    | Factor: NF-kappaB1; motif: KGGRNITTCM                                     | TF:M07221         | 2105  | 1.50E-02 | 38  |
| TF    | Factor: Sox-9; motif: NNNNAACAATRGNN                                      | TF:M00410         | 3323  | 1.50E-02 | 52  |
| TF    | Factor: ZABC1; motif: NNTGNMCTTTGNCCYNNN                                  | TF:M12683         | 3689  | 1.50E-02 | 56  |
| TF    | Factor: TEF-3:C/EBPdelta; motif: RGWATGYNRTTRCGYAAAY                      | TF:M08413         | 5118  | 1.50E-02 | 71  |
| TF    | Factor: c-Ets-2; motif: NNCTTCCTNNN                                       | TF:M07379         | 2966  | 1.50E-02 | 48  |
| TF    | Factor: Oct-1; motif: NNNNNNNWATGCAAATNNWNNA                              | TF:M00138         | 2024  | 1.50E-02 | 37  |
| TF    | Factor: CEBPA; motif: NNATTGCACAATNN                                      | TF:M12502         | 2530  | 1.50E-02 | 43  |
| TF    | Factor: Fra-2; motif: TGASTCANCN  | TF:M03870         | 3056  | 1.50E-02 | 49  |
| TF    | Factor: oct-2; motif: NNWNATGCAAATNN                                      | TF:M03836         | 3147  | 1.50E-02 | 50  |
| GO:BP | regulation of blood coagulation   | GO:0030193        | 58    | 1.60E-02 | 6   |
| GO:BP | muscle tissue morphogenesis   | GO:0060415        | 58    | 1.60E-02 | 6   |
| GO:BP | cellular component organization or biogenesis                             | GO:0071840        | 6398  | 1.60E-02 | 83  |
| GO:BP | lymphocyte differentiation  | GO:0030098        | 353   | 1.60E-02 | 13  |
| GO:BP | anion transport   | GO:0006820        | 465   | 1.60E-02 | 15  |
| TF    | Factor: c-Fos; motif: NNTGASTCATN   | TF:M07090         | 3604  | 1.60E-02 | 55  |
| TF    | Factor: E2F-1:TBR2; motif: NGGTGNNANGGCGCANNNTNCRNNN                      | TF:M08523         | 11259 | 1.60E-02 | 129 |
| TF    | Factor: JUND; motif: NNATGACTCATNN  | TF:M12524         | 3514  | 1.60E-02 | 54  |
| TF    | Factor: MAF; motif: NGCTGAGTCAN   | TF:M00983         | 5128  | 1.60E-02 | 71  |
| TF    | Factor: ctcf; motif: NNNCCASYAGRKGGCRSYNN                                 | TF:M09602         | 6837  | 1.60E-02 | 88  |
| TF    | Factor: NF-1A; motif: NGCCARN; match class: 1                             | TF:M03554_1       | 626   | 1.60E-02 | 18  |

|       |   |                      |      |          |     |
|-------|---|----------------------|------|----------|-----|
| TF    | Factor: BTEB2; motif: GNAGGGGGNGGGSSNN                    | TF:M03814            | 4838 | 1.60E-02 | 68  |
| TF    | Factor: VDR; motif: RRGTCANNRGRKTC; match class: 1        | TF:M09671_1          | 2116 | 1.60E-02 | 38  |
| GO:BP | regulation of endopeptidase activity                      | GO:0052548           | 354  | 1.70E-02 | 13  |
| GO:BP | positive regulation of cell adhesion                      | GO:0045785           | 409  | 1.70E-02 | 14  |
| GO:BP | heart valve development                                   | GO:0003170           | 59   | 1.70E-02 | 6   |
| TF    | Factor: Tbx3; motif: AGGTGTNR                             | TF:M08786            | 3157 | 1.70E-02 | 50  |
| TF    | Factor: Tax/CREB; motif: RTGACGCATAYCCCC; match class: 1  | TF:M00115_1          | 2627 | 1.70E-02 | 44  |
| TF    | Factor: c-Fos; motif: RTGASTCAY                           | TF:M04693            | 2202 | 1.70E-02 | 39  |
| TF    | Factor: AhR:Arnt; motif: GRGKATYGCGTGMCWNSCC              | TF:M00237            | 5832 | 1.70E-02 | 78  |
| TF    | Factor: E2F-7; motif: GRGGCGGAANN                         | TF:M09896            | 9398 | 1.70E-02 | 112 |
| MIRNA | hsa-miR-670-3p  | MIRNA:hsa-miR-670-3p | 186  | 1.70E-02 | 9   |
| GO:BP | positive regulation of cellular protein metabolic process | GO:0032270           | 1284 | 1.80E-02 | 27  |
| GO:BP | positive regulation of apoptotic process                  | GO:0043065           | 469  | 1.80E-02 | 15  |
| GO:BP | cellular zinc ion homeostasis                             | GO:0006882           | 35   | 1.80E-02 | 5   |
| GO:BP | middle ear morphogenesis                                  | GO:0042474           | 17   | 1.80E-02 | 4   |
| GO:BP | kidney mesenchyme development                             | GO:0072074           | 17   | 1.80E-02 | 4   |
| GO:BP | negative regulation of cell migration                     | GO:0030336           | 255  | 1.80E-02 | 11  |
| GO:CC | platelet alpha granule                                    | GO:0031091           | 82   | 1.80E-02 | 6   |
| TF    | Factor: DATF1; motif: SNGGRRGCVWNGGG; match class: 1      | TF:M09724_1          | 2633 | 1.80E-02 | 44  |
| TF    | Factor: AP-2alpha; motif: GCCNNNRGS                       | TF:M00469            | 4949 | 1.80E-02 | 69  |
| TF    | Factor: p53; motif: RGRCWWGYCYNGRCWWGYYY; match class: 1  | TF:M01652_1          | 4757 | 1.80E-02 | 67  |
| TF    | Factor: C-JUN:FOSB; motif: NATGACTCAY                     | TF:M08936            | 2723 | 1.80E-02 | 45  |
| TF    | Factor: Sox-3; motif: SNNACAATRK                          | TF:M11617            | 3258 | 1.80E-02 | 51  |
| CORUM | Calprotectin heterotetramer                               | CORUM:6826           | 2    | 1.80E-02 | 2   |
| CORUM | NOS3-CAV1 complex   | CORUM:5714           | 2    | 1.80E-02 | 2   |
| GO:BP | mononuclear cell migration                                | GO:0071674           | 165  | 1.90E-02 | 9   |

|       |  |                    |      |          |     |
|-------|--|--------------------|------|----------|-----|
| GO:BP | regulation of hemostasis                                     | GO:1900046         | 60   | 1.90E-02 | 6   |
| GO:BP | heterocycle biosynthetic process                             | GO:0018130         | 3595 | 1.90E-02 | 54  |
| GO:BP | regulation of tube diameter                                  | GO:0035296         | 126  | 1.90E-02 | 8   |
| GO:BP | blood vessel diameter maintenance                            | GO:0097746         | 126  | 1.90E-02 | 8   |
| GO:CC | membrane raft  | GO:0045121         | 312  | 1.90E-02 | 11  |
| GO:CC | membrane microdomain   | GO:0098857         | 313  | 1.90E-02 | 11  |
| KEGG  | Focal adhesion   | KEGG:04510         | 195  | 1.90E-02 | 8   |
| REAC  | Metallothioneins bind metals                                 | REAC:R-HSA-5661231 | 9    | 1.90E-02 | 3   |
| TF    | Factor: alpha-CP1; motif: CAGCCAATGAG                        | TF:M00687          | 2044 | 1.90E-02 | 37  |
| TF    | Factor: YY1; motif: NGCCATYTTKGRCNWWNNGTGCK                  | TF:M12276          | 8868 | 1.90E-02 | 107 |
| TF    | Factor: NF-1C; motif: NTTGGCNNNNTGCCARN; match class: 1      | TF:M11728_1        | 967  | 1.90E-02 | 23  |
| TF    | Factor: C/EBPbeta; motif: RNRTKDNGMAAKNN                     | TF:M00109          | 2642 | 1.90E-02 | 44  |
| TF    | Factor: Oct3; motif: NNTTATGYWAATKARN                        | TF:M11932          | 2470 | 1.90E-02 | 42  |
| TF    | Factor: GATA-1; motif: NNCWGATARNNN                          | TF:M00128          | 2048 | 1.90E-02 | 37  |
| TF    | Factor: PBX3; motif: TGANTGRCRGS                             | TF:M10030          | 1884 | 1.90E-02 | 35  |
| GO:BP | regulation of lymphocyte activation                          | GO:0051249         | 415  | 2.00E-02 | 14  |
| GO:BP | negative regulation of extrinsic apoptotic signaling pathway | GO:2001237         | 91   | 2.00E-02 | 7   |
| GO:BP | autocrine signaling  | GO:0035425         | 6    | 2.00E-02 | 3   |
| GO:BP | glomerular mesangial cell differentiation                    | GO:0072008         | 6    | 2.00E-02 | 3   |
| GO:BP | regulation of tube size                                      | GO:0035150         | 127  | 2.00E-02 | 8   |
| GO:CC | side of membrane   | GO:0098552         | 492  | 2.00E-02 | 14  |
| GO:CC | collagen type I trimer                                       | GO:0005584         | 2    | 2.00E-02 | 2   |
| GO:CC | interleukin-18 receptor complex                              | GO:0045092         | 2    | 2.00E-02 | 2   |
| TF    | Factor: Kaiso; motif: NTCCTGCNAN                             | TF:M01119          | 3633 | 2.00E-02 | 55  |
| TF    | Factor: PPARGAMMA:RXR-ALPHA; motif: NNRGGTCAAWAGGTCAN        | TF:M08962          | 4100 | 2.00E-02 | 60  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: SNA; motif: GCCACCTGNCNGYN                              | TF:M03566   | 1969 | 2.00E-02 | 36  |
| TF    | Factor: PMX1; motif: TAATHA; match class: 1                     | TF:M03560_1 | 8561 | 2.00E-02 | 104 |
| TF    | Factor: MAZ; motif: GGGMGGGGS; match class: 1                   | TF:M10432_1 | 4198 | 2.00E-02 | 61  |
| TF    | Factor: ESR1; motif: NNNNMAGGTACCCCTGACCY; match class: 1       | TF:M02261_1 | 2053 | 2.00E-02 | 37  |
| GO:BP | aromatic compound biosynthetic process                          | GO:0019438  | 3605 | 2.10E-02 | 54  |
| GO:BP | response to progesterone  | GO:0032570  | 36   | 2.10E-02 | 5   |
| GO:BP | semi-lunar valve development                                    | GO:1905314  | 36   | 2.10E-02 | 5   |
| GO:BP | protein metabolic process                                       | GO:0019538  | 4947 | 2.10E-02 | 68  |
| TF    | Factor: p73; motif: NNRCAWGYCCARRCWTCYC                         | TF:M10025   | 5463 | 2.10E-02 | 74  |
| TF    | Factor: beta-catenin; motif: CTTTGATN; match class: 1           | TF:M07599_1 | 1809 | 2.10E-02 | 34  |
| TF    | Factor: ZNF394; motif: NRARWRGAANNAMWGNAAK; match class: 1      | TF:M10147_1 | 1493 | 2.10E-02 | 30  |
| TF    | Factor: TFAP2A; motif: NGCCYSAGGCN                              | TF:M04147   | 4684 | 2.10E-02 | 66  |
| GO:BP | cellular response to lipopolysaccharide                         | GO:0071222  | 168  | 2.20E-02 | 9   |
| GO:BP | negative regulation of biosynthetic process                     | GO:0009890  | 1454 | 2.20E-02 | 29  |
| GO:BP | positive regulation of nucleic acid-templated transcription     | GO:1903508  | 1456 | 2.20E-02 | 29  |
| GO:BP | positive regulation of transcription, DNA-templated             | GO:0045893  | 1456 | 2.20E-02 | 29  |
| TF    | Factor: C/EBPbeta; motif: NRTRYGCAATN                           | TF:M09881   | 2226 | 2.20E-02 | 39  |
| TF    | Factor: AP4; motif: NMNCAGCTGGN; match class: 1                 | TF:M12580_1 | 1119 | 2.20E-02 | 25  |
| TF    | Factor: SOX10; motif: NNAACAAAGNN; match class: 1               | TF:M09819_1 | 906  | 2.20E-02 | 22  |
| TF    | Factor: AR; motif: NNGNRRRGNACANNGTGTTCTNNNNN N; match class: 1 | TF:M00953_1 | 159  | 2.20E-02 | 9   |
| TF    | Factor: WT1; motif: SMCNCCNSC                                   | TF:M01118   | 6380 | 2.20E-02 | 83  |
| TF    | Factor: SF1; motif: NTGRCCTTGAMCT                               | TF:M12661   | 1979 | 2.20E-02 | 36  |
| GO:BP | kidney epithelium development                                   | GO:0072073  | 129  | 2.30E-02 | 8   |
| GO:BP | positive regulation of RNA biosynthetic process                 | GO:1902680  | 1458 | 2.30E-02 | 29  |
| TF    | Factor: E2F1; motif: GSGCGGGAAN; match class: 1                 | TF:M12597_1 | 9447 | 2.30E-02 | 112 |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: KLF15; motif: GAGNNGGGGNGTDG              | TF:M01714   | 1981 | 2.30E-02 | 36  |
| TF    | Factor: STAT5A; motif: NAWTTCYNGGAANYN            | TF:M00457   | 3468 | 2.30E-02 | 53  |
| TF    | Factor: DEC1; motif: CNCACRTGASC                  | TF:M03572   | 5982 | 2.30E-02 | 79  |
| TF    | Factor: ER-alpha; motif: ARGSTGACC                | TF:M04881   | 3378 | 2.30E-02 | 52  |
| TF    | Factor: NKX2B; motif: CACTTNA                     | TF:M02109   | 8588 | 2.30E-02 | 104 |
| GO:BP | zinc ion homeostasis                              | GO:0055069  | 37   | 2.40E-02 | 5   |
| GO:BP | response to purine-containing compound            | GO:0014074  | 130  | 2.40E-02 | 8   |
| GO:BP | regulation of hydrolase activity                  | GO:0051336  | 870  | 2.40E-02 | 21  |
| GO:CC | specific granule membrane                         | GO:0035579  | 86   | 2.40E-02 | 6   |
| KEGG  | Bladder cancer                                    | KEGG:05219  | 39   | 2.40E-02 | 4   |
| TF    | Factor: CEBPA; motif: ATTGCAYAAYN                 | TF:M07205   | 2066 | 2.40E-02 | 37  |
| TF    | Factor: HIF-1alpha; motif: NCACGT                 | TF:M02012   | 5985 | 2.40E-02 | 79  |
| TF    | Factor: ZBTB37; motif: TGGCTTTGGY                 | TF:M12688   | 3380 | 2.40E-02 | 52  |
| TF    | Factor: Six-2; motif: NNGTATCRNN                  | TF:M11030   | 5986 | 2.40E-02 | 79  |
| TF    | Factor: NR1B1; motif: NRGGTCANRRGGTCAN            | TF:M11792   | 4126 | 2.40E-02 | 60  |
| TF    | Factor: Pax-5; motif: RRNGRNGCAN; match class: 1  | TF:M03577_1 | 2236 | 2.40E-02 | 39  |
| GO:BP | regulation of phosphorylation                     | GO:0042325  | 1159 | 2.50E-02 | 25  |
| GO:BP | regulation of coagulation                         | GO:0050818  | 63   | 2.50E-02 | 6   |
| KEGG  | Human papillomavirus infection                    | KEGG:05165  | 314  | 2.50E-02 | 10  |
| TF    | Factor: NFATc1; motif: NATGGAANWNANTTTYCMN        | TF:M04051   | 4704 | 2.50E-02 | 66  |
| TF    | Factor: NFATc2; motif: NTTTCCATNNATGGAAN          | TF:M11986   | 5194 | 2.50E-02 | 71  |
| TF    | Factor: GR; motif: RGRACATTNTGTYC; match class: 1 | TF:M04750_1 | 1428 | 2.50E-02 | 29  |
| TF    | Factor: POU3F2; motif: WTATGCWAATKAG              | TF:M11904   | 2582 | 2.50E-02 | 43  |
| TF    | Factor: DPRX; motif: NNGGATTANN                   | TF:M04306   | 4131 | 2.50E-02 | 60  |
| TF    | Factor: POU4F3; motif: CTAATYW                    | TF:M07061   | 5993 | 2.50E-02 | 79  |
| TF    | Factor: p63; motif: NNRCAWGYCTGGRCWTGYN           | TF:M09643   | 3386 | 2.50E-02 | 52  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: Fli-1:ETV7; motif: NSMGGAMGGATNTCCGNN                 | TF:M08283   | 2670  | 2.50E-02 | 44  |
| TF    | Factor: ER71:SREBP-2; motif: NTSACGTGACGGAARY                 | TF:M08457   | 10905 | 2.50E-02 | 125 |
| TF    | Factor: TTF-1; motif: NNNCNCTTGASNNN                          | TF:M02034   | 3206  | 2.50E-02 | 50  |
| GO:BP | negative regulation of ion transport                          | GO:0043271  | 131   | 2.60E-02 | 8   |
| GO:BP | negative regulation of intrinsic apoptotic signaling pathway  | GO:2001243  | 95    | 2.60E-02 | 7   |
| TF    | Factor: SREBP; motif: NNNNYCACNCCANNN                         | TF:M01168   | 5699  | 2.60E-02 | 76  |
| TF    | Factor: ATF2; motif: NTGACRTCAYC                              | TF:M12581   | 3762  | 2.60E-02 | 56  |
| TF    | Factor: Fli-1:C/EBPbeta; motif: RNCGGAWRTTGCGCAAY             | TF:M08281   | 6613  | 2.60E-02 | 85  |
| TF    | Factor: DEC; motif: SCCCAMGTGAAGN                             | TF:M00997   | 7759  | 2.60E-02 | 96  |
| TF    | Factor: Gli2; motif: NTGGGTGGTCNN                             | TF:M07455   | 2502  | 2.60E-02 | 42  |
| GO:BP | regulation of actin filament-based movement                   | GO:1903115  | 38    | 2.70E-02 | 5   |
| GO:BP | positive regulation of molecular function                     | GO:0044093  | 1394  | 2.70E-02 | 28  |
| GO:CC | ficolin-1-rich granule membrane                               | GO:0101003  | 55    | 2.70E-02 | 5   |
| TF    | Factor: POU2F2; motif: NTATGCWAATN                            | TF:M04072   | 1912  | 2.70E-02 | 35  |
| TF    | Factor: c-Jun; motif: NNNNRRTGASTCAN                          | TF:M07102   | 4236  | 2.70E-02 | 61  |
| TF    | Factor: TATA; motif: STATAAAWRNNNNNN                          | TF:M00252   | 3672  | 2.70E-02 | 55  |
| TF    | Factor: DB1; motif: GGRRRRGRRGGGGGNGRRR; match class: 1       | TF:M10107_1 | 2504  | 2.70E-02 | 42  |
| TF    | Factor: beta-catenin; motif: CTTTGATN                         | TF:M07599   | 6721  | 2.70E-02 | 86  |
| TF    | Factor: p73; motif: NGRCATGYTGNRCWTGYYN                       | TF:M09644   | 3034  | 2.70E-02 | 48  |
| GO:BP | muscle organ morphogenesis                                    | GO:0048644  | 64    | 2.80E-02 | 6   |
| GO:BP | negative regulation of ion transmembrane transporter activity | GO:0032413  | 64    | 2.80E-02 | 6   |
| GO:BP | negative regulation of cell motility                          | GO:2000146  | 267   | 2.80E-02 | 11  |
| TF    | Factor: GABP-alpha; motif: AACCGGAAR; match class: 1          | TF:M04748_1 | 9377  | 2.80E-02 | 111 |
| TF    | Factor: Sp1; motif: NNGGGCGGGGNN; match class: 1              | TF:M00932_1 | 5909  | 2.80E-02 | 78  |
| TF    | Factor: C/EBPepsilon; motif: HAANMTTKCNWMAC                   | TF:M01868   | 2507  | 2.80E-02 | 42  |
| TF    | Factor: Sox-18; motif: NACAAYGS                               | TF:M11623   | 4529  | 2.80E-02 | 64  |

|       |  |             |      |          |    |
|-------|--|-------------|------|----------|----|
| TF    | Factor: ATF3; motif: GRTGACKCA                     | TF:M12582   | 6319 | 2.80E-02 | 82 |
| GO:MF | SMAD binding                                       | GO:0046332  | 76   | 2.90E-02 | 6  |
| GO:BP | positive regulation of leukocyte activation        | GO:0002696  | 319  | 2.90E-02 | 12 |
| TF    | Factor: GATA-2; motif: NTGNNNNNNNAGATAAGN          | TF:M09937   | 2338 | 2.90E-02 | 40 |
| TF    | Factor: ESR1; motif: STGACCTN                      | TF:M12602   | 2862 | 2.90E-02 | 46 |
| TF    | Factor: NFATc2; motif: NTTTCCGCGGAAAN              | TF:M11983   | 7146 | 2.90E-02 | 90 |
| TF    | Factor: E2A; motif: NRMCASCTGCNNN                  | TF:M02088   | 2511 | 2.90E-02 | 42 |
| TF    | Factor: Helios; motif: NNTWGGGANNN                 | TF:M01003   | 3131 | 2.90E-02 | 49 |
| TF    | Factor: Dlx-7; motif: NTCRTTAN                     | TF:M10600   | 6220 | 2.90E-02 | 81 |
| TF    | Factor: RFX1; motif: NNGTNRNCRNWRGYAACNN           | TF:M00280   | 5716 | 2.90E-02 | 76 |
| TF    | Factor: LRH-1; motif: TCAAGGTCRTGACCTTGA           | TF:M11831   | 3042 | 2.90E-02 | 48 |
| TF    | Factor: Prep-1; motif: GRBTGANAGATN                | TF:M07464   | 3683 | 2.90E-02 | 55 |
| TF    | Factor: TEAD3; motif: RCATTCW                      | TF:M04144   | 994  | 2.90E-02 | 23 |
| TF    | Factor: Oct-2; motif: NTGCATATGCAN; match class: 1 | TF:M11899_1 | 3591 | 2.90E-02 | 54 |
| TF    | Factor: Msx-1; motif: WNGNAATTANV                  | TF:M08822   | 5618 | 2.90E-02 | 75 |
| GO:BP | leukocyte mediated immunity                        | GO:0002443  | 320  | 3.00E-02 | 12 |
| TF    | Factor: T-box; motif: NASGTGTNAN                   | TF:M12021   | 3685 | 3.00E-02 | 55 |
| TF    | Factor: JUNB:FRA-2; motif: NRTGASTCAT              | TF:M08923   | 2428 | 3.00E-02 | 41 |
| TF    | Factor: STAT1; motif: TTCNRGGAAN                   | TF:M07064   | 2258 | 3.00E-02 | 39 |
| GO:BP | negative regulation of cation channel activity     | GO:2001258  | 39   | 3.10E-02 | 5  |
| GO:BP | programmed necrotic cell death                     | GO:0097300  | 39   | 3.10E-02 | 5  |
| GO:BP | cellular response to molecule of bacterial origin  | GO:0071219  | 176  | 3.10E-02 | 9  |
| TF    | Factor: GLI; motif: MCVNNGACCACCAV                 | TF:M03871   | 3048 | 3.10E-02 | 48 |
| TF    | Factor: LRF; motif: RCGACCACCNN; match class: 1    | TF:M12230_1 | 2432 | 3.10E-02 | 41 |
| TF    | Factor: ERR1; motif: NTGACCTTGRNN                  | TF:M04873   | 2694 | 3.10E-02 | 44 |
| TF    | Factor: Oct3; motif: NATGCAANN                     | TF:M01307   | 3322 | 3.10E-02 | 51 |

|       |  |                   |       |          |     |
|-------|--|-------------------|-------|----------|-----|
| GO:CC | apical part of cell                                      | GO:0045177        | 391   | 3.20E-02 | 12  |
| REAC  | Signaling by PDGF  | REAC:R-HSA-186797 | 53    | 3.20E-02 | 5   |
| TF    | Factor: RARA; motif: AGGTCAANNARAGGTCA                   | TF:M04483         | 3600  | 3.20E-02 | 54  |
| TF    | Factor: C/EBPgamma; motif: NRTRSRMAAKN                   | TF:M01869         | 2608  | 3.20E-02 | 43  |
| TF    | Factor: AP-1; motif: RGTGACTMANN                         | TF:M00188         | 2609  | 3.20E-02 | 43  |
| TF    | Factor: MR; motif: NGNACRNNNYGTNCN                       | TF:M11849         | 3788  | 3.20E-02 | 56  |
| GO:MF | RAGE receptor binding                                    | GO:0050786        | 9     | 3.30E-02 | 3   |
| TF    | Factor: foxm1; motif: TGTTTRCTYWNN                       | TF:M09930         | 5734  | 3.30E-02 | 76  |
| TF    | Factor: RAR-gamma; motif: TGACCTBYNKN                    | TF:M03562         | 3697  | 3.30E-02 | 55  |
| TF    | Factor: HES-1; motif: GNCACGTGNC; match class: 1         | TF:M08767_1       | 6962  | 3.30E-02 | 88  |
| TF    | Factor: RUNX2; motif: WRACCGCANWAACCGCAN; match class: 1 | TF:M04107_1       | 6039  | 3.30E-02 | 79  |
| TF    | Factor: STAT6; motif: NNYTTCCY                           | TF:M00500         | 4076  | 3.30E-02 | 59  |
| TF    | Factor: HAIRYLIKE; motif: NNNNCANGTG                     | TF:M08885         | 5339  | 3.40E-02 | 72  |
| TF    | Factor: Brachyury; motif: NTNNCANNNRGTGTGAANN            | TF:M09878         | 3240  | 3.40E-02 | 50  |
| TF    | Factor: Fra-1; motif: NATGASTCAYM                        | TF:M11284         | 2615  | 3.40E-02 | 43  |
| TF    | Factor: NF-1C; motif: NTTGGCNNNTGCCARN; match class: 1   | TF:M11729_1       | 794   | 3.40E-02 | 20  |
| TF    | Factor: Fra-2; motif: NNRTGAGTCAYN                       | TF:M09923         | 3611  | 3.40E-02 | 54  |
| GO:BP | response to oxygen levels                                | GO:0070482        | 325   | 3.50E-02 | 12  |
| TF    | Factor: HOXB5; motif: RTCRTTAN                           | TF:M10698         | 3800  | 3.50E-02 | 56  |
| TF    | Factor: Dlx-3; motif: NTCRTTAN                           | TF:M10609         | 3800  | 3.50E-02 | 56  |
| TF    | Factor: E2F-4; motif: NGGCGGGAARN                        | TF:M07084         | 10196 | 3.50E-02 | 118 |
| GO:BP | growth   | GO:0040007        | 893   | 3.60E-02 | 21  |
| GO:BP | pulmonary valve development                              | GO:0003177        | 20    | 3.60E-02 | 4   |
| REAC  | Biological oxidations                                    | REAC:R-HSA-211859 | 169   | 3.60E-02 | 8   |
| REAC  | Dissolution of Fibrin Clot                               | REAC:R-HSA-75205  | 11    | 3.60E-02 | 3   |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: NFATc2; motif: TTTTCCATGGAAAA; match class: 1 | TF:M11985_1 | 3803 | 3.60E-02 | 56  |
| TF    | Factor: C/EBPalpha; motif: ATTGCGYAAY                 | TF:M07412   | 2888 | 3.60E-02 | 46  |
| GO:BP | cellular nitrogen compound biosynthetic process       | GO:0044271  | 4249 | 3.70E-02 | 60  |
| GO:BP | negative regulation of cellular component movement    | GO:0051271  | 275  | 3.70E-02 | 11  |
| TF    | Factor: ZNF342; motif: NRGTTGGWCANT                   | TF:M12076   | 1229 | 3.70E-02 | 26  |
| TF    | Factor: Fra-1; motif: NNNTGAGTCAYN                    | TF:M09922   | 3807 | 3.70E-02 | 56  |
| TF    | Factor: T3R-beta; motif: NNRGGTCRTGACCYNN             | TF:M11815   | 4668 | 3.70E-02 | 65  |
| GO:BP | in utero embryonic development                        | GO:0001701  | 383  | 3.80E-02 | 13  |
| GO:BP | response to metal ion                                 | GO:0010038  | 328  | 3.80E-02 | 12  |
| GO:CC | plasma membrane region                                | GO:0098590  | 1176 | 3.80E-02 | 23  |
| TF    | Factor: DPF2; motif: NYCACYTCCYCNYYCY; match class: 1 | TF:M09760_1 | 2803 | 3.80E-02 | 45  |
| TF    | Factor: GCMA; motif: ATGCGGGCGGAARKG; match class: 1  | TF:M08487_1 | 8249 | 3.80E-02 | 100 |
| TF    | Factor: POU5F1; motif: NNATGCAAANN                    | TF:M09782   | 2982 | 3.80E-02 | 47  |
| TF    | Factor: PDEF; motif: MCCGGATNTN                       | TF:M02075   | 2453 | 3.80E-02 | 41  |
| TF    | Factor: SPI1; motif: NGRGGAAGTN                       | TF:M02078   | 3073 | 3.80E-02 | 48  |
| TF    | Factor: MSANTD3; motif: SNNCACTCAC                    | TF:M12406   | 3999 | 3.80E-02 | 58  |
| TF    | Factor: FOXO1A; motif: RWMAACAGGAAGTN; match class: 1 | TF:M08302_1 | 2282 | 3.80E-02 | 39  |
| GO:BP | nephron epithelium development                        | GO:0072009  | 101  | 3.90E-02 | 7   |
| TF    | Factor: DMBX1; motif: NNGGATTANN                      | TF:M04305   | 4383 | 3.90E-02 | 62  |
| TF    | Factor: BRCA2; motif: TGMICYCWGN                      | TF:M12723   | 3259 | 3.90E-02 | 50  |
| GO:BP | negative regulation of blood coagulation              | GO:0030195  | 41   | 4.00E-02 | 5   |
| TF    | Factor: IRF; motif: RAAANTGAAAN                       | TF:M00972   | 1623 | 4.00E-02 | 31  |
| TF    | Factor: AML2; motif: CCRCACCAYDN                      | TF:M01854   | 2372 | 4.00E-02 | 40  |
| TF    | Factor: CDP:HOXA13; motif: ATCGATYAYSICRTAAA          | TF:M08201   | 6582 | 4.00E-02 | 84  |
| GO:CC | basement membrane                                     | GO:0005604  | 95   | 4.10E-02 | 6   |
| TF    | Factor: REST; motif: NNNNGGNGCTGTCCATGGTGCT           | TF:M01256   | 2374 | 4.10E-02 | 40  |

|       |   |                      |      |          |     |
|-------|---|----------------------|------|----------|-----|
| TF    | Factor: ER-alpha; motif: NAGGTCACSGTGACCTN          | TF:M11843            | 3172 | 4.10E-02 | 49  |
| TF    | Factor: HOXA6; motif: NYMATTAN                      | TF:M08772            | 6482 | 4.10E-02 | 83  |
| TF    | Factor: TEF-1; motif: NRCATWCCN; match class: 1     | TF:M12042_1          | 672  | 4.20E-02 | 18  |
| TF    | Factor: Cdx-2; motif: NRTYRTAAAN                    | TF:M10851            | 1953 | 4.20E-02 | 35  |
| TF    | Factor: STAT3; motif: NGNNATTTCCSGBAARTGNNN         | TF:M00225            | 2815 | 4.20E-02 | 45  |
| TF    | Factor: E2A; motif: CAGNTGNN                        | TF:M07353            | 2292 | 4.20E-02 | 39  |
| GO:BP | defense response to bacterium                       | GO:0042742           | 183  | 4.30E-02 | 9   |
| TF    | Factor: MR; motif: NGNACRNNNYGTNCN; match class: 1  | TF:M11849_1          | 3732 | 4.30E-02 | 55  |
| TF    | Factor: Sox-4; motif: BCWTTGT                       | TF:M07268            | 4591 | 4.30E-02 | 64  |
| TF    | Factor: E2F-4; motif: NNTTCCC GCCNN; match class: 1 | TF:M04823_1          | 7533 | 4.30E-02 | 93  |
| GO:BP | negative regulation of proteolysis                  | GO:0045861           | 280  | 4.40E-02 | 11  |
| GO:BP | entry into host                                     | GO:0044409           | 141  | 4.40E-02 | 8   |
| GO:BP | cell development                                    | GO:0048468           | 1919 | 4.40E-02 | 34  |
| REAC  | MET activates PTK2 signaling                        | REAC:R-HSA-8874081   | 30   | 4.40E-02 | 4   |
| TF    | Factor: FOXJ2; motif: NNTGTTGTAAAYAN                | TF:M11584            | 3923 | 4.40E-02 | 57  |
| TF    | Factor: REST; motif: CCNNGGTGCTGAA                  | TF:M03883            | 3090 | 4.40E-02 | 48  |
| TF    | Factor: Spic; motif: NGNGGAASTN; match class: 1     | TF:M02077_1          | 2042 | 4.40E-02 | 36  |
| MIRNA | hsa-miR-204-5p                                      | MIRNA:hsa-miR-204-5p | 372  | 4.40E-02 | 12  |
| GO:BP | response to interferon-alpha                        | GO:0035455           | 21   | 4.50E-02 | 4   |
| GO:BP | negative regulation of hemostasis                   | GO:1900047           | 42   | 4.50E-02 | 5   |
| GO:BP | anion transmembrane transport                       | GO:0098656           | 231  | 4.50E-02 | 10  |
| GO:CC | aggresome   | GO:0016235           | 33   | 4.50E-02 | 4   |
| TF    | Factor: AP-2alpha; motif: NTNSCCTGRGGSNAN           | TF:M09590            | 4694 | 4.50E-02 | 65  |
| TF    | Factor: NF-E4; motif: CHCCCTCKCCWG                  | TF:M02105            | 2471 | 4.50E-02 | 41  |
| TF    | Factor: Hey2; motif: NNCACGYGNN; match class: 1     | TF:M11052_1          | 8713 | 4.50E-02 | 104 |
| TF    | Factor: Nkx3-2; motif: TRAGTG                       | TF:M01181            | 8070 | 4.50E-02 | 98  |

|       |  |                    |      |          |     |
|-------|--|--------------------|------|----------|-----|
| TF    | Factor: NFATc2; motif: NTTTCCATNNATGGAAAN; match class: 1            | TF:M11986_1        | 4990 | 4.50E-02 | 68  |
| GO:BP | positive regulation of response to external stimulus                 | GO:0032103         | 390  | 4.60E-02 | 13  |
| TF    | Factor: B-ATF; motif: NNAYGACACN                                     | TF:M11301          | 6607 | 4.60E-02 | 84  |
| TF    | Factor: isx; motif: NTCRTTAA   | TF:M10956          | 8396 | 4.60E-02 | 101 |
| GO:MF | oxygen carrier activity  | GO:0005344         | 10   | 4.70E-02 | 3   |
| GO:BP | negative regulation of transcription by RNA polymerase II            | GO:0000122         | 841  | 4.80E-02 | 20  |
| REAC  | Response to metal ions   | REAC:R-HSA-5660526 | 12   | 4.80E-02 | 3   |
| TF    | Factor: ERF:C/EBPdelta; motif: NNCGGAWRTTGCGCAAY                     | TF:M08233          | 4997 | 4.80E-02 | 68  |
| TF    | Factor: myogenin; motif: CRCTGTTBNNTTGGCAGSNGCCA RCH; match class: 1 | TF:M00056_1        | 3842 | 4.80E-02 | 56  |
| TF    | Factor: Sox-9; motif: MACARWGNNNYCNTTNW; match class: 1              | TF:M08838_1        | 552  | 4.80E-02 | 16  |
| GO:BP | response to corticosteroid   | GO:0031960         | 143  | 4.90E-02 | 8   |
| GO:BP | lymphocyte mediated immunity   | GO:0002449         | 233  | 4.90E-02 | 10  |
| TF    | Factor: E2F-4; motif: AATGGCGCCAAA                                   | TF:M04518          | 4902 | 4.90E-02 | 67  |
| TF    | Factor: BEN; motif: CWGCGAYA   | TF:M01241          | 6926 | 4.90E-02 | 87  |
| TF    | Factor: HSF1; motif: RGAANRTTCYRGAAN                                 | TF:M11656          | 1721 | 4.90E-02 | 32  |
| GO:MF | interleukin-18 receptor activity                                     | GO:0042008         | 2    | 5.00E-02 | 2   |
| GO:MF | heme binding   | GO:0020037         | 121  | 5.00E-02 | 7   |

*Table A33. KCL BrainBank enrichment for Cluster 2 with gProfiler2. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term. GO:BP – Gene Ontology Biological Process, GO:CC – Gene Ontology Cellular Components, GO:MF – Gene Ontology Molecular Function, KEGG: Kyoto Encyclopaedia of Genes and Genomes, REAC: Reactome, TF: Transfac.*

| Source | Term Name                                    | Term ID           | Term Size | p adjusted | Intersection Size |
|--------|--|-------------------|-----------|------------|-------------------|
| GO:BP  | immune response                              | GO:0006955        | 1363      | 6.00E-58   | 106               |
| GO:BP  | immune system process                        | GO:0002376        | 2161      | 5.50E-57   | 127               |
| GO:BP  | regulation of immune system process          | GO:0002682        | 1217      | 2.60E-47   | 91                |
| GO:CC  | cell periphery                               | GO:0071944        | 5188      | 2.20E-46   | 173               |
| GO:BP  | defense response                             | GO:0006952        | 1343      | 7.40E-42   | 89                |
| GO:CC  | plasma membrane                              | GO:0005886        | 4761      | 7.20E-41   | 158               |
| REAC   | Immune System                                | REAC:R-HSA-168256 | 1770      | 1.60E-40   | 98                |
| GO:BP  | regulation of immune response                | GO:0050776        | 741       | 8.30E-40   | 68                |
| GO:CC  | integral component of membrane               | GO:0016021        | 4917      | 4.20E-37   | 155               |
| GO:BP  | leukocyte activation                         | GO:0045321        | 795       | 8.10E-37   | 67                |
| GO:CC  | intrinsic component of membrane              | GO:0031224        | 5051      | 2.50E-36   | 156               |
| GO:BP  | cell activation                              | GO:0001775        | 914       | 5.80E-35   | 69                |
| GO:BP  | positive regulation of immune system process | GO:0002684        | 764       | 7.70E-35   | 64                |
| GO:CC  | membrane                                     | GO:0016020        | 8518      | 3.60E-34   | 203               |
| REAC   | Innate Immune System                         | REAC:R-HSA-168249 | 914       | 8.80E-33   | 66                |
| GO:BP  | response to external stimulus                | GO:0009605        | 2310      | 2.40E-32   | 101               |
| GO:BP  | response to stimulus                         | GO:0050896        | 7482      | 1.60E-30   | 184               |
| GO:BP  | inflammatory response                        | GO:0006954        | 651       | 1.20E-28   | 54                |
| GO:BP  | immune effector process                      | GO:0002252        | 513       | 1.50E-28   | 49                |
| GO:BP  | regulation of cell activation                | GO:0050865        | 541       | 1.60E-28   | 50                |
| GO:MF  | signaling receptor activity                  | GO:0038023        | 1139      | 5.80E-28   | 67                |
| GO:MF  | molecular transducer activity                | GO:0060089        | 1139      | 5.80E-28   | 67                |
| GO:MF  | transmembrane signaling receptor activity    | GO:0004888        | 947       | 2.40E-27   | 61                |
| GO:BP  | response to biotic stimulus                  | GO:0009607        | 1182      | 3.60E-27   | 68                |
| GO:BP  | defense response to other organism           | GO:0098542        | 842       | 1.10E-26   | 58                |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| GO:BP | positive regulation of response to stimulus                               | GO:0048584         | 1882 | 1.30E-26 | 84  |
| KEGG  | Staphylococcus aureus infection   | KEGG:05150         | 60   | 1.40E-26 | 22  |
| GO:BP | response to other organism  | GO:0051707         | 1142 | 2.20E-26 | 66  |
| GO:BP | response to external biotic stimulus                                      | GO:0043207         | 1145 | 2.60E-26 | 66  |
| GO:BP | regulation of response to stimulus  | GO:0048583         | 3512 | 4.20E-26 | 115 |
| GO:BP | regulation of leukocyte activation  | GO:0002694         | 500  | 6.40E-26 | 46  |
| GO:BP | leukocyte activation involved in immune response                          | GO:0002366         | 253  | 3.60E-25 | 35  |
| GO:BP | biological process involved in interspecies interaction between organisms | GO:0044419         | 1282 | 4.40E-25 | 68  |
| GO:BP | cell activation involved in immune response                               | GO:0002263         | 257  | 6.20E-25 | 35  |
| GO:BP | lymphocyte activation   | GO:0046649         | 652  | 1.00E-24 | 50  |
| GO:BP | biological adhesion   | GO:0022610         | 1393 | 1.60E-24 | 70  |
| GO:BP | positive regulation of immune response                                    | GO:0050778         | 464  | 3.50E-24 | 43  |
| GO:CC | intrinsic component of plasma membrane                                    | GO:0031226         | 1541 | 3.60E-24 | 72  |
| GO:CC | integral component of plasma membrane                                     | GO:0005887         | 1466 | 5.70E-24 | 70  |
| GO:BP | cell adhesion   | GO:0007155         | 1388 | 7.60E-24 | 69  |
| GO:BP | regulation of multicellular organismal process                            | GO:0051239         | 2403 | 2.70E-23 | 90  |
| GO:BP | regulation of cytokine production   | GO:0001817         | 646  | 5.10E-23 | 48  |
| GO:BP | cytokine production   | GO:0001816         | 652  | 7.70E-23 | 48  |
| REAC  | Neutrophil degranulation  | REAC:R-HSA-6798695 | 446  | 1.80E-22 | 40  |
| GO:BP | innate immune response  | GO:0045087         | 667  | 2.10E-22 | 48  |
| GO:BP | signaling   | GO:0023052         | 5550 | 3.40E-22 | 141 |
| GO:BP | myeloid leukocyte activation  | GO:0002274         | 205  | 5.50E-22 | 30  |
| GO:BP | response to stress  | GO:0006950         | 3345 | 7.90E-22 | 105 |
| GO:BP | cell communication  | GO:0007154         | 5601 | 8.50E-22 | 141 |
| GO:BP | positive regulation of biological process                                 | GO:0048518         | 5512 | 1.90E-21 | 139 |

|       |   |             |           |              |     |
|-------|---|-------------|-----------|--------------|-----|
| GO:BP | biological regulation                                   | GO:0065007  | 1083<br>7 | 2.70E-<br>21 | 209 |
| GO:BP | signal transduction                                     | GO:0007165  | 5094      | 4.50E-<br>21 | 132 |
| GO:BP | regulation of biological process                        | GO:0050789  | 1021<br>3 | 4.60E-<br>21 | 201 |
| GO:CC | extracellular region                                    | GO:0005576  | 3516      | 6.80E-<br>21 | 105 |
| GO:BP | adaptive immune response                                | GO:0002250  | 390       | 8.10E-<br>21 | 37  |
| GO:CC | vesicle   | GO:0031982  | 3591      | 9.60E-<br>21 | 106 |
| GO:BP | activation of immune response                           | GO:0002253  | 298       | 1.90E-<br>20 | 33  |
| GO:BP | negative regulation of immune system process            | GO:0002683  | 375       | 2.30E-<br>20 | 36  |
| GO:BP | multicellular organismal process                        | GO:0032501  | 6431      | 2.80E-<br>20 | 150 |
| GO:BP | cellular response to stimulus                           | GO:0051716  | 6392      | 4.60E-<br>20 | 149 |
| GO:CC | cytoplasmic vesicle                                     | GO:0031410  | 2275      | 6.90E-<br>20 | 81  |
| GO:CC | intracellular vesicle                                   | GO:0097708  | 2277      | 7.20E-<br>20 | 81  |
| GO:BP | response to bacterium                                   | GO:0009617  | 504       | 8.50E-<br>20 | 40  |
| GO:BP | regulation of cellular process                          | GO:0050794  | 9657      | 1.40E-<br>19 | 191 |
| GO:BP | immune response-regulating signaling pathway            | GO:0002764  | 396       | 1.50E-<br>19 | 36  |
| GO:CC | cell surface  | GO:0009986  | 741       | 1.80E-<br>19 | 46  |
| GO:BP | leukocyte mediated immunity                             | GO:0002443  | 320       | 1.90E-<br>19 | 33  |
| GO:BP | phagocytosis  | GO:0006909  | 229       | 2.40E-<br>19 | 29  |
| GO:BP | positive regulation of multicellular organismal process | GO:0051240  | 1298      | 1.10E-<br>18 | 60  |
| TF    | Factor: GATAD2A; motif: CCTKTG; match class: 1          | TF:M09726_1 | 7641      | 2.00E-<br>18 | 163 |
| TF    | Factor: PEA3; motif: ACWTCK                             | TF:M00655   | 8027      | 2.20E-<br>18 | 168 |
| TF    | Factor: AML1; motif: TGTGGT                             | TF:M02084   | 1026<br>8 | 7.00E-<br>18 | 195 |
| TF    | Factor: AML1; motif: TGTGGT                             | TF:M00751   | 1026<br>8 | 7.00E-<br>18 | 195 |
| TF    | Factor: AML1a; motif: TGTGGT                            | TF:M00271   | 1026<br>8 | 7.00E-<br>18 | 195 |
| GO:BP | T cell activation                                       | GO:0042110  | 448       | 9.30E-<br>18 | 36  |
| TF    | Factor: Smad2; motif: AGACAN; match class: 1            | TF:M03580_1 | 7607      | 1.00E-<br>17 | 161 |

|       |   |             |           |              |     |
|-------|---|-------------|-----------|--------------|-----|
| REAC  | REACTOME root term                                  | REAC:000000 | 9607      | 1.90E-<br>17 | 184 |
| GO:CC | secretory granule                                   | GO:0030141  | 760       | 2.20E-<br>17 | 44  |
| GO:CC | secretory granule membrane                          | GO:0030667  | 287       | 2.40E-<br>17 | 29  |
| TF    | Factor: SRY; motif: AACAAATNR                       | TF:M08976   | 1174<br>0 | 2.70E-<br>17 | 211 |
| TF    | Factor: ZBTB39; motif: CNCTGY                       | TF:M12689   | 1347<br>7 | 4.60E-<br>17 | 230 |
| TF    | Factor: PEA3; motif: NNCAGGAARNN                    | TF:M09915   | 1084<br>9 | 4.90E-<br>17 | 200 |
| GO:BP | leukocyte migration                                 | GO:0050900  | 329       | 5.60E-<br>17 | 31  |
| TF    | Factor: NMYC; motif: CAYCTG                         | TF:M01808   | 1095<br>1 | 5.90E-<br>17 | 201 |
| GO:BP | regulation of lymphocyte activation                 | GO:0051249  | 415       | 6.60E-<br>17 | 34  |
| GO:BP | positive regulation of cytokine production          | GO:0001819  | 416       | 7.10E-<br>17 | 34  |
| TF    | Factor: GATAD2A; motif: CCTKTG                      | TF:M09726   | 1308<br>9 | 9.30E-<br>17 | 225 |
| TF    | Factor: Spi-B; motif: TTCYBC; match class: 1        | TF:M03851_1 | 1709<br>5 | 9.60E-<br>17 | 267 |
| TF    | Factor: Spi-B; motif: TTCYBC                        | TF:M03851   | 1711<br>0 | 1.10E-<br>16 | 267 |
| GO:BP | leukocyte cell-cell adhesion                        | GO:0007159  | 338       | 1.20E-<br>16 | 31  |
| TF    | Transfac  | TF:M00000   | 1711<br>4 | 1.20E-<br>16 | 267 |
| GO:BP | leukocyte proliferation                             | GO:0070661  | 286       | 1.30E-<br>16 | 29  |
| GO:BP | myeloid cell activation involved in immune response | GO:0002275  | 87        | 1.30E-<br>16 | 19  |
| GO:CC | extracellular space                                 | GO:0005615  | 2749      | 1.50E-<br>16 | 84  |
| GO:BP | cell surface receptor signaling pathway             | GO:0007166  | 2456      | 1.70E-<br>16 | 80  |
| KEGG  | Systemic lupus erythematosus                        | KEGG:05322  | 104       | 1.90E-<br>16 | 19  |
| GO:CC | vesicle membrane                                    | GO:0012506  | 1138      | 2.30E-<br>16 | 52  |
| GO:CC | cellular anatomical entity                          | GO:0110165  | 1686<br>9 | 4.70E-<br>16 | 261 |
| TF    | Factor: PU.1; motif: AGGAAG                         | TF:M02031   | 1548<br>6 | 5.00E-<br>16 | 249 |
| TF    | Factor: Elf-1; motif: AGGAAG                        | TF:M01266   | 1548<br>6 | 5.00E-<br>16 | 249 |
| GO:BP | cell-cell adhesion                                  | GO:0098609  | 828       | 5.40E-<br>16 | 45  |
| GO:CC | cytoplasmic vesicle membrane                        | GO:0030659  | 1119      | 5.80E-<br>16 | 51  |



|       |  |                    |       |          |     |
|-------|--|--------------------|-------|----------|-----|
| GO:BP | positive regulation of cell activation         | GO:0050867         | 330   | 6.40E-16 | 30  |
| TF    | Factor: Sox-18; motif: CAAWGBB                 | TF:M03848          | 15043 | 7.10E-16 | 244 |
| TF    | Factor: ZBTB39; motif: CNCTGY; match class: 1  | TF:M12689_1        | 8347  | 1.10E-15 | 166 |
| TF    | Factor: ZNF35; motif: SSAAKA                   | TF:M07479          | 16059 | 1.20E-15 | 254 |
| GO:CC | cellular_component                             | GO:0005575         | 16974 | 1.30E-15 | 261 |
| TF    | Factor: Kid3; motif: CCACN                     | TF:M01160          | 17056 | 1.30E-15 | 264 |
| KEGG  | KEGG root term                                 | KEGG:00000         | 7044  | 1.40E-15 | 145 |
| KEGG  | Leishmaniasis                                  | KEGG:05140         | 71    | 2.70E-15 | 16  |
| TF    | Factor: Smad2; motif: AGACAN                   | TF:M03580          | 13070 | 3.40E-15 | 221 |
| KEGG  | Tuberculosis                                   | KEGG:05152         | 162   | 4.80E-15 | 21  |
| GO:BP | cell population proliferation                  | GO:0008283         | 1750  | 6.00E-15 | 64  |
| GO:BP | regulation of developmental process            | GO:0050793         | 2221  | 6.10E-15 | 73  |
| GO:BP | regulation of immune effector process          | GO:0002697         | 302   | 6.10E-15 | 28  |
| TF    | Factor: NMYC; motif: CAYCTG; match class: 1    | TF:M01808_1        | 5049  | 7.70E-15 | 119 |
| GO:MF | molecular_function                             | GO:0003674         | 16562 | 8.40E-15 | 255 |
| TF    | Factor: ING4; motif: CCACCA                    | TF:M01743          | 13898 | 9.40E-15 | 229 |
| GO:BP | lymphocyte proliferation                       | GO:0046651         | 261   | 1.70E-14 | 26  |
| GO:CC | side of membrane                               | GO:0098552         | 492   | 1.70E-14 | 33  |
| REAC  | Adaptive Immune System                         | REAC:R-HSA-1280218 | 709   | 2.20E-14 | 39  |
| GO:BP | mononuclear cell proliferation                 | GO:0032943         | 264   | 2.30E-14 | 26  |
| GO:MF | immune receptor activity                       | GO:0140375         | 122   | 2.30E-14 | 19  |
| TF    | Factor: Sox-18; motif: CAAWGBB; match class: 1 | TF:M03848_1        | 10894 | 2.40E-14 | 194 |
| GO:BP | positive regulation of leukocyte activation    | GO:0002696         | 319   | 2.60E-14 | 28  |
| GO:CC | secretory vesicle                              | GO:0099503         | 920   | 2.80E-14 | 44  |
| TF    | Factor: ETV4; motif: NCAGGAAGNN                | TF:M12556          | 9336  | 2.80E-14 | 175 |
| GO:BP | regulation of response to external stimulus    | GO:0032101         | 839   | 3.10E-14 | 43  |

|       |  |                   |       |          |     |
|-------|--|-------------------|-------|----------|-----|
| KEGG  | Neutrophil extracellular trap formation                                  | KEGG:04613        | 159   | 4.90E-14 | 20  |
| TF    | Factor: Kid3; motif: CCACN; match class: 1                               | TF:M01160_1       | 16941 | 5.00E-14 | 259 |
| TF    | Factor: PU.1; motif: NNNNYYACTTCCTCTTTY                                  | TF:M01172         | 3663  | 5.80E-14 | 96  |
| GO:BP | regulation of leukocyte cell-cell adhesion                               | GO:1903037        | 302   | 6.30E-14 | 27  |
| GO:BP | immune response-regulating cell surface receptor signaling pathway       | GO:0002768        | 251   | 7.50E-14 | 25  |
| TF    | Factor: Zbtb44; motif: CKGTGA  | TF:M05405         | 11777 | 7.50E-14 | 203 |
| TF    | Factor: PARP; motif: TTTCYN  | TF:M02027         | 14025 | 8.10E-14 | 228 |
| KEGG  | Phagosome  | KEGG:04145        | 143   | 9.40E-14 | 19  |
| TF    | Factor: BRN1; motif: HAATGCN   | TF:M03813         | 11080 | 1.70E-13 | 194 |
| GO:BP | positive regulation of immune effector process                           | GO:0002699        | 211   | 1.90E-13 | 23  |
| GO:BP | regulation of tumor necrosis factor superfamily cytokine production      | GO:1903555        | 145   | 2.00E-13 | 20  |
| GO:BP | tumor necrosis factor superfamily cytokine production                    | GO:0071706        | 145   | 2.00E-13 | 20  |
| GO:BP | response to chemical   | GO:0042221        | 3698  | 2.30E-13 | 95  |
| GO:BP | regulation of cell population proliferation                              | GO:0042127        | 1482  | 2.50E-13 | 56  |
| REAC  | Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell | REAC:R-HSA-198933 | 101   | 2.70E-13 | 17  |
| TF    | Factor: ZNF35; motif: SSAAKA; match class: 1                             | TF:M07479_1       | 13256 | 3.30E-13 | 218 |
| TF    | Factor: Lyl-1; motif: NCAKCTGYTNYCNN                                     | TF:M09977         | 11924 | 3.30E-13 | 203 |
| GO:BP | cellular process   | GO:0009987        | 15441 | 3.60E-13 | 241 |
| GO:CC | external side of plasma membrane   | GO:0009897        | 291   | 4.30E-13 | 25  |
| GO:BP | regulation of leukocyte proliferation                                    | GO:0070663        | 219   | 4.40E-13 | 23  |
| GO:BP | anatomical structure development   | GO:0048856        | 5153  | 5.60E-13 | 116 |
| TF    | Factor: IRF-4; motif: GAAARTA  | TF:M01883         | 6944  | 6.30E-13 | 141 |
| GO:CC | endomembrane system  | GO:0012505        | 4326  | 6.50E-13 | 102 |
| GO:BP | positive regulation of leukocyte cell-cell adhesion                      | GO:1903039        | 223   | 6.60E-13 | 23  |
| GO:BP | negative regulation of biological process                                | GO:0048519        | 4967  | 7.60E-13 | 113 |
| TF    | Factor: FOXO1A; Elk-1; motif: RWMAACAGGAAGTN                             | TF:M08299         | 6145  | 7.60E-13 | 130 |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:BP | immune response-activating cell surface receptor signaling pathway | GO:0002429  | 226   | 8.80E-13 | 23  |
| GO:BP | immune response-activating signal transduction                     | GO:0002757  | 226   | 8.80E-13 | 23  |
| GO:BP | biological_process   | GO:0008150  | 16323 | 9.90E-13 | 249 |
| GO:BP | cellular response to biotic stimulus                               | GO:0071216  | 203   | 1.00E-12 | 22  |
| GO:BP | regulation of cell-cell adhesion                                   | GO:0022407  | 400   | 1.10E-12 | 29  |
| TF    | Factor: SRY; motif: ACAATANCATTGTT                                 | TF:M04555   | 5745  | 1.20E-12 | 124 |
| GO:BP | regulation of leukocyte mediated immunity                          | GO:0002703  | 205   | 1.30E-12 | 22  |
| GO:BP | chemotaxis   | GO:0006935  | 538   | 1.30E-12 | 33  |
| TF    | Factor: c-Ets-1; motif: RCAGGAAGTGNNNTNS                           | TF:M00339   | 5893  | 1.30E-12 | 126 |
| TF    | Factor: FOXO1A:PDEF; motif: WNCCGGATGTTDN                          | TF:M08486   | 9927  | 1.30E-12 | 178 |
| TF    | Factor: PARP; motif: TTTCYN; match class: 1                        | TF:M02027_1 | 10180 | 1.30E-12 | 181 |
| GO:BP | developmental process  | GO:0032502  | 5648  | 1.50E-12 | 122 |
| GO:BP | taxis  | GO:0042330  | 542   | 1.70E-12 | 33  |
| GO:BP | regulation of myeloid leukocyte mediated immunity                  | GO:0002886  | 57    | 1.80E-12 | 14  |
| GO:BP | regulation of tumor necrosis factor production                     | GO:0032680  | 141   | 1.80E-12 | 19  |
| GO:BP | tumor necrosis factor production                                   | GO:0032640  | 141   | 1.80E-12 | 19  |
| TF    | Factor: PU.1; motif: AGGAAG; match class: 1                        | TF:M02031_1 | 11933 | 2.00E-12 | 201 |
| TF    | Factor: Elf-1; motif: AGGAAG; match class: 1                       | TF:M01266_1 | 11933 | 2.00E-12 | 201 |
| TF    | Factor: ZNF333; motif: ATAAT                                       | TF:M01230   | 13185 | 2.20E-12 | 215 |
| TF    | Factor: Sox-17; motif: TTGTYT                                      | TF:M03803   | 13366 | 2.20E-12 | 217 |
| GO:BP | regulation of multicellular organismal development                 | GO:2000026  | 1218  | 2.30E-12 | 49  |
| TF    | Factor: SMAD3; motif: TGTCTGTCT                                    | TF:M00701   | 3555  | 2.30E-12 | 91  |
| TF    | Factor: sin3A; motif: TGTCNNGGTGCTG                                | TF:M04756   | 12573 | 2.50E-12 | 208 |
| GO:BP | regulation of localization   | GO:0032879  | 2549  | 2.70E-12 | 74  |
| GO:BP | positive regulation of cellular process                            | GO:0048522  | 5061  | 2.90E-12 | 113 |
| GO:BP | negative regulation of cell activation                             | GO:0050866  | 190   | 3.20E-12 | 21  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: Cdx-1; motif: TTTATK                      | TF:M02086   | 12282 | 4.60E-12 | 204 |
| TF    | Factor: Sox-17; motif: TTGTYT; match class: 1     | TF:M03803_1 | 7955  | 4.70E-12 | 152 |
| TF    | Factor: SMAD3; motif: CAGACAS                     | TF:M07429   | 5352  | 4.90E-12 | 117 |
| GO:BP | negative regulation of cellular process           | GO:0048523  | 4412  | 5.00E-12 | 103 |
| TF    | Factor: SATB1; motif: NTTTTAT                     | TF:M03564   | 13565 | 6.00E-12 | 218 |
| TF    | Factor: CPBP; motif: SNCCCNN                      | TF:M01822   | 16885 | 6.40E-12 | 253 |
| GO:BP | regulation of leukocyte migration                 | GO:0002685  | 197   | 6.70E-12 | 21  |
| GO:BP | regulation of T cell activation                   | GO:0050863  | 304   | 6.80E-12 | 25  |
| TF    | Factor: myogenin; motif: CAGCTG                   | TF:M02101   | 11284 | 7.30E-12 | 192 |
| TF    | Factor: myogenin; motif: CAGCTG; match class: 1   | TF:M02101_1 | 11284 | 7.30E-12 | 192 |
| GO:MF | binding   | GO:0005488  | 15390 | 7.60E-12 | 235 |
| KEGG  | Hematopoietic cell lineage                        | KEGG:04640  | 78    | 7.80E-12 | 14  |
| GO:BP | macrophage activation                             | GO:0042116  | 94    | 7.90E-12 | 16  |
| TF    | Factor: PEBP2beta; motif: TGTGGTY                 | TF:M03841   | 6476  | 7.90E-12 | 132 |
| GO:BP | regulation of cell adhesion                       | GO:0030155  | 687   | 8.00E-12 | 36  |
| GO:BP | cellular response to molecule of bacterial origin | GO:0071219  | 176   | 9.00E-12 | 20  |
| TF    | Factor: C-Jun; motif: TGACTC                      | TF:M03541   | 9625  | 9.40E-12 | 172 |
| TF    | Factor: GR; motif: AGAACAN                        | TF:M07355   | 4913  | 9.90E-12 | 110 |
| TF    | Factor: MEL1; motif: GATGAG                       | TF:M08793   | 10128 | 9.90E-12 | 178 |
| GO:BP | hemopoiesis                                       | GO:0030097  | 815   | 1.00E-11 | 39  |
| GO:BP | myeloid leukocyte mediated immunity               | GO:0002444  | 96    | 1.10E-11 | 16  |
| GO:BP | vesicle-mediated transport                        | GO:0016192  | 1466  | 1.10E-11 | 53  |
| GO:BP | leukocyte differentiation                         | GO:0002521  | 507   | 1.20E-11 | 31  |
| GO:BP | regulation of lymphocyte proliferation            | GO:0050670  | 203   | 1.20E-11 | 21  |
| KEGG  | Cell adhesion molecules                           | KEGG:04514  | 139   | 1.20E-11 | 17  |
| TF    | Factor: c-Ets-2; motif: CTTCTG                    | TF:M01207   | 8932  | 1.40E-11 | 163 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: Elk-1; motif: CTTCKG                    | TF:M07252   | 8932  | 1.40E-11 | 163 |
| GO:BP | regulation of mononuclear cell proliferation    | GO:0032944  | 205   | 1.50E-11 | 21  |
| TF    | Factor: Pax-4; motif: DTTTCCACCN                | TF:M04624   | 13570 | 1.50E-11 | 217 |
| GO:BP | cellular developmental process                  | GO:0048869  | 3759  | 1.60E-11 | 92  |
| GO:BP | positive regulation of cell-cell adhesion       | GO:0022409  | 259   | 1.70E-11 | 23  |
| TF    | Factor: Smad2; motif: TGTCTGNCACCT              | TF:M09656   | 5444  | 1.70E-11 | 117 |
| GO:BP | defense response to bacterium                   | GO:0042742  | 183   | 1.90E-11 | 20  |
| TF    | Factor: Smad3; motif: NGNCAGACASNNN             | TF:M01888   | 3489  | 1.90E-11 | 88  |
| TF    | Factor: Pax-4; motif: NNNNNYACCCB               | TF:M00378   | 15748 | 1.90E-11 | 240 |
| TF    | Factor: AP-4; motif: AWCAGCTGWT                 | TF:M11206   | 6263  | 2.20E-11 | 128 |
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1 | TF:M11206_1 | 6263  | 2.20E-11 | 128 |
| GO:BP | response to molecule of bacterial origin        | GO:0002237  | 292   | 2.50E-11 | 24  |
| TF    | Factor: p300; motif: CTGNCTYMAN                 | TF:M07266   | 6955  | 2.80E-11 | 137 |
| GO:BP | system development                              | GO:0048731  | 4335  | 3.20E-11 | 100 |
| GO:BP | hematopoietic or lymphoid organ development     | GO:0048534  | 846   | 3.40E-11 | 39  |
| TF    | Factor: GKLf; motif: CCTCCYN                    | TF:M01835   | 13756 | 3.40E-11 | 218 |
| TF    | Factor: ETV4; motif: NCAGGAAGNN; match class: 1 | TF:M12556_1 | 3399  | 3.50E-11 | 86  |
| GO:BP | cell differentiation                            | GO:0030154  | 3683  | 3.80E-11 | 90  |
| KEGG  | Complement and coagulation cascades             | KEGG:04610  | 70    | 3.80E-11 | 13  |
| TF    | Factor: Oct3; motif: NYWTTSWTATGCAAAT           | TF:M09646   | 4663  | 3.80E-11 | 105 |
| GO:MF | protein binding                                 | GO:0005515  | 13368 | 4.40E-11 | 211 |
| TF    | Factor: Zbtb44; motif: CKGTGA; match class: 1   | TF:M05405_1 | 5881  | 4.60E-11 | 122 |
| TF    | Factor: PEA3; motif: ACWTCK; match class: 1     | TF:M00655_1 | 2384  | 5.00E-11 | 69  |
| GO:MF | carbohydrate binding                            | GO:0030246  | 236   | 5.20E-11 | 21  |
| GO:BP | negative regulation of leukocyte activation     | GO:0002695  | 169   | 5.40E-11 | 19  |
| TF    | Factor: nerf; motif: YRNCAGGAAGYRGSTBDS         | TF:M00531   | 6635  | 5.40E-11 | 132 |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:BP | regulation of phagocytosis                       | GO:0050764  | 88    | 5.60E-11 | 15  |
| TF    | Factor: SPI1; motif: NNNAAAGAGGAAGTGANNNN        | TF:M12497   | 1992  | 5.60E-11 | 62  |
| TF    | Factor: Elk-1; motif: GGAAGN                     | TF:M03819   | 12382 | 6.10E-11 | 202 |
| TF    | Factor: MAFB; motif: NTCAGCN                     | TF:M08888   | 8591  | 6.40E-11 | 157 |
| GO:BP | humoral immune response                          | GO:0006959  | 171   | 6.70E-11 | 19  |
| TF    | Factor: PEA3; motif: NNCAGGAARNN; match class: 1 | TF:M09915_1 | 4914  | 6.90E-11 | 108 |
| GO:BP | leukocyte degranulation                          | GO:0043299  | 73    | 7.40E-11 | 14  |
| TF    | Factor: NF1C; motif: WGCCARR                     | TF:M09763   | 9428  | 8.30E-11 | 167 |
| TF    | Factor: STAT; motif: NNNNNTTCTKGGA               | TF:M00777   | 4378  | 8.60E-11 | 100 |
| GO:BP | cellular response to cytokine stimulus           | GO:0071345  | 744   | 8.80E-11 | 36  |
| TF    | Factor: FOXO1A;Net; motif: RWMAACAGGAAGTN        | TF:M08302   | 7909  | 9.00E-11 | 148 |
| TF    | Factor: JUNB:C-JUN; motif: NATGACKCAT            | TF:M08944   | 4454  | 9.60E-11 | 101 |
| GO:BP | response to cytokine                             | GO:0034097  | 833   | 1.00E-10 | 38  |
| GO:CC | tertiary granule membrane                        | GO:0070821  | 68    | 1.10E-10 | 13  |
| TF    | Factor: NFATc2; motif: GGAAAA                    | TF:M01281   | 13979 | 1.10E-10 | 219 |
| TF    | Factor: NFATc3; motif: GGAAAA                    | TF:M01886   | 13979 | 1.10E-10 | 219 |
| TF    | Factor: NFATc2; motif: GGAAAA                    | TF:M03555   | 13979 | 1.10E-10 | 219 |
| TF    | Factor: Sox-9; motif: NNNACAATRG                 | TF:M11626   | 5446  | 1.10E-10 | 115 |
| GO:BP | multicellular organism development               | GO:0007275  | 4634  | 1.20E-10 | 103 |
| TF    | Factor: IRF-7; motif: AAGWGAA                    | TF:M01884   | 9133  | 1.20E-10 | 163 |
| TF    | Factor: PMX1; motif: TAATHA                      | TF:M03560   | 11838 | 1.20E-10 | 195 |
| TF    | Factor: PU.1; motif: NRAAAGAGGAAGTGRNN           | TF:M10073   | 2088  | 1.40E-10 | 63  |
| TF    | Factor: AML1; motif: TGTGGT; match class: 1      | TF:M00751_1 | 4420  | 1.60E-10 | 100 |
| TF    | Factor: AML1; motif: TGTGGT; match class: 1      | TF:M02084_1 | 4420  | 1.60E-10 | 100 |
| TF    | Factor: AML1a; motif: TGTGGT; match class: 1     | TF:M00271_1 | 4420  | 1.60E-10 | 100 |
| GO:BP | positive regulation of cell communication        | GO:0010647  | 1569  | 1.70E-10 | 53  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | positive regulation of signaling                        | GO:0023056  | 1573  | 1.90E-10 | 53  |
| GO:CC | extracellular vesicle                                   | GO:1903561  | 1921  | 1.90E-10 | 58  |
| GO:CC | extracellular organelle                                 | GO:0043230  | 1922  | 1.90E-10 | 58  |
| GO:CC | extracellular membrane-bounded organelle                | GO:0065010  | 1922  | 1.90E-10 | 58  |
| TF    | Factor: SPI1; motif: AGGAAGT                            | TF:M02278   | 5850  | 1.90E-10 | 120 |
| TF    | Factor: PEA3; motif: AGGAAGT                            | TF:M03579   | 5850  | 1.90E-10 | 120 |
| TF    | Factor: C-ets-1; motif: AGGAAGN                         | TF:M01870   | 5850  | 1.90E-10 | 120 |
| TF    | Factor: Fli-1; motif: MGGAAGT                           | TF:M07382   | 5850  | 1.90E-10 | 120 |
| GO:CC | bounding membrane of organelle                          | GO:0098588  | 2037  | 2.00E-10 | 60  |
| TF    | Factor: T3R-beta; motif: NTGACCTYRNYRAGGTCAN            | TF:M11818   | 10182 | 2.00E-10 | 175 |
| GO:CC | tertiary granule  | GO:0070820  | 151   | 2.10E-10 | 17  |
| TF    | Factor: AP-4; motif: ANCATATGNT                         | TF:M11207   | 2574  | 2.10E-10 | 71  |
| TF    | Factor: YY1; motif: NGCCATYTTKGRCNWVWNGTGCK             | TF:M12276   | 8868  | 2.10E-10 | 159 |
| TF    | Factor: GTF2IRD1-isoform2; motif: GGGATRRNR             | TF:M01229   | 13062 | 2.20E-10 | 208 |
| GO:BP | T cell proliferation                                    | GO:0042098  | 183   | 2.30E-10 | 19  |
| GO:BP | immune system development                               | GO:0002520  | 899   | 2.30E-10 | 39  |
| TF    | Factor: FOSB;JUND; motif: NNTNACTNATN                   | TF:M08928   | 5006  | 2.40E-10 | 108 |
| TF    | Factor: MEL1; motif: GATGAG; match class: 1             | TF:M08793_1 | 4116  | 2.60E-10 | 95  |
| GO:BP | positive regulation of response to external stimulus    | GO:0032103  | 390   | 2.70E-10 | 26  |
| TF    | Factor: Pax-6; motif: CTGACCTGGAAC TM                   | TF:M00979   | 8330  | 2.70E-10 | 152 |
| TF    | Factor: HOXA3; motif: NNNNRNTAATTARY                    | TF:M01337   | 13550 | 3.00E-10 | 213 |
| GO:BP | myeloid leukocyte migration                             | GO:0097529  | 186   | 3.10E-10 | 19  |
| TF    | Factor: SPI1; motif: AAAAAGCGGAAGTW                     | TF:M03994   | 1851  | 3.40E-10 | 58  |
| TF    | Factor: ZNF462; motif: YYYCTSCWG                        | TF:M12707   | 8440  | 3.70E-10 | 153 |
| GO:BP | negative regulation of multicellular organismal process | GO:0051241  | 913   | 3.80E-10 | 39  |
| GO:CC | extracellular exosome                                   | GO:0070062  | 1901  | 4.10E-10 | 57  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:MF | protein-containing complex binding  | GO:0044877  | 1204  | 4.20E-10 | 44  |
| TF    | Factor: AP-4; motif: AHCATRTGKT   | TF:M11213   | 3359  | 4.20E-10 | 83  |
| TF    | Factor: SRY; motif: TTGTTT  | TF:M03854   | 12068 | 4.20E-10 | 196 |
| TF    | Factor: FOXO1A; motif: AAACAA   | TF:M03823   | 12068 | 4.20E-10 | 196 |
| GO:BP | locomotion  | GO:0040011  | 1669  | 5.30E-10 | 54  |
| GO:BP | cellular response to lipopolysaccharide   | GO:0071222  | 168   | 6.00E-10 | 18  |
| GO:BP | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | GO:0002460  | 247   | 6.10E-10 | 21  |
| GO:BP | B cell activation   | GO:0042113  | 247   | 6.10E-10 | 21  |
| GO:BP | leukocyte chemotaxis  | GO:0030595  | 193   | 6.10E-10 | 19  |
| GO:BP | regulation of transport   | GO:0051049  | 1622  | 6.20E-10 | 53  |
| GO:BP | positive regulation of lymphocyte activation  | GO:0051251  | 277   | 6.50E-10 | 22  |
| GO:CC | endocytic vesicle membrane  | GO:0030666  | 187   | 6.70E-10 | 18  |
| TF    | Factor: SMAD; motif: TNGNCAGACWN  | TF:M00974   | 3788  | 7.60E-10 | 89  |
| TF    | Factor: DREF; motif: CTYYCWCTTCCY   | TF:M09725   | 6415  | 7.90E-10 | 126 |
| GO:BP | positive regulation of cell adhesion  | GO:0045785  | 409   | 8.00E-10 | 26  |
| TF    | Factor: c-Ets-2; motif: CTTCTG; match class: 1  | TF:M01207_1 | 3080  | 8.00E-10 | 78  |
| TF    | Factor: Elk-1; motif: CTTCKG; match class: 1  | TF:M07252_1 | 3080  | 8.00E-10 | 78  |
| TF    | Factor: HES-5; motif: NCACACKY  | TF:M11069   | 9505  | 8.90E-10 | 165 |
| GO:BP | localization  | GO:0051179  | 5792  | 9.40E-10 | 117 |
| TF    | Factor: T3R-beta; motif: NTGACCTYRNYRAGGTCAN; match class: 1  | TF:M11818_1 | 9678  | 9.50E-10 | 167 |
| TF    | Factor: GATA-5; motif: TATCTN   | TF:M02006   | 7582  | 9.50E-10 | 141 |
| TF    | Factor: MafG; motif: CMATGACTCAGAGA   | TF:M07048   | 5916  | 1.00E-09 | 119 |
| GO:BP | cellular response to chemical stimulus  | GO:0070887  | 2745  | 1.10E-09 | 72  |
| GO:BP | positive regulation of developmental process  | GO:0051094  | 1182  | 1.10E-09 | 44  |
| TF    | Factor: egr-3; motif: GTGGGY  | TF:M03818   | 11653 | 1.10E-09 | 190 |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: TFII-I; motif: NAGGAAGTGN  | TF:M04636   | 11048 | 1.10E-09 | 183 |
| TF    | Factor: C/EBP; motif: NNNTKNNNAAN  | TF:M00770   | 4639  | 1.20E-09 | 101 |
| GO:BP | positive regulation of T cell activation                                     | GO:0050870  | 202   | 1.40E-09 | 19  |
| GO:BP | positive regulation of signal transduction                                   | GO:0009967  | 1394  | 1.50E-09 | 48  |
| GO:BP | positive regulation of gene expression                                       | GO:0010628  | 1001  | 1.50E-09 | 40  |
| TF    | Factor: HSF4; motif: CTGCMRN   | TF:M07322   | 14568 | 1.50E-09 | 222 |
| GO:BP | transport  | GO:0006810  | 4269  | 1.60E-09 | 95  |
| TF    | Factor: SRY; motif: TTGTTT; match class: 1                                   | TF:M03854_1 | 7628  | 1.60E-09 | 141 |
| TF    | Factor: FOXO1A; motif: AAACAA; match class: 1                                | TF:M03823_1 | 7628  | 1.60E-09 | 141 |
| TF    | Factor: SRY; motif: AACAAATNR; match class: 1                                | TF:M08976_1 | 6555  | 1.60E-09 | 127 |
| TF    | Factor: Sox-4; motif: AACAAA   | TF:M03849   | 12223 | 1.70E-09 | 196 |
| GO:BP | establishment of localization  | GO:0051234  | 4416  | 1.80E-09 | 97  |
| GO:BP | positive regulation of tumor necrosis factor superfamily cytokine production | GO:1903557  | 91    | 1.80E-09 | 14  |
| TF    | Factor: THAP1; motif: YTGCCCNNA  | TF:M07407   | 9580  | 1.80E-09 | 165 |
| TF    | Factor: Erg; motif: MCAGGAAA   | TF:M07284   | 9694  | 2.40E-09 | 166 |
| GO:BP | regulation of molecular function   | GO:0065009  | 2797  | 2.60E-09 | 72  |
| TF    | Factor: SREBP-1; motif: CACSCCA  | TF:M00749   | 7520  | 2.60E-09 | 139 |
| TF    | Factor: Six-6; motif: NNSTATCRNN   | TF:M11037   | 4351  | 2.70E-09 | 96  |
| GO:CC | endocytic vesicle  | GO:0030139  | 325   | 2.80E-09 | 22  |
| TF    | Factor: FOXM1; motif: NAGASTGATTA  | TF:M04611   | 7843  | 2.80E-09 | 143 |
| GO:BP | positive regulation of transport   | GO:0051050  | 838   | 2.90E-09 | 36  |
| TF    | Factor: BCL-11A; motif: NAAAGAGGAAGTGARAN                                    | TF:M09595   | 3159  | 2.90E-09 | 78  |
| TF    | Factor: RARG; motif: RAGGTCAASYARAGGTCA                                      | TF:M04485   | 4222  | 3.00E-09 | 94  |
| TF    | Factor: POU2F1; Gscl; motif: NNGATTANNATKCANNNN                              | TF:M08404   | 5279  | 3.10E-09 | 109 |
| TF    | Factor: HLTF; motif: AGSCARAAAGYRGSTGS                                       | TF:M04613   | 6765  | 3.10E-09 | 129 |
| TF    | Factor: Erg; motif: NRRSAGGAAGNGG  | TF:M09907   | 10225 | 3.20E-09 | 172 |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: MEF-2C; motif: TATTTWT                          | TF:M02025   | 10824 | 3.30E-09 | 179 |
| TF    | Factor: Sox-10; motif: NACAAWG                          | TF:M02116   | 12073 | 4.40E-09 | 193 |
| TF    | Factor: ZXDA; motif: NAGGGTG                            | TF:M06203   | 6420  | 4.50E-09 | 124 |
| TF    | Factor: ZXDB; motif: NAGGGTG                            | TF:M06202   | 6420  | 4.50E-09 | 124 |
| TF    | Factor: ZBRK1; motif: NGNNNGGTNAWAAAARRGCNG             | TF:M10468   | 9361  | 5.20E-09 | 161 |
| TF    | Factor: SREBP; motif: VNNVTCACCCYA                      | TF:M00776   | 5467  | 5.20E-09 | 111 |
| GO:BP | response to lipopolysaccharide                          | GO:0032496  | 277   | 5.60E-09 | 21  |
| GO:BP | regulation of cell differentiation                      | GO:0045595  | 1400  | 6.30E-09 | 47  |
| GO:BP | neutrophil activation involved in immune response       | GO:0002283  | 17    | 6.80E-09 | 8   |
| TF    | Factor: RelA-p65; motif: AAASCCC                        | TF:M04849   | 5419  | 7.00E-09 | 110 |
| TF    | Factor: myogenin; motif: RGCAGSTG                       | TF:M00712   | 6086  | 7.20E-09 | 119 |
| TF    | Factor: JUND; motif: NATGAGTCAT                         | TF:M08934   | 3610  | 7.30E-09 | 84  |
| GO:BP | regulation of hydrolase activity                        | GO:0051336  | 870   | 8.50E-09 | 36  |
| GO:BP | regulation of leukocyte degranulation                   | GO:0043300  | 50    | 8.60E-09 | 11  |
| GO:BP | regulation of catalytic activity                        | GO:0050790  | 2138  | 8.70E-09 | 60  |
| GO:BP | synapse pruning   | GO:0098883  | 11    | 9.40E-09 | 7   |
| TF    | Factor: SRY; motif: TCAATAMCATTGA                       | TF:M04557   | 8365  | 9.50E-09 | 148 |
| GO:BP | cell chemotaxis   | GO:0060326  | 255   | 1.00E-08 | 20  |
| TF    | Factor: SPI1; motif: NNAAWGNGGAASTNNNN                  | TF:M01203   | 2304  | 1.00E-08 | 63  |
| TF    | Factor: AP-4; motif: ANCATATGNT                         | TF:M11209   | 2930  | 1.20E-08 | 73  |
| TF    | Factor: PU.1; motif: WGAGGAAG                           | TF:M00658   | 3851  | 1.30E-08 | 87  |
| GO:BP | lymphocyte activation involved in immune response       | GO:0002285  | 175   | 1.40E-08 | 17  |
| TF    | Factor: Erg; motif: NRRSAGGAAGNGG; match class: 1       | TF:M09907_1 | 4480  | 1.50E-08 | 96  |
| TF    | Factor: NFATc2; motif: NTTTCRTNNAYGGAAN; match class: 1 | TF:M11984_1 | 9477  | 1.50E-08 | 161 |
| TF    | Factor: DREF; motif: CTYYCWCTTCY; match class: 1        | TF:M09725_1 | 1747  | 1.50E-08 | 53  |
| TF    | Factor: ING4; motif: CCACCA; match class: 1             | TF:M01743_1 | 8903  | 1.50E-08 | 154 |

|       |  |                    |      |          |     |
|-------|--|--------------------|------|----------|-----|
| TF    | Factor: NFATc1; motif: NTTTCRTNNAYGGAAAN; match class: 1 | TF:M11979_1        | 7539 | 1.50E-08 | 137 |
| GO:BP | cell killing   | GO:001906          | 128  | 1.60E-08 | 15  |
| GO:BP | animal organ development                                 | GO:0048513         | 3102 | 1.70E-08 | 75  |
| GO:CC | specific granule   | GO:0042581         | 145  | 1.70E-08 | 15  |
| TF    | Factor: MEIS1B:HOXA9; motif: TGACASTTTWAYRR              | TF:M00421          | 5493 | 1.70E-08 | 110 |
| TF    | Factor: STAT5A; motif: TTCCNRGAANNNNNTTCCNNGRR           | TF:M00460          | 6618 | 1.70E-08 | 125 |
| GO:BP | cell migration   | GO:0016477         | 1339 | 1.80E-08 | 45  |
| GO:BP | mononuclear cell differentiation                         | GO:1903131         | 397  | 1.90E-08 | 24  |
| GO:BP | regulation of vesicle-mediated transport                 | GO:0060627         | 509  | 1.90E-08 | 27  |
| GO:BP | positive regulation of tumor necrosis factor production  | GO:0032760         | 88   | 2.00E-08 | 13  |
| KEGG  | Intestinal immune network for IgA production             | KEGG:04672         | 39   | 2.00E-08 | 9   |
| GO:BP | regulation of defense response                           | GO:0031347         | 551  | 2.10E-08 | 28  |
| KEGG  | Pertussis  | KEGG:05133         | 72   | 2.20E-08 | 11  |
| TF    | Factor: GR; motif: GGTACAANN TGTYCTK                     | TF:M00205          | 5664 | 2.20E-08 | 112 |
| REAC  | Cytokine Signaling in Immune system                      | REAC:R-HSA-1280215 | 634  | 2.30E-08 | 29  |
| TF    | Factor: SPDEF; motif: NASATCCKGNW                        | TF:M12650          | 1491 | 2.30E-08 | 48  |
| TF    | Factor: NFATc2; motif: NTTTCRTNNAYGGAAAN                 | TF:M11984          | 9531 | 2.40E-08 | 161 |
| TF    | Factor: NFE2L1; motif: NNNATGACTCAGCANW                  | TF:M12499          | 8308 | 2.60E-08 | 146 |
| TF    | Factor: Spic; motif: NGNGGAASN                           | TF:M02077          | 7359 | 2.70E-08 | 134 |
| KEGG  | Viral myocarditis  | KEGG:05416         | 56   | 3.00E-08 | 10  |
| TF    | Factor: Tbx5; motif: TNAGGTGTKV; match class: 1          | TF:M01020_1        | 3443 | 3.00E-08 | 80  |
| GO:BP | response to organic substance                            | GO:0010033         | 2758 | 3.10E-08 | 69  |
| GO:CC | MHC class II protein complex                             | GO:0042613         | 15   | 3.10E-08 | 7   |
| TF    | Factor: GATA-3; motif: AGATAAGATCT                       | TF:M12193          | 5254 | 3.10E-08 | 106 |
| TF    | Factor: Nfe2l1; motif: TGYNNAGTCATT                      | TF:M07390          | 5626 | 3.30E-08 | 111 |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: six-4; motif: ANNNATGACACCCNNNNN                                | TF:M01374   | 5406 | 3.30E-08 | 108 |
| GO:BP | regulation of hemopoiesis   | GO:1903706  | 338  | 3.40E-08 | 22  |
| TF    | Factor: Sox-4; motif: AACAAA; match class: 1                            | TF:M03849_1 | 7618 | 3.40E-08 | 137 |
| GO:BP | interleukin-8 production  | GO:0032637  | 73   | 3.50E-08 | 12  |
| GO:BP | regulation of interleukin-8 production                                  | GO:0032677  | 73   | 3.50E-08 | 12  |
| TF    | Factor: Tbx5; motif: TNAGGTGTKV   | TF:M01020   | 9490 | 3.60E-08 | 160 |
| TF    | Factor: c-Ets; motif: KRCAGGAARTRNKT                                    | TF:M00340   | 4483 | 3.70E-08 | 95  |
| TF    | Factor: BRN1; motif: HAATGCN; match class: 1                            | TF:M03813_1 | 5787 | 3.80E-08 | 113 |
| TF    | Factor: NKX2-2; motif: NNNCCACTCAANN                                    | TF:M12456   | 8199 | 4.20E-08 | 144 |
| TF    | Factor: Spi-B; motif: NRAAAGAGGAAGTGARA                                 | TF:M10074   | 1415 | 4.60E-08 | 46  |
| TF    | Factor: PU.1; motif: NRAAAGAGGAAGTGARA                                  | TF:M09659   | 2208 | 4.70E-08 | 60  |
| TF    | Factor: ZNF273; motif: GAGAGGAGCTAC                                     | TF:M10460   | 1122 | 4.70E-08 | 180 |
| TF    | Factor: GCMa:FOXO1A; motif: GTMAATAMGGGTRN                              | TF:M08318   | 1002 | 4.90E-08 | 166 |
| TF    | Factor: AP-4; motif: ANCATATGNT   | TF:M11211   | 2515 | 5.00E-08 | 65  |
| TF    | Factor: c-Jun; motif: NATGACKCATN                                       | TF:M11267   | 2641 | 5.10E-08 | 67  |
| GO:BP | antigen processing and presentation of peptide antigen via MHC class II | GO:0002495  | 31   | 5.20E-08 | 9   |
| TF    | Factor: NR1B1; motif: NRGGTCANNRGGTCAN                                  | TF:M11795   | 6883 | 5.40E-08 | 127 |
| KEGG  | Rheumatoid arthritis  | KEGG:05323  | 78   | 5.50E-08 | 11  |
| TF    | Factor: FOXP1; motif: CTGTTTNYTYTKN                                     | TF:M09855   | 6424 | 5.50E-08 | 121 |
| TF    | Factor: SMAD; motif: TGCTGNNN   | TF:M08897   | 3891 | 5.60E-08 | 86  |
| TF    | Factor: NFATc4; motif: NGGAAAAAN  | TF:M07301   | 3354 | 5.70E-08 | 78  |
| GO:BP | mononuclear cell migration  | GO:0071674  | 165  | 5.90E-08 | 16  |
| TF    | Factor: C/EBPbeta; motif: TKNNNGCAANN                                   | TF:M01896   | 3827 | 6.00E-08 | 85  |
| TF    | Factor: Elf-1; motif: RNWMBAGGAART                                      | TF:M00746   | 2905 | 6.20E-08 | 71  |
| GO:BP | negative regulation of response to external stimulus                    | GO:0032102  | 349  | 6.40E-08 | 22  |
| GO:MF | sialic acid binding   | GO:0033691  | 16   | 6.50E-08 | 7   |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: NFATc1; motif: NTTTC CRTNNAYGGAAAN  | TF:M11979         | 7686  | 6.50E-08 | 137 |
| KEGG  | Osteoclast differentiation  | KEGG:04380        | 124   | 6.60E-08 | 13  |
| GO:BP | secretion   | GO:0046903        | 843   | 6.90E-08 | 34  |
| TF    | Factor: Spi-B; motif: NAWGRGGAAGTR  | TF:M11374         | 2170  | 6.90E-08 | 59  |
| TF    | Factor: VDR; motif: RRTGNMICYTNNTGAMCCNYNT  | TF:M00966         | 8419  | 7.20E-08 | 146 |
| GO:BP | microglial cell activation  | GO:0001774        | 45    | 7.40E-08 | 10  |
| GO:BP | humoral immune response mediated by circulating immunoglobulin                            | GO:0002455        | 45    | 7.40E-08 | 10  |
| TF    | Factor: p53; motif: NGRCWTGYCY  | TF:M00272         | 3572  | 7.40E-08 | 81  |
| TF    | Factor: Erm; motif: NRRSAGGAARNGRN  | TF:M09916         | 5923  | 7.40E-08 | 114 |
| GO:BP | lymphocyte differentiation  | GO:0030098        | 353   | 7.90E-08 | 22  |
| TF    | Factor: NKX25; motif: NNANCCACTTRAAWTT  | TF:M01414         | 8271  | 8.20E-08 | 144 |
| TF    | Factor: NFATc2; motif: TTTTCCA  | TF:M02265         | 6464  | 8.30E-08 | 121 |
| TF    | Factor: TEF-1; motif: GRRATG  | TF:M00704         | 10603 | 8.50E-08 | 172 |
| TF    | Factor: HMGIIY; motif: NNKKNAWTTTNYTNN  | TF:M01010         | 6852  | 8.60E-08 | 126 |
| GO:BP | positive regulation of phagocytosis   | GO:0050766        | 61    | 8.70E-08 | 11  |
| TF    | Factor: Sox-9; motif: NNNNAACAATRGNN  | TF:M00410         | 3323  | 9.40E-08 | 77  |
| GO:BP | neutrophil activation   | GO:0042119        | 33    | 9.70E-08 | 9   |
| GO:BP | complement activation, classical pathway  | GO:0006958        | 33    | 9.70E-08 | 9   |
| REAC  | GPCR ligand binding   | REAC:R-HSA-500792 | 388   | 1.00E-07 | 22  |
| TF    | Factor: IRF-2; motif: NAANYGAAASYR  | TF:M08775         | 7180  | 1.00E-07 | 130 |
| TF    | Factor: FOXO1A:ETV7; motif: NWMAACAGGAMNNNCTTCNN  | TF:M08304         | 12194 | 1.00E-07 | 190 |
| GO:BP | regulation of leukocyte differentiation   | GO:1902105        | 259   | 1.10E-07 | 19  |
| GO:MF | immunoglobulin binding  | GO:0019865        | 17    | 1.10E-07 | 7   |
| TF    | Factor: T3R-beta; motif: RTGACCTYACRTGACCTYA  | TF:M11819         | 5885  | 1.10E-07 | 113 |
| TF    | Factor: ZNF436; motif: TCCTCCAGGAAGCCY  | TF:M10477         | 12825 | 1.10E-07 | 197 |
| GO:BP | antigen processing and presentation of peptide or polysaccharide antigen via MHC class II | GO:0002504        | 34    | 1.30E-07 | 9   |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: AP-4; motif: AHCATRTGKT; match class: 1     | TF:M11213_1 | 2446  | 1.30E-07 | 63  |
| TF    | Factor: ER71:E2A; motif: CASSTGNACCGAWRYN           | TF:M08568   | 15994 | 1.30E-07 | 231 |
| TF    | Factor: ZABC1; motif: ATTCNAC                       | TF:M01306   | 8006  | 1.40E-07 | 140 |
| TF    | Factor: CRX; motif: YTAATC                          | TF:M01712   | 9480  | 1.40E-07 | 158 |
| TF    | Factor: GLI4; motif: RGGCCTTGAATGCCANGCYMA          | TF:M10514   | 11095 | 1.40E-07 | 177 |
| TF    | Factor: ZNF644; motif: TCCWGCCTCTSN                 | TF:M09737   | 6371  | 1.50E-07 | 119 |
| GO:BP | regulation of metabolic process                     | GO:0019222  | 6103  | 1.60E-07 | 115 |
| TF    | Factor: rfx3:SREBP-2; motif: ATGGYAACRTCACGTGAY     | TF:M08412   | 9163  | 1.60E-07 | 154 |
| TF    | Factor: C/EBPgamma:Elf-1; motif: TKRCGHAATWSCGGAAGT | TF:M08676   | 7465  | 1.60E-07 | 133 |
| TF    | Factor: GR; motif: CNNNNTGTYCTNN                    | TF:M01836   | 4890  | 1.60E-07 | 99  |
| TF    | Factor: Cdx-1; motif: TTTATK; match class: 1        | TF:M02086_1 | 8108  | 1.70E-07 | 141 |
| KEGG  | Asthma  | KEGG:05310  | 22    | 1.80E-07 | 7   |
| GO:BP | regulation of T cell proliferation                  | GO:0042129  | 152   | 1.90E-07 | 15  |
| TF    | Factor: Smad2; motif: TGTCTGNCWCCT                  | TF:M10059   | 5342  | 1.90E-07 | 105 |
| GO:BP | cellular response to organic substance              | GO:0071310  | 2188  | 2.00E-07 | 58  |
| TF    | Factor: TFP4; motif: AWCAGCTGWT                     | TF:M04192   | 4548  | 2.00E-07 | 94  |
| TF    | Factor: NFATc2; motif: GGAAAA; match class: 1       | TF:M03555_1 | 9439  | 2.00E-07 | 157 |
| TF    | Factor: NFATc3; motif: GGAAAA; match class: 1       | TF:M01886_1 | 9439  | 2.00E-07 | 157 |
| TF    | Factor: NFATc2; motif: GGAAAA; match class: 1       | TF:M01281_1 | 9439  | 2.00E-07 | 157 |
| GO:BP | positive regulation of leukocyte migration          | GO:0002687  | 128   | 2.10E-07 | 14  |
| TF    | Factor: c-Jun; motif: NATGACTCATN                   | TF:M11265   | 3855  | 2.10E-07 | 84  |
| GO:BP | positive regulation of molecular function           | GO:0044093  | 1394  | 2.40E-07 | 44  |
| TF    | Factor: LBP-1; motif: CAGCTGS                       | TF:M00644   | 7824  | 2.40E-07 | 137 |
| TF    | Factor: Smad4; motif: NCAGACAN                      | TF:M07368   | 3322  | 2.40E-07 | 76  |
| GO:BP | positive regulation of catalytic activity           | GO:0043085  | 1031  | 2.50E-07 | 37  |
| TF    | Factor: TTF1; motif: ASTCAAGTRK                     | TF:M00432   | 4425  | 2.50E-07 | 92  |

|       |  |                   |           |          |     |
|-------|--|-------------------|-----------|----------|-----|
| TF    | Factor: CPBP; motif: SNCCCN; match class: 1                | TF:M01822_1       | 1646<br>4 | 2.50E-07 | 235 |
| TF    | Factor: C/EBPalpha; motif: NRTTGTGCAAYNN                   | TF:M09596         | 4356      | 2.50E-07 | 91  |
| TF    | Factor: Tbx3; motif: NAGGTGTSAN                            | TF:M12024         | 3800      | 2.60E-07 | 83  |
| TF    | Factor: ITF-2; motif: NNCACCTGNN                           | TF:M04191         | 4572      | 2.60E-07 | 94  |
| TF    | Factor: B-ATF; motif: NNATGACACN                           | TF:M11300         | 7440      | 2.70E-07 | 132 |
| GO:BP | negative regulation of response to stimulus                | GO:0048585        | 1510      | 2.80E-07 | 46  |
| TF    | Factor: PPARgamma:RXRalpha; motif: AAGTAGGTCACNGTGACCYACTT | TF:M00515         | 6738      | 2.80E-07 | 123 |
| TF    | Factor: HOXA13; motif: ATAAMA                              | TF:M01292         | 1135<br>3 | 2.80E-07 | 179 |
| TF    | Factor: SPI1; motif: NGRGGAAGTN                            | TF:M02078         | 3073      | 2.90E-07 | 72  |
| GO:BP | positive regulation of metabolic process                   | GO:0009893        | 3369      | 3.20E-07 | 76  |
| TF    | Factor: ZNF342; motif: TRSTGGACRNT                         | TF:M12075         | 5465      | 3.30E-07 | 106 |
| TF    | Factor: Elk-1; motif: GGAAGN; match class: 1               | TF:M03819_1       | 6527      | 3.40E-07 | 120 |
| GO:BP | regulation of cell communication                           | GO:0010646        | 3111      | 3.50E-07 | 72  |
| GO:MF | G protein-coupled receptor activity                        | GO:0004930        | 495       | 3.50E-07 | 24  |
| TF    | Factor: ZNF684; motif: MAAGGGGTGGACTGT                     | TF:M10550         | 1342<br>6 | 3.50E-07 | 202 |
| REAC  | Class A/1 (Rhodopsin-like receptors)                       | REAC:R-HSA-373076 | 272       | 3.90E-07 | 18  |
| TF    | Factor: Ikaros; motif: TGGGAGN                             | TF:M07260         | 1183<br>2 | 3.90E-07 | 184 |
| GO:BP | regulation of inflammatory response                        | GO:0050727        | 313       | 4.00E-07 | 20  |
| TF    | Factor: AP-4:Max; motif: NCAGCTGNNNNNNNCACGTGN             | TF:M08674         | 1002<br>5 | 4.00E-07 | 163 |
| TF    | Factor: SMAD3; motif: CAGACAS; match class: 1              | TF:M07429_1       | 1137      | 4.00E-07 | 39  |
| TF    | Factor: NR3C1; motif: NRGWACAYNRTGTWCYN                    | TF:M04476         | 6162      | 4.10E-07 | 115 |
| TF    | Factor: RXR:RAR; motif: RGKTCANNRAGAGTCA                   | TF:M02272         | 5486      | 4.10E-07 | 106 |
| GO:BP | regulation of signaling                                    | GO:0023051        | 3125      | 4.30E-07 | 72  |
| TF    | Factor: Ets; motif: ACTTCCTS                               | TF:M00971         | 2036      | 4.60E-07 | 55  |
| TF    | Factor: MZF-1; motif: TGGGGAR                              | TF:M01733         | 1004<br>3 | 4.70E-07 | 163 |
| GO:BP | cell death   | GO:0008219        | 1881      | 4.90E-07 | 52  |

|       |   |             |           |          |     |
|-------|---|-------------|-----------|----------|-----|
| GO:BP | granulocyte activation  | GO:0036230  | 39        | 5.10E-07 | 9   |
| GO:BP | toll-like receptor signaling pathway  | GO:0002224  | 113       | 5.10E-07 | 13  |
| TF    | Factor: NFATc1; motif: TTCCAYWRTGGAAA   | TF:M04052   | 5658      | 5.30E-07 | 108 |
| TF    | Factor: gsh-1; motif: NTMATNRN  | TF:M10750   | 6650      | 5.30E-07 | 121 |
| TF    | Factor: TR4; motif: ACCCCGS   | TF:M04934   | 1599<br>7 | 5.40E-07 | 229 |
| TF    | Factor: AP-4; motif: RNCAGCTGC  | TF:M00927   | 5587      | 5.50E-07 | 107 |
| GO:BP | antigen processing and presentation of exogenous peptide antigen via MHC class II | GO:0019886  | 27        | 5.70E-07 | 8   |
| TF    | Factor: Oct-2; motif: NTGCATATGCAN; match class: 1                                | TF:M11899_1 | 3591      | 5.90E-07 | 79  |
| TF    | Factor: SRY; motif: AACAAATANCATTGTT; match class: 1                              | TF:M04555_1 | 2669      | 6.00E-07 | 65  |
| TF    | Factor: AR; motif: GGAACGGWACATGTTCT  | TF:M08190   | 6740      | 6.00E-07 | 122 |
| TF    | Factor: ipf1; motif: TGATTGATK  | TF:M10031   | 7448      | 6.10E-07 | 131 |
| GO:BP | negative regulation of immune response  | GO:0050777  | 165       | 6.20E-07 | 15  |
| GO:BP | positive regulation of interleukin-8 production                                   | GO:0032757  | 55        | 6.20E-07 | 10  |
| GO:BP | lipopolysaccharide-mediated signaling pathway                                     | GO:0031663  | 55        | 6.20E-07 | 10  |
| GO:BP | secretion by cell   | GO:0032940  | 728       | 6.30E-07 | 30  |
| TF    | Factor: c-Maf; motif: NWNNTGCTGACKNNNNNNN   | TF:M01070   | 5525      | 6.30E-07 | 106 |
| TF    | Factor: ERF:FOXO1A; motif: RTMACAGGAARNS  | TF:M08241   | 6745      | 6.30E-07 | 122 |
| TF    | Factor: GTF2IRD1-isoform2; motif: GGGATTRNR; match class: 1                       | TF:M01229_1 | 7936      | 6.60E-07 | 137 |
| GO:CC | specific granule membrane   | GO:0035579  | 86        | 7.00E-07 | 11  |
| TF    | Factor: T3R-beta; motif: NRGGTCAAAGGTCRN  | TF:M11814   | 1217<br>7 | 7.20E-07 | 187 |
| TF    | Factor: AP-4; motif: ANCATATGNT; match class: 1                                   | TF:M11209_1 | 2183      | 7.40E-07 | 57  |
| KEGG  | B cell receptor signaling pathway   | KEGG:04662  | 77        | 7.50E-07 | 10  |
| TF    | Factor: ARP-1; motif: TGARCCYTTGAMCCCW  | TF:M00155   | 4662      | 7.50E-07 | 94  |
| GO:BP | negative regulation of lymphocyte activation                                      | GO:0051250  | 141       | 7.60E-07 | 14  |
| GO:CC | MHC protein complex   | GO:0042611  | 22        | 7.70E-07 | 7   |
| GO:BP | cell motility   | GO:0048870  | 1504      | 7.90E-07 | 45  |



|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | localization of cell                                      | GO:0051674  | 1504  | 7.90E-07 | 45  |
| TF    | Factor: Sox-18; motif: NACAAYGS                           | TF:M11623   | 4529  | 8.50E-07 | 92  |
| TF    | Factor: c-Ets-1; motif: RCAGGAAGTGNNNTNS; match class: 1  | TF:M00339_1 | 1273  | 8.60E-07 | 41  |
| GO:BP | regulation of secretion                                   | GO:0051046  | 562   | 9.00E-07 | 26  |
| GO:BP | interferon-gamma production                               | GO:0032609  | 96    | 9.60E-07 | 12  |
| TF    | Factor: NFATc2; motif: NTTCCATNNATGGAAAN                  | TF:M11986   | 5194  | 9.60E-07 | 101 |
| GO:BP | G protein-coupled receptor signaling pathway              | GO:0007186  | 836   | 9.90E-07 | 32  |
| TF    | Factor: Nkx3-2; motif: TRAGTG                             | TF:M01181   | 8070  | 1.10E-06 | 138 |
| TF    | Factor: c-Ets-2; motif: NNCTTCCTNNN                       | TF:M07379   | 2966  | 1.10E-06 | 69  |
| TF    | Factor: STAT3; motif: NNTCCRRGGAANNNNN                    | TF:M01595   | 6729  | 1.10E-06 | 121 |
| GO:BP | T cell activation involved in immune response             | GO:0002286  | 98    | 1.20E-06 | 12  |
| GO:CC | organelle membrane  | GO:0031090  | 3469  | 1.20E-06 | 74  |
| GO:MF | signaling receptor binding                                | GO:0005102  | 1265  | 1.20E-06 | 39  |
| TF    | Factor: TFII-I; motif: NAGGAAGTGN; match class: 1         | TF:M04636_1 | 4849  | 1.20E-06 | 96  |
| TF    | Factor: FOXJ2; motif: NNTGTTGTAAAYAN                      | TF:M11584   | 3923  | 1.20E-06 | 83  |
| TF    | Factor: ZNF333; motif: ATAAT; match class: 1              | TF:M01230_1 | 9656  | 1.20E-06 | 157 |
| GO:BP | phagocytosis, engulfment                                  | GO:0006911  | 59    | 1.30E-06 | 10  |
| GO:MF | MHC class II protein complex binding                      | GO:0023026  | 23    | 1.30E-06 | 7   |
| TF    | Factor: c-Myb; motif: NNWGRCAGTTRN                        | TF:M09990   | 9243  | 1.30E-06 | 152 |
| TF    | Factor: MYB; motif: NAACNGNCN                             | TF:M00913   | 4422  | 1.30E-06 | 90  |
| TF    | Factor: Sox-10; motif: MAANRRNNNCWTTGTGTT; match class: 1 | TF:M10065_1 | 1512  | 1.30E-06 | 45  |
| GO:BP | regulation of B cell activation                           | GO:0050864  | 122   | 1.40E-06 | 13  |
| TF    | Factor: JunD; motif: NATGASTCATS                          | TF:M11268   | 2342  | 1.40E-06 | 59  |
| TF    | Factor: HNRPUL1; motif: NCNCAGN                           | TF:M09746   | 12084 | 1.40E-06 | 185 |
| TF    | Factor: NR1B2; motif: NTGACCY                             | TF:M02111   | 8513  | 1.40E-06 | 143 |
| TF    | Factor: sin3A; motif: TGTCNNGGTGCTG; match class: 1       | TF:M04756_1 | 6912  | 1.50E-06 | 123 |

|       |  |                   |      |          |     |
|-------|--|-------------------|------|----------|-----|
| GO:BP | negative regulation of leukocyte proliferation           | GO:0070664        | 79   | 1.60E-06 | 11  |
| GO:BP | positive regulation of intracellular signal transduction | GO:1902533        | 902  | 1.60E-06 | 33  |
| TF    | Factor: NFATc1; motif: NTTTCRTNNAYGGAAAN                 | TF:M11981         | 5462 | 1.60E-06 | 104 |
| TF    | Factor: NFATc1; motif: NTTTCRTNNAYGGAAAN; match class: 1 | TF:M11981_1       | 4945 | 1.60E-06 | 97  |
| TF    | Factor: RORbeta; motif: TGACCYA                          | TF:M01722         | 5168 | 1.60E-06 | 100 |
| TF    | Factor: Six-3; motif: NNGTATCRNN                         | TF:M11034         | 3061 | 1.60E-06 | 70  |
| TF    | Factor: Oct3; motif: CYWTTSWNATGCAAAT                    | TF:M10036         | 3465 | 1.70E-06 | 76  |
| TF    | Factor: T-bet; motif: NNGNRGGTGTGRN                      | TF:M10089         | 5395 | 1.70E-06 | 103 |
| TF    | Factor: c-MAF; motif: CNNNCTCAGCA                        | TF:M03816         | 4956 | 1.80E-06 | 97  |
| TF    | Factor: MyoD; motif: CGNCAGCTGTYN                        | TF:M11187         | 1698 | 1.80E-06 | 48  |
| KEGG  | Graft-versus-host disease                                | KEGG:05332        | 30   | 1.90E-06 | 7   |
| GO:BP | detection of external biotic stimulus                    | GO:0098581        | 20   | 2.00E-06 | 7   |
| TF    | Factor: Sox-10; motif: AACAAATRGNCYATTGTT                | TF:M11632         | 4174 | 2.00E-06 | 86  |
| TF    | Factor: CART1; motif: NGNNYTAATTARTNNNN                  | TF:M01362         | 3756 | 2.00E-06 | 80  |
| GO:BP | positive regulation of cell population proliferation     | GO:0008284        | 813  | 2.10E-06 | 31  |
| TF    | Factor: p53; motif: RGRCAWGNCY                           | TF:M00761         | 2560 | 2.10E-06 | 62  |
| TF    | Factor: PMX1; motif: TAATHA; match class: 1              | TF:M03560_1       | 8561 | 2.20E-06 | 143 |
| TF    | Factor: SMAD5; motif: GSGGCAGM                           | TF:M03846         | 7589 | 2.20E-06 | 131 |
| TF    | Factor: C/EBPbeta; motif: RTTGCGCAA; match class: 1      | TF:M04690_1       | 3216 | 2.20E-06 | 72  |
| TF    | Factor: beta-catenin; motif: GDMATCAAAGM                 | TF:M03539         | 3217 | 2.20E-06 | 72  |
| TF    | Factor: six4; motif: NCGTATCRTN                          | TF:M11024         | 4469 | 2.20E-06 | 90  |
| TF    | Factor: Rarb; motif: AGGTCANNYARAGGTCA                   | TF:M08035         | 4979 | 2.30E-06 | 97  |
| TF    | Factor: AP-4; motif: ANCATATGNT; match class: 1          | TF:M11207_1       | 1827 | 2.30E-06 | 50  |
| REAC  | Regulation of Complement cascade                         | REAC:R-HSA-977606 | 38   | 2.40E-06 | 8   |
| GO:BP | regulation of neutrophil activation                      | GO:1902563        | 12   | 2.50E-06 | 6   |
| GO:CC | lysosome   | GO:0005764        | 688  | 2.50E-06 | 27  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:CC | lytic vacuole                                    | GO:0000323  | 688   | 2.50E-06 | 27  |
| KEGG  | Allograft rejection                              | KEGG:05330  | 31    | 2.50E-06 | 7   |
| TF    | Factor: Sox-10; motif: CWTTGT                    | TF:M03138   | 11286 | 2.50E-06 | 175 |
| TF    | Factor: TCF-1; motif: CTTTGW                     | TF:M03857   | 11286 | 2.50E-06 | 175 |
| TF    | Factor: Fli-1; motif: RCAGGAAGTGR                | TF:M07089   | 4264  | 2.50E-06 | 87  |
| GO:BP | respiratory burst                                | GO:0045730  | 32    | 2.60E-06 | 8   |
| TF    | Factor: GR; motif: NNNNNNCNNTNTGTNCTNN           | TF:M00192   | 6349  | 2.60E-06 | 115 |
| TF    | Factor: CDP:HOXA13; motif: ATCGATYAYSICRTAAA     | TF:M08201   | 6582  | 2.60E-06 | 118 |
| TF    | Factor: egr-3; motif: GTGGGY; match class: 1     | TF:M03818_1 | 5816  | 2.70E-06 | 108 |
| GO:BP | regulation of mononuclear cell migration         | GO:0071675  | 105   | 2.80E-06 | 12  |
| GO:CC | membrane raft                                    | GO:0045121  | 312   | 2.90E-06 | 18  |
| GO:BP | cell junction disassembly                        | GO:0150146  | 21    | 3.00E-06 | 7   |
| GO:CC | membrane microdomain                             | GO:0098857  | 313   | 3.00E-06 | 18  |
| TF    | Factor: GR; motif: RGNACANKNTGTNCY               | TF:M09625   | 7867  | 3.00E-06 | 134 |
| TF    | Factor: Oct-2; motif: NTATGCWAATN                | TF:M11896   | 4354  | 3.10E-06 | 88  |
| TF    | Factor: SRY; motif: AAACWAM                      | TF:M00148   | 7951  | 3.10E-06 | 135 |
| TF    | Factor: ETS LIKE; motif: NACTTCCTNN              | TF:M08881   | 2714  | 3.10E-06 | 64  |
| GO:BP | export from cell                                 | GO:0140352  | 780   | 3.20E-06 | 30  |
| TF    | Factor: CSX; motif: TSYCACTTSM                   | TF:M01043   | 5382  | 3.20E-06 | 102 |
| GO:BP | regulation of anatomical structure morphogenesis | GO:0022603  | 878   | 3.30E-06 | 32  |
| TF    | Factor: IRF-4; motif: RGGAASWGR                  | TF:M04818   | 8202  | 3.30E-06 | 138 |
| TF    | Factor: MEL1; motif: GARGAT                      | TF:M08794   | 9275  | 3.30E-06 | 151 |
| TF    | Factor: ER-beta; motif: GTCANASTGRCCYNR          | TF:M01875   | 5536  | 3.30E-06 | 104 |
| GO:BP | positive regulation of cell differentiation      | GO:0045597  | 782   | 3.40E-06 | 30  |
| GO:BP | endocytosis                                      | GO:0006897  | 555   | 3.40E-06 | 25  |
| TF    | Factor: SRY; motif: AACAAATNNNCATTGTT            | TF:M04556   | 6458  | 3.50E-06 | 116 |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:BP | mast cell degranulation                                    | GO:0043303  | 48    | 3.70E-06 | 9   |
| GO:BP | regulation of signal transduction                          | GO:0009966  | 2751  | 3.70E-06 | 64  |
| GO:BP | intracellular signal transduction                          | GO:0035556  | 2497  | 3.90E-06 | 60  |
| GO:MF | cargo receptor activity                                    | GO:0038024  | 77    | 3.90E-06 | 10  |
| TF    | Factor: TEF; motif: ATGTTWAYATAA                           | TF:M00672   | 4809  | 3.90E-06 | 94  |
| TF    | Factor: BRCA2; motif: TGMCYCWGN                            | TF:M12723   | 3259  | 3.90E-06 | 72  |
| TF    | Factor: Msx-2; motif: NNNGACYAATTAGYNNNT; match class: 1   | TF:M01393_1 | 3193  | 3.90E-06 | 71  |
| GO:BP | regulation of interleukin-6 production                     | GO:0032675  | 133   | 4.00E-06 | 13  |
| GO:BP | interleukin-6 production                                   | GO:0032635  | 133   | 4.00E-06 | 13  |
| GO:BP | regulation of toll-like receptor signaling pathway         | GO:0034121  | 66    | 4.00E-06 | 10  |
| TF    | Factor: ESRRA; motif: CAAGGTCANNYSAAAGTCA                  | TF:M04458   | 9722  | 4.10E-06 | 156 |
| TF    | Factor: CDP; motif: NATYGATSSS                             | TF:M00106   | 5335  | 4.20E-06 | 101 |
| TF    | Factor: rfx3:SRF; motif: TRGCAACNNNNNCCNWATANGN            | TF:M08623   | 12775 | 4.20E-06 | 191 |
| GO:BP | regulation of protein metabolic process                    | GO:0051246  | 2316  | 4.50E-06 | 57  |
| GO:BP | positive regulation of interleukin-6 production            | GO:0032755  | 87    | 4.50E-06 | 11  |
| TF    | Factor: IRX5; motif: NWACAYRACAWN                          | TF:M04378   | 3270  | 4.50E-06 | 72  |
| GO:BP | MHC class II protein complex assembly                      | GO:0002399  | 13    | 4.60E-06 | 6   |
| GO:BP | peptide antigen assembly with MHC class II protein complex | GO:0002503  | 13    | 4.60E-06 | 6   |
| TF    | Factor: TEAD1; motif: NNACATTCCAGNN                        | TF:M12500   | 5045  | 4.60E-06 | 97  |
| TF    | Factor: HOXD4; motif: RTCRTTAN                             | TF:M10710   | 2741  | 4.60E-06 | 64  |
| TF    | Factor: c-Myc; motif: NCCACGTGCNN                          | TF:M09992   | 4899  | 4.60E-06 | 95  |
| GO:BP | plasma membrane invagination                               | GO:0099024  | 67    | 4.70E-06 | 10  |
| GO:BP | immunoglobulin mediated immune response                    | GO:0016064  | 110   | 4.70E-06 | 12  |
| GO:BP | regulation of leukocyte chemotaxis                         | GO:0002688  | 110   | 4.70E-06 | 12  |
| TF    | Factor: Lyl-1; motif: NCAKCTGYTNYCENN; match class: 1      | TF:M09977_1 | 6570  | 4.80E-06 | 117 |
| TF    | Factor: C/EBPbeta; motif: NKNTTGCNYYAAYNN                  | TF:M00117   | 3480  | 4.80E-06 | 75  |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: SREBP-2; motif: RTGGGGTGAY  | TF:M07406         | 5054  | 5.00E-06 | 97  |
| TF    | Factor: C/EBP; motif: NTRCNAANN   | TF:M00912         | 4188  | 5.30E-06 | 85  |
| GO:BP | mast cell activation involved in immune response                          | GO:0002279        | 50    | 5.40E-06 | 9   |
| GO:BP | complement activation   | GO:0006956        | 50    | 5.40E-06 | 9   |
| GO:BP | mast cell mediated immunity   | GO:0002448        | 50    | 5.40E-06 | 9   |
| GO:BP | regulation of cell migration  | GO:0030334        | 847   | 5.40E-06 | 31  |
| REAC  | Signaling by GPCR   | REAC:R-HSA-372790 | 615   | 5.50E-06 | 25  |
| TF    | Factor: GSX2; motif: NNYMATTANN   | TF:M04328         | 5063  | 5.50E-06 | 97  |
| TF    | Factor: C-Jun; motif: TGA CTC; match class: 1                             | TF:M03541_1       | 3560  | 5.50E-06 | 76  |
| TF    | Factor: NFATc2; motif: NTTCCATNNATGGAAAN; match class: 1                  | TF:M11986_1       | 4990  | 5.60E-06 | 96  |
| TF    | Factor: SAP-1a; motif: CWTCKGT  | TF:M03844         | 2306  | 5.60E-06 | 57  |
| TF    | Factor: ER71; motif: CWTCTGT  | TF:M07282         | 2306  | 5.60E-06 | 57  |
| TF    | Factor: Oct-2; motif: NYATGCAAATN   | TF:M10034         | 5065  | 5.60E-06 | 97  |
| TF    | Factor: CDP:SRF; motif: NCCWTAYAAAGGTMNKRATCRATN                          | TF:M08520         | 8843  | 5.70E-06 | 145 |
| TF    | Factor: PPARgamma:RXRalpha; motif: AAGTAGGTACNGTGACCYACTT; match class: 1 | TF:M00515_1       | 3841  | 5.70E-06 | 80  |
| GO:BP | B cell mediated immunity  | GO:0019724        | 112   | 5.80E-06 | 12  |
| TF    | Factor: Spi-B; motif: NAWGCGGAAGTN  | TF:M11375         | 2309  | 5.80E-06 | 57  |
| TF    | Factor: Sox-10; motif: AACAAATGGNCCATTGTT                                 | TF:M11633         | 3089  | 5.90E-06 | 69  |
| TF    | Factor: Thap1; motif: SCGCCATSTTKGNTNMGGGCARNN                            | TF:M04723         | 10537 | 5.90E-06 | 165 |
| KEGG  | Inflammatory bowel disease  | KEGG:05321        | 52    | 6.10E-06 | 8   |
| KEGG  | Type I diabetes mellitus  | KEGG:04940        | 35    | 6.10E-06 | 7   |
| GO:BP | regulation of cell death  | GO:0010941        | 1440  | 6.80E-06 | 42  |
| TF    | Factor: FOXO1A:PDEF; motif: WNCCGGATGTTDN; match class: 1                 | TF:M08486_1       | 3785  | 6.80E-06 | 79  |
| GO:MF | IgG binding   | GO:0019864        | 9     | 6.90E-06 | 5   |
| TF    | Factor: Oct-2; motif: NTATGCGCATAN  | TF:M11895         | 3303  | 6.90E-06 | 72  |

|       |  |                    |       |          |     |
|-------|--|--------------------|-------|----------|-----|
| TF    | Factor: CSX; motif: NNCACCTGNRN                      | TF:M02108          | 5994  | 7.10E-06 | 109 |
| TF    | Factor: Pax-5; motif: RRNGRNGCAN                     | TF:M03577          | 7727  | 7.20E-06 | 131 |
| TF    | Factor: SATB1; motif: NTTTTAT; match class: 1        | TF:M03564_1        | 10054 | 7.40E-06 | 159 |
| TF    | Factor: Oct-4; motif: ATTGWSWTGCWAAWN                | TF:M01124          | 4945  | 7.50E-06 | 95  |
| TF    | Factor: MEF-2C; motif: TATTTWT; match class: 1       | TF:M02025_1        | 6386  | 7.50E-06 | 114 |
| TF    | Factor: ZBTB44; motif: MACWGCAGS                     | TF:M12352          | 5619  | 7.60E-06 | 104 |
| GO:BP | programmed cell death                                | GO:0012501         | 1737  | 7.80E-06 | 47  |
| TF    | Factor: GATA-3; motif: AGATAA                        | TF:M01878          | 8472  | 7.90E-06 | 140 |
| TF    | Factor: Spi-B; motif: RAAWGRGGAAGTN                  | TF:M11376          | 613   | 8.00E-06 | 26  |
| TF    | Factor: CTCF; motif: CANNWRRTGGCAG                   | TF:M04745          | 7022  | 8.10E-06 | 122 |
| REAC  | Interferon gamma signaling                           | REAC:R-HSA-877300  | 83    | 8.20E-06 | 10  |
| TF    | Factor: Bcl-6; motif: NTTYCTAGRA                     | TF:M02085          | 4154  | 8.20E-06 | 84  |
| TF    | Factor: C/EBPalpha; motif: NNNTTNNGCAANN             | TF:M01866          | 4299  | 8.30E-06 | 86  |
| GO:BP | regulated exocytosis                                 | GO:0045055         | 231   | 8.60E-06 | 16  |
| TF    | Factor: Tbx5; motif: NNAGGTGTNANN                    | TF:M01019          | 4960  | 8.80E-06 | 95  |
| GO:BP | positive regulation of phosphate metabolic process   | GO:0045937         | 817   | 9.20E-06 | 30  |
| GO:BP | positive regulation of phosphorus metabolic process  | GO:0010562         | 817   | 9.20E-06 | 30  |
| GO:CC | cytoplasm  | GO:0005737         | 11064 | 9.20E-06 | 167 |
| TF    | Factor: Spi-B; motif: AAAAWGMGGAAGTWNSN              | TF:M01204          | 663   | 9.30E-06 | 27  |
| TF    | Factor: HOXD4; motif: RTCRTTAN                       | TF:M10713          | 3124  | 9.40E-06 | 69  |
| KEGG  | Legionellosis  | KEGG:05134         | 55    | 9.60E-06 | 8   |
| TF    | Factor: C-FOS; motif: NATGAGTCATN                    | TF:M08946          | 2153  | 9.60E-06 | 54  |
| GO:BP | lymphocyte mediated immunity                         | GO:0002449         | 233   | 9.70E-06 | 16  |
| TF    | Factor: SRY; motif: TCAATAMCATTGA; match class: 1    | TF:M04557_1        | 3956  | 9.70E-06 | 81  |
| TF    | Factor: PPARGAMMA:RXR-ALPHA; motif: NNRGGTCAAAGGTCAN | TF:M08962          | 4100  | 9.90E-06 | 83  |
| REAC  | Antimicrobial peptides                               | REAC:R-HSA-6803157 | 30    | 1.00E-05 | 7   |

|       |   |                      |       |          |     |
|-------|---|----------------------|-------|----------|-----|
| TF    | Factor: Oct-2; motif: NTGCATATGCAN                        | TF:M11899            | 4532  | 1.00E-05 | 89  |
| TF    | Factor: SMAD3; motif: TGTCTGTCT; match class: 1           | TF:M00701_1          | 575   | 1.00E-05 | 25  |
| TF    | Factor: TBX2; motif: NNNGTGTSNN                           | TF:M12026            | 6418  | 1.00E-05 | 114 |
| TF    | Factor: FOXO1A;Net; motif: RWMAACAGGAAGTN; match class: 1 | TF:M08302_1          | 2282  | 1.00E-05 | 56  |
| TF    | Factor: Fra-1; motif: ACTCATG                             | TF:M04897            | 2096  | 1.00E-05 | 53  |
| TF    | Factor: IRF-4; motif: NAANGRGGAASTGAAASN                  | TF:M09959            | 2865  | 1.00E-05 | 65  |
| TF    | Factor: C/EBPbeta; motif: RTTGCGCAA                       | TF:M04690            | 3752  | 1.10E-05 | 78  |
| TF    | Factor: ZNF549; motif: NTGCTKYCMW                         | TF:M12355            | 5656  | 1.10E-05 | 104 |
| TF    | Factor: NF-E4; motif: GTGAGGS                             | TF:M08826            | 10022 | 1.10E-05 | 158 |
| GO:BP | regulation of interferon-gamma production                 | GO:0032649           | 95    | 1.20E-05 | 11  |
| GO:BP | positive regulation of leukocyte differentiation          | GO:1902107           | 146   | 1.20E-05 | 13  |
| GO:BP | positive regulation of hemopoiesis                        | GO:1903708           | 146   | 1.20E-05 | 13  |
| GO:CC | clathrin-coated endocytic vesicle membrane                | GO:0030669           | 66    | 1.20E-05 | 9   |
| MIRNA | hsa-miR-335-5p  | MIRNA:hsa-miR-335-5p | 2271  | 1.20E-05 | 54  |
| REAC  | Complement cascade  | REAC:R-HSA-166658    | 46    | 1.20E-05 | 8   |
| TF    | Factor: TCF-7; motif: TCAAAG                              | TF:M00805            | 10201 | 1.20E-05 | 160 |
| TF    | Factor: TCF-3; motif: CTTTGA                              | TF:M03858            | 10201 | 1.20E-05 | 160 |
| TF    | Factor: OLIG2; motif: CCAKCTGYTYNNNNNNN                   | TF:M10019            | 3416  | 1.20E-05 | 73  |
| TF    | Factor: Erg; motif: NACAGGAARTN                           | TF:M11390            | 2358  | 1.20E-05 | 57  |
| GO:BP | response to wounding                                      | GO:0009611           | 505   | 1.30E-05 | 23  |
| GO:BP | negative regulation of lymphocyte proliferation           | GO:0050672           | 74    | 1.30E-05 | 10  |
| GO:BP | membrane invagination                                     | GO:0010324           | 74    | 1.30E-05 | 10  |
| GO:BP | negative regulation of mononuclear cell proliferation     | GO:0032945           | 74    | 1.30E-05 | 10  |
| GO:BP | peptide antigen assembly with MHC protein complex         | GO:0002501           | 15    | 1.30E-05 | 6   |
| GO:MF | MHC protein complex binding                               | GO:0023023           | 31    | 1.30E-05 | 7   |
| TF    | Factor: RXRA; motif: RRGTCATGACCYY                        | TF:M04490            | 6522  | 1.30E-05 | 115 |

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|-------|--|-------------|-------|----------|-----|
| KEGG  | Autoimmune thyroid disease                                     | KEGG:05320  | 39    | 1.40E-05 | 7   |
| TF    | Factor: MRF4; motif: CASCTGC                                   | TF:M03831   | 7565  | 1.40E-05 | 128 |
| TF    | Factor: HTF4; motif: CASCTGB                                   | TF:M02018   | 7565  | 1.40E-05 | 128 |
| TF    | Factor: MafB; motif: GNTGAC                                    | TF:M01227   | 10227 | 1.40E-05 | 160 |
| GO:BP | regulation of neutrophil degranulation                         | GO:0043313  | 8     | 1.50E-05 | 5   |
| GO:BP | positive regulation of apoptotic cell clearance                | GO:2000427  | 8     | 1.50E-05 | 5   |
| TF    | Factor: POU2F1;GscI; motif: NNGATTANNATKCANNNN; match class: 1 | TF:M08404_1 | 1404  | 1.50E-05 | 41  |
| TF    | Factor: myogenin; motif: CRSGTGTTBNNTTGGCAGSNGCCA RCH          | TF:M00056   | 9551  | 1.50E-05 | 152 |
| GO:BP | response to lipid  | GO:0033993  | 787   | 1.60E-05 | 29  |
| TF    | Factor: JunD; motif: NRTGAGTCAYN                               | TF:M09964   | 4213  | 1.60E-05 | 84  |
| TF    | Factor: RelA-p65; motif: BCWGGGRANNK                           | TF:M04811   | 6469  | 1.60E-05 | 114 |
| GO:BP | antigen processing and presentation of peptide antigen         | GO:0048002  | 76    | 1.70E-05 | 10  |
| GO:BP | antigen receptor-mediated signaling pathway                    | GO:0050851  | 179   | 1.70E-05 | 14  |
| TF    | Factor: DBP; motif: TTRCATAANN                                 | TF:M07038   | 4582  | 1.70E-05 | 89  |
| TF    | Factor: Sox-8; motif: NGAACAATRN                               | TF:M11629   | 1030  | 1.70E-05 | 34  |
| TF    | Factor: TBP; motif: NGNNTATAAAA                                | TF:M03581   | 5782  | 1.70E-05 | 105 |
| GO:BP | cytokine-mediated signaling pathway                            | GO:0019221  | 430   | 1.80E-05 | 21  |
| TF    | Factor: T3R-beta; motif: NRGGTCAAAGGTCAN                       | TF:M11816   | 10084 | 1.80E-05 | 158 |
| TF    | Factor: msc; motif: NRMCAATGNYN                                | TF:M11146   | 2641  | 1.80E-05 | 61  |
| TF    | Factor: Pax-4; motif: NNNNNYCACCCB; match class: 1             | TF:M00378_1 | 13163 | 1.80E-05 | 193 |
| TF    | Factor: Sox-30; motif: NAACAATN                                | TF:M11641   | 1945  | 1.80E-05 | 50  |
| TF    | Factor: KLF4; motif: MCACACCCTNN                               | TF:M09808   | 3175  | 1.80E-05 | 69  |
| TF    | Factor: C/EBPgamma; motif: YTBATTCARAAW                        | TF:M00622   | 5635  | 1.80E-05 | 103 |
| TF    | Factor: znf136; motif: CAAGAATWCTATAYCCAG                      | TF:M10535   | 6878  | 1.80E-05 | 119 |
| KEGG  | Transcriptional misregulation in cancer                        | KEGG:05202  | 166   | 1.90E-05 | 12  |

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|-------|--|-------------------|-------|----------|-----|
| TF    | Factor: HSF4; motif: CTGCMRN; match class: 1           | TF:M07322_1       | 10436 | 1.90E-05 | 162 |
| TF    | Factor: JunD; motif: SATGACTCATN                       | TF:M11269         | 3179  | 1.90E-05 | 69  |
| TF    | Factor: CLOCK; motif: NNCAYGYGYN                       | TF:M11046         | 2134  | 1.90E-05 | 53  |
| TF    | Factor: HOXA3; motif: NNNNRNTAATTARY; match class: 1   | TF:M01337_1       | 10095 | 1.90E-05 | 158 |
| GO:BP | regulation of cellular protein metabolic process       | GO:0032268        | 2160  | 2.00E-05 | 53  |
| TF    | Factor: B-ATF; motif: NNATGACACN; match class: 1       | TF:M11300_1       | 2135  | 2.00E-05 | 53  |
| GO:BP | MHC protein complex assembly                           | GO:0002396        | 16    | 2.10E-05 | 6   |
| GO:BP | regulation of cell motility                            | GO:2000145        | 898   | 2.10E-05 | 31  |
| TF    | Factor: FOXO1A; Eif-1; motif: NAGAAAACCGAANM           | TF:M08295         | 10193 | 2.10E-05 | 159 |
| TF    | Factor: DRI1; motif: AATTAA                            | TF:M01654         | 9177  | 2.10E-05 | 147 |
| TF    | Factor: Dlx-5; motif: AATTAN                           | TF:M03546         | 9177  | 2.10E-05 | 147 |
| REAC  | G alpha (i) signalling events                          | REAC:R-HSA-418594 | 276   | 2.20E-05 | 16  |
| TF    | Factor: Pit-1; motif: NMTTCATAAWTATWNMNA               | TF:M00802         | 3743  | 2.20E-05 | 77  |
| TF    | Factor: HMX2; motif: SCACTTANC                         | TF:M10646         | 6195  | 2.30E-05 | 110 |
| TF    | Factor: foxm1; motif: TGTTRCTYWNN                      | TF:M09930         | 5734  | 2.30E-05 | 104 |
| TF    | Factor: LHX3; motif: ATTAAW                            | TF:M02097         | 10034 | 2.30E-05 | 157 |
| TF    | Factor: GR; motif: NNTGTYCT                            | TF:M00921         | 1600  | 2.30E-05 | 44  |
| GO:BP | negative regulation of cytokine production             | GO:0001818        | 248   | 2.40E-05 | 16  |
| GO:BP | positive regulation of macromolecule metabolic process | GO:0010604        | 3089  | 2.40E-05 | 67  |
| GO:BP | regulation of cell killing                             | GO:0031341        | 79    | 2.40E-05 | 10  |
| REAC  | Hemostasis   | REAC:R-HSA-109582 | 570   | 2.40E-05 | 23  |
| TF    | Factor: Octamer; motif: TNATTTGCATN                    | TF:M00795         | 3752  | 2.40E-05 | 77  |
| TF    | Factor: Oct-1; motif: NNNNNNNWATGCAAATNNNNWNA          | TF:M00138         | 2024  | 2.40E-05 | 51  |
| GO:BP | regulation of macromolecule metabolic process          | GO:0060255        | 5629  | 2.50E-05 | 102 |
| TF    | Factor: HES-5; motif: NCACACKY; match class: 1         | TF:M11069_1       | 3616  | 2.50E-05 | 75  |
| GO:BP | complement-mediated synapse pruning                    | GO:0150062        | 4     | 2.60E-05 | 4   |

|       |  |            |      |          |     |
|-------|--|------------|------|----------|-----|
| TF    | Factor: ELF3; motif: NNCCACTTCTGNN                 | TF:M12544  | 3272 | 2.60E-05 | 70  |
| GO:BP | myeloid cell differentiation                       | GO:0030099 | 360  | 2.70E-05 | 19  |
| TF    | Factor: C/EBPdelta; motif: TTGCNNMAN               | TF:M03571  | 3137 | 2.70E-05 | 68  |
| TF    | Factor: TEF-3; motif: GNTATTTTT                    | TF:M07270  | 8541 | 2.70E-05 | 139 |
| TF    | Factor: Foxc1; motif: TTVYTTTNW                    | TF:M07254  | 6449 | 2.70E-05 | 113 |
| TF    | Factor: B-ATF; motif: NNAYGACACN                   | TF:M11301  | 6607 | 2.70E-05 | 115 |
| TF    | Factor: AP-2; motif: NNGCCTK                       | TF:M01859  | 6687 | 2.80E-05 | 116 |
| TF    | Factor: Fli-1; motif: NNRGGMAGGAAGRRRGR            | TF:M09920  | 8216 | 2.80E-05 | 135 |
| TF    | Factor: Six-2; motif: NNGTATCRNN                   | TF:M11030  | 5986 | 2.80E-05 | 107 |
| TF    | Factor: NR1B1; motif: NRGGNCRTGACCTN               | TF:M11796  | 9466 | 2.80E-05 | 150 |
| GO:MF | peptide binding                                    | GO:0042277 | 282  | 2.90E-05 | 16  |
| KEGG  | Coronavirus disease - COVID-19                     | KEGG:05171 | 206  | 2.90E-05 | 13  |
| TF    | Factor: FXR:RXR-ALPHA; motif: NRGGTCANRGGKN        | TF:M08955  | 8470 | 2.90E-05 | 138 |
| TF    | Factor: LXR; motif: NTGACCKNNAGTRACCYN             | TF:M03795  | 5609 | 3.00E-05 | 102 |
| TF    | Factor: ipf1; motif: CATTAR                        | TF:M01275  | 7333 | 3.00E-05 | 124 |
| GO:BP | regulation of phosphate metabolic process          | GO:0019220 | 1289 | 3.10E-05 | 38  |
| TF    | Factor: Oct-1; motif: NNNNATGCAAATNAN              | TF:M00195  | 3014 | 3.10E-05 | 66  |
| GO:BP | regulation of phosphorus metabolic process         | GO:0051174 | 1291 | 3.20E-05 | 38  |
| GO:BP | positive regulation of superoxide anion generation | GO:0032930 | 17   | 3.20E-05 | 6   |
| GO:BP | cellular defense response                          | GO:0006968 | 43   | 3.20E-05 | 8   |
| GO:BP | regulation of mast cell activation                 | GO:0033003 | 43   | 3.20E-05 | 8   |
| TF    | Factor: IRF-4; motif: AAGTTTC                      | TF:M04855  | 6624 | 3.20E-05 | 115 |
| TF    | Factor: Six-1; motif: NCGTATCRNN                   | TF:M11029  | 1980 | 3.20E-05 | 50  |
| TF    | Factor: AR; motif: RGGWACAYNGTGTWCYN               | TF:M04453  | 6079 | 3.20E-05 | 108 |
| TF    | Factor: HOXB2; motif: RTCATTAN                     | TF:M10739  | 3153 | 3.20E-05 | 68  |
| GO:CC | vacuole  | GO:0005773 | 781  | 3.30E-05 | 27  |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: MGA; motif: AGGTGTGA                        | TF:M04117         | 1738  | 3.30E-05 | 46  |
| TF    | Factor: TBX1; motif: AGGTGTGA                       | TF:M04126         | 1738  | 3.30E-05 | 46  |
| TF    | Factor: Tbx5; motif: AGGTGTGA                       | TF:M04137         | 1738  | 3.30E-05 | 46  |
| TF    | Factor: TBX15; motif: AGGTGTGA                      | TF:M04122         | 1738  | 3.30E-05 | 46  |
| TF    | Factor: TBX4; motif: AGGTGTGA                       | TF:M04135         | 1738  | 3.30E-05 | 46  |
| TF    | Factor: MEF-2D; motif: WAAATAR                      | TF:M02026         | 6393  | 3.30E-05 | 112 |
| TF    | Factor: GCMa:C/EBPbeta; motif: ATGCGGGTNNRTTGCACAAY | TF:M08575         | 5928  | 3.30E-05 | 106 |
| GO:BP | mast cell activation                                | GO:0045576        | 61    | 3.40E-05 | 9   |
| TF    | Factor: Pax-4; motif: DTTTTCCACCN; match class: 1   | TF:M04624_1       | 8077  | 3.40E-05 | 133 |
| TF    | Factor: NF-1C; motif: NYTGGCANNYNGCCARN             | TF:M10002         | 5930  | 3.40E-05 | 106 |
| GO:BP | regulation of biological quality                    | GO:0065008        | 3465  | 3.50E-05 | 72  |
| TF    | Factor: SREBP-1; motif: CACSCCA; match class: 1     | TF:M00749_1       | 2428  | 3.50E-05 | 57  |
| TF    | Factor: Ikaros; motif: TGGGAGN; match class: 1      | TF:M07260_1       | 6245  | 3.50E-05 | 110 |
| TF    | Factor: C/EBPalpha; motif: NRTTGTGCAAYN             | TF:M09880         | 2890  | 3.60E-05 | 64  |
| GO:BP | regulation of angiogenesis                          | GO:0045765        | 256   | 3.70E-05 | 16  |
| REAC  | Cell surface interactions at the vascular wall      | REAC:R-HSA-202733 | 123   | 3.70E-05 | 11  |
| TF    | Factor: HELIOS; motif: RNARRRGGAASTGARAN            | TF:M09745         | 2894  | 3.80E-05 | 64  |
| TF    | Factor: TCF11:MafG; motif: NNNNATGACTCAGCANTTNG     | TF:M00284         | 3651  | 3.80E-05 | 75  |
| TF    | Factor: FOXO1A:HOXA10; motif: RWMAACANCRTWAA        | TF:M08482         | 3442  | 3.80E-05 | 72  |
| GO:BP | positive regulation of defense response             | GO:0031349        | 257   | 3.90E-05 | 16  |
| TF    | Factor: Six-1; motif: NNGTATCRNN                    | TF:M11026         | 5183  | 3.90E-05 | 96  |
| TF    | Factor: Zic3; motif: NGGGKGGTC                      | TF:M00450         | 12380 | 3.90E-05 | 183 |
| TF    | Factor: LBX2; motif: CTNRRANSTAATTA; match class: 1 | TF:M04383_1       | 1933  | 4.10E-05 | 49  |
| TF    | Factor: FAC1; motif: NNNCAMAACACRNA                 | TF:M00456         | 6812  | 4.10E-05 | 117 |
| TF    | Factor: msc; motif: NRMCAATGNYN; match class: 1     | TF:M11146_1       | 2505  | 4.20E-05 | 58  |
| TF    | Factor: Dlx-3; motif: NTCRTTAN                      | TF:M10609         | 3800  | 4.20E-05 | 77  |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| TF    | Factor: HOXB5; motif: RTCRTTAN                    | TF:M10698   | 3800  | 4.20E-05 | 77  |
| TF    | Factor: nanog; motif: NYWTTGWNATGCAAAATN          | TF:M09639   | 1458  | 4.30E-05 | 41  |
| TF    | Factor: Sox-10; motif: NACAAWG; match class: 1    | TF:M02116_1 | 6582  | 4.30E-05 | 114 |
| TF    | Factor: POU2F1; motif: ATTTGCATN                  | TF:M07058   | 2707  | 4.50E-05 | 61  |
| TF    | Factor: NFATC3; motif: WNTTTCRRNN                 | TF:M08001   | 1404  | 4.50E-05 | 40  |
| GO:BP | regulation of vasculature development             | GO:1901342  | 260   | 4.60E-05 | 16  |
| GO:BP | pattern recognition receptor signaling pathway    | GO:0002221  | 163   | 4.70E-05 | 13  |
| TF    | Factor: c-Jun; motif: NATGASTCATN; match class: 1 | TF:M11264_1 | 3183  | 4.70E-05 | 68  |
| TF    | Factor: SALL2; motif: GGGTGGG                     | TF:M04595   | 11697 | 4.70E-05 | 175 |
| TF    | Factor: MAF; motif: NGCTGAGTCAN                   | TF:M00983   | 5128  | 4.70E-05 | 95  |
| TF    | Factor: Six-3; motif: NNRTATCRNN                  | TF:M11035   | 1522  | 4.80E-05 | 42  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT                   | TF:M11210   | 3956  | 4.80E-05 | 79  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1   | TF:M11210_1 | 3956  | 4.80E-05 | 79  |
| GO:BP | negative regulation of inflammatory response      | GO:0050728  | 135   | 4.90E-05 | 12  |
| TF    | Factor: FOXJ2; motif: AYMATAATATTKN               | TF:M00423   | 5662  | 4.90E-05 | 102 |
| TF    | Factor: Ngn-2; motif: RACATATGTY                  | TF:M11132   | 673   | 5.40E-05 | 26  |
| TF    | Factor: Erg; motif: MCAGGAAA; match class: 1      | TF:M07284_1 | 3752  | 5.40E-05 | 76  |
| TF    | Factor: ZBTB2; motif: TCCKCCTSR                   | TF:M07437   | 3263  | 5.40E-05 | 69  |
| GO:BP | regulation of locomotion                          | GO:0040012  | 937   | 5.60E-05 | 31  |
| TF    | Factor: CTCF; motif: NNNNANASYGCCMYCTAGTGG        | TF:M04689   | 4847  | 5.70E-05 | 91  |
| TF    | Factor: SMAD4; motif: GKSRKKCAGMCANCY             | TF:M00733   | 7655  | 5.70E-05 | 127 |
| TF    | Factor: Tbx1; motif: NNAGGTGTGAAN                 | TF:M12035   | 2399  | 5.80E-05 | 56  |
| TF    | Factor: OCT-x; motif: CTNATTTGCATAY               | TF:M00210   | 3408  | 5.90E-05 | 71  |
| TF    | Factor: Oct3; motif: NNTTATGYWAATKARN             | TF:M11932   | 2470  | 6.40E-05 | 57  |
| TF    | Factor: GATA-1; motif: NNNNNGATANKGGN             | TF:M00126   | 3277  | 6.40E-05 | 69  |
| TF    | Factor: TEF-1; motif: GRRATG; match class: 1      | TF:M00704_1 | 4564  | 6.50E-05 | 87  |

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|-------|---|--------------------|------|----------|-----|
| TF    | Factor: IRF-4; motif: GAAARTA; match class: 1               | TF:M01883_1        | 2342 | 6.50E-05 | 55  |
| TF    | Factor: PRDM16; motif: KGGTCATRACCM                         | TF:M05946          | 6003 | 6.50E-05 | 106 |
| GO:BP | regulation of apoptotic cell clearance                      | GO:2000425         | 10   | 6.60E-05 | 5   |
| TF    | Factor: Nrf-2; motif: NTGCTGAGTCAKN                         | TF:M00821          | 3984 | 6.60E-05 | 79  |
| GO:BP | exocytosis  | GO:0006887         | 342  | 6.70E-05 | 18  |
| TF    | Factor: FOXJ2; motif: NNTGTTGTAAYAN                         | TF:M11585          | 4568 | 6.70E-05 | 87  |
| REAC  | FCGR activation   | REAC:R-HSA-2029481 | 13   | 6.80E-05 | 5   |
| GO:BP | positive regulation of myeloid leukocyte mediated immunity  | GO:0002888         | 19   | 6.90E-05 | 6   |
| TF    | Factor: AP-4; motif: AWCAGCTGWT                             | TF:M11208          | 3562 | 6.90E-05 | 73  |
| TF    | Factor: TBX15; motif: NAGGTGTGAN                            | TF:M12040          | 2218 | 6.90E-05 | 53  |
| TF    | Factor: GSX1; motif: NNYMATTANN; match class: 1             | TF:M04327_1        | 4571 | 6.90E-05 | 87  |
| GO:BP | regulation of interleukin-1 beta production                 | GO:0032651         | 88   | 7.00E-05 | 10  |
| GO:BP | interleukin-1 beta production                               | GO:0032611         | 88   | 7.00E-05 | 10  |
| TF    | Factor: FOXO1A;Elk-1; motif: RWMAACAGGAAGTN; match class: 1 | TF:M08299_1        | 1312 | 7.00E-05 | 38  |
| TF    | Factor: Blimp-1; motif: NACTTTCAC                           | TF:M04731          | 3425 | 7.10E-05 | 71  |
| TF    | Factor: Msx-2; motif: TWWTTGGDGABN                          | TF:M03797          | 4137 | 7.20E-05 | 81  |
| TF    | Factor: NeuroD-2; motif: RMCATATGKY                         | TF:M01287          | 2032 | 7.30E-05 | 50  |
| TF    | Factor: Oct-2; motif: NNNATTATGCAW                          | TF:M11894          | 2946 | 7.30E-05 | 64  |
| GO:BP | positive regulation of hydrolase activity                   | GO:0051345         | 511  | 7.40E-05 | 22  |
| GO:BP | regulation of secretion by cell                             | GO:1903530         | 511  | 7.40E-05 | 22  |
| GO:BP | cellular response to lipid                                  | GO:0071396         | 511  | 7.40E-05 | 22  |
| TF    | Factor: SPIB; motif: NNTCACTTCCTCTTN                        | TF:M12498          | 1908 | 7.40E-05 | 48  |
| TF    | Factor: ATF-4; motif: GGATGATGCATCC                         | TF:M11334          | 5176 | 7.50E-05 | 95  |
| TF    | Factor: EVX1; motif: NTCATTAN                               | TF:M10864          | 4360 | 7.60E-05 | 84  |
| TF    | Factor: GATA-3; motif: AGATAA; match class: 1               | TF:M01878_1        | 3293 | 7.80E-05 | 69  |
| GO:BP | regulation of mast cell degranulation                       | GO:0043304         | 32   | 7.90E-05 | 7   |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| GO:BP | detection of biotic stimulus                                     | GO:0009595  | 32   | 7.90E-05 | 7   |
| TF    | Factor: NF1C; motif: WGCCARR; match class: 1                     | TF:M09763_1 | 3644 | 7.90E-05 | 74  |
| TF    | Factor: Pax-2; motif: NNNNGTCANGNRTKANNNN                        | TF:M00098   | 6494 | 7.90E-05 | 112 |
| GO:BP | apoptotic process  | GO:0006915  | 1692 | 8.20E-05 | 44  |
| TF    | Factor: PU.1; motif: ACTTCCTCT                                   | TF:M04711   | 1495 | 8.50E-05 | 41  |
| TF    | Factor: Spic; motif: NGNGGAASTN; match class: 1                  | TF:M02077_1 | 2042 | 8.50E-05 | 50  |
| GO:BP | cellular response to oxygen-containing compound                  | GO:1901701  | 1062 | 8.60E-05 | 33  |
| GO:CC | phagocytic vesicle   | GO:0045335  | 136  | 8.70E-05 | 11  |
| TF    | Factor: POU3F2; motif: WTATGCWAATKA                              | TF:M04079   | 2624 | 8.70E-05 | 59  |
| TF    | Factor: GSX2; motif: NNYMATTANN; match class: 1                  | TF:M04328_1 | 3165 | 8.80E-05 | 67  |
| GO:BP | positive regulation of leukocyte mediated immunity               | GO:0002705  | 115  | 8.90E-05 | 11  |
| GO:CC | clathrin-coated endocytic vesicle                                | GO:0045334  | 83   | 9.10E-05 | 9   |
| TF    | Factor: FOXO1A:ETV7; motif: NWMAACAGGAMNNNCTTCNN; match class: 1 | TF:M08304_1 | 6512 | 9.20E-05 | 112 |
| GO:BP | blood vessel morphogenesis                                       | GO:0048514  | 563  | 9.30E-05 | 23  |
| TF    | Factor: ZNF462; motif: YYYCTSCWG; match class: 1                 | TF:M12707_1 | 3033 | 9.30E-05 | 65  |
| GO:CC | clathrin-coated vesicle membrane                                 | GO:0030665  | 109  | 9.50E-05 | 10  |
| TF    | Factor: TORC2; motif: TGGGCTKKD                                  | TF:M07341   | 4235 | 9.50E-05 | 82  |
| TF    | Factor: Oct-1; motif: NNNRTAATNANN                               | TF:M00137   | 5582 | 9.50E-05 | 100 |
| TF    | Factor: c-Jun; motif: NNNNRRTGASTCAN                             | TF:M07102   | 4236 | 9.60E-05 | 82  |
| GO:BP | regulation of superoxide anion generation                        | GO:0032928  | 20   | 9.80E-05 | 6   |
| TF    | Factor: Pax-6; motif: NNNNTTCACGCWTGANTKNNN                      | TF:M00097   | 9552 | 9.80E-05 | 149 |
| TF    | Factor: GATA-1; motif: NCWGATAACA                                | TF:M00346   | 3594 | 9.90E-05 | 73  |
| GO:BP | negative regulation of cell population proliferation             | GO:0008285  | 660  | 1.00E-04 | 25  |
| GO:BP | angiogenesis   | GO:0001525  | 477  | 1.00E-04 | 21  |
| TF    | Factor: CDP; motif: ATCGATNNNNNATCRAT                            | TF:M03950   | 3384 | 1.00E-04 | 70  |
| TF    | Factor: TBR2; motif: AGGTGTGAA                                   | TF:M01774   | 743  | 1.00E-04 | 27  |

|       |  |              |       |          |     |
|-------|--|--------------|-------|----------|-----|
| TF    | Factor: SATB1; motif: AKWAWTAAHGRYMNWW                         | TF:M01723    | 2569  | 1.00E-04 | 58  |
| TF    | Factor: GATA-3; motif: AGATAAGATCT; match class: 1             | TF:M12193_1  | 1274  | 1.00E-04 | 37  |
| GO:BP | positive regulation of cell killing                            | GO:0031343   | 50    | 1.10E-04 | 8   |
| GO:BP | regulation of endopeptidase activity                           | GO:0052548   | 354   | 1.10E-04 | 18  |
| MIRNA | MIRNA root   | MIRNA:000000 | 13878 | 1.10E-04 | 195 |
| TF    | Factor: E2F-3; motif: NNITTTGGCGCCAAACT                        | TF:M03962    | 9734  | 1.10E-04 | 151 |
| TF    | Factor: CTF/NF1; motif: TTGGCN                                 | TF:M02050    | 9395  | 1.10E-04 | 147 |
| TF    | Factor: COUP-TF1; motif: TGACCTY                               | TF:M03542    | 4395  | 1.10E-04 | 84  |
| TF    | Factor: NR1B1; motif: RAGGTCA                                  | TF:M08963    | 4395  | 1.10E-04 | 84  |
| TF    | Factor: RXR-ALPHA; motif: RAGGTCA                              | TF:M08968    | 4395  | 1.10E-04 | 84  |
| TF    | Factor: ESE-1; motif: SATKGCGGATGCN                            | TF:M11381    | 13896 | 1.10E-04 | 198 |
| TF    | Factor: ZNF592; motif: NSARNATGGAGKN                           | TF:M09766    | 6223  | 1.10E-04 | 108 |
| TF    | Factor: MAF; motif: NGCTGAGTCAN; match class: 1                | TF:M00983_1  | 952   | 1.10E-04 | 31  |
| GO:BP | regulation of intracellular signal transduction                | GO:1902531   | 1594  | 1.20E-04 | 42  |
| GO:BP | detection of molecule of bacterial origin                      | GO:0032490   | 11    | 1.20E-04 | 5   |
| GO:BP | positive regulation of protein phosphorylation                 | GO:0001934   | 666   | 1.20E-04 | 25  |
| GO:BP | negative regulation of defense response                        | GO:0031348   | 209   | 1.20E-04 | 14  |
| GO:BP | regulation of mast cell activation involved in immune response | GO:0033006   | 34    | 1.20E-04 | 7   |
| GO:CC | plasma membrane protein complex                                | GO:0098797   | 534   | 1.20E-04 | 21  |
| GO:MF | lipid binding  | GO:0008289   | 723   | 1.20E-04 | 25  |
| GO:MF | amide binding  | GO:0033218   | 354   | 1.20E-04 | 17  |
| TF    | Factor: ITF-2; motif: NGCAGSTGKS                               | TF:M09962    | 4254  | 1.20E-04 | 82  |
| TF    | Factor: AP-4; motif: NCAGCTGYNGNCN                             | TF:M01860    | 5298  | 1.20E-04 | 96  |
| TF    | Factor: E2F2; motif: NNITTTGGCGCCAAAAWN                        | TF:M03959    | 7017  | 1.20E-04 | 118 |
| TF    | Factor: STAT1; motif: NTTCCNGGA                                | TF:M04721    | 6860  | 1.20E-04 | 116 |
| TF    | Factor: TEF5; motif: NNWGGWATKTTT                              | TF:M08903    | 1515  | 1.20E-04 | 41  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: HLF; motif: AGSCARAAAGYRGSTGS; match class: 1        | TF:M04613_1 | 1635 | 1.20E-04 | 43  |
| TF    | Factor: T-box; motif: NASGTGTNAN                             | TF:M12021   | 3685 | 1.20E-04 | 74  |
| TF    | Factor: AP-1; motif: NNNTGAGTCAKCN                           | TF:M00517   | 4189 | 1.20E-04 | 81  |
| GO:BP | regulation of cellular component movement                    | GO:0051270  | 972  | 1.30E-04 | 31  |
| GO:BP | anatomical structure formation involved in morphogenesis     | GO:0048646  | 1026 | 1.30E-04 | 32  |
| GO:BP | regulation of response to stress                             | GO:0080134  | 1192 | 1.30E-04 | 35  |
| GO:BP | regulation of microglial cell mediated cytotoxicity          | GO:1904149  | 5    | 1.30E-04 | 4   |
| GO:BP | microglial cell mediated cytotoxicity                        | GO:0090634  | 5    | 1.30E-04 | 4   |
| GO:BP | regulation of hippocampal neuron apoptotic process           | GO:0110089  | 5    | 1.30E-04 | 4   |
| GO:BP | hippocampal neuron apoptotic process                         | GO:0110088  | 5    | 1.30E-04 | 4   |
| GO:CC | primary lysosome   | GO:0005766  | 141  | 1.30E-04 | 11  |
| GO:CC | azurophil granule  | GO:0042582  | 141  | 1.30E-04 | 11  |
| TF    | Factor: HOXB5; motif: NNYMATTANN                             | TF:M04349   | 4707 | 1.30E-04 | 88  |
| TF    | Factor: Six-2; motif: NNGTAWCRNN                             | TF:M11032   | 9253 | 1.30E-04 | 145 |
| TF    | Factor: DEC; motif: SCCCAMGTGAAGN                            | TF:M00997   | 7759 | 1.30E-04 | 127 |
| TF    | Factor: AP-2rep; motif: CAGTGGG                              | TF:M00468   | 6084 | 1.30E-04 | 106 |
| TF    | Factor: GSX1; motif: NNYMATTANN                              | TF:M04327   | 4712 | 1.30E-04 | 88  |
| TF    | Factor: SUHW1; motif: TCTCTCCAGTRTGAATTCTCTGAT               | TF:M10541   | 6086 | 1.30E-04 | 106 |
| GO:BP | T cell differentiation                                       | GO:0030217  | 245  | 1.40E-04 | 15  |
| GO:BP | regulation of programmed cell death                          | GO:0043067  | 1308 | 1.40E-04 | 37  |
| GO:CC | endosome   | GO:0005768  | 949  | 1.40E-04 | 29  |
| TF    | Factor: Msx-1; motif: NNNNANTAATTANTNN                       | TF:M01412   | 2525 | 1.40E-04 | 57  |
| TF    | Factor: AP-1; motif: NTGASTCAG                               | TF:M00199   | 4054 | 1.40E-04 | 79  |
| TF    | Factor: Six-1; motif: NCGTATCRNN                             | TF:M11028   | 1949 | 1.40E-04 | 48  |
| GO:BP | regulation of pattern recognition receptor signaling pathway | GO:0062207  | 95   | 1.50E-04 | 10  |
| TF    | Factor: Sox-10; motif: MAANRRNNNCWTTGTT                      | TF:M10065   | 5861 | 1.50E-04 | 103 |



|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| TF    | Factor: Ngn-2; motif: RACATATGTY                    | TF:M11131          | 708  | 1.50E-04 | 26  |
| TF    | Factor: IRF-8; motif: AGTTTCW                       | TF:M01665          | 3988 | 1.50E-04 | 78  |
| TF    | Factor: T-bet; motif: NNGNRGGTGTGRN; match class: 1 | TF:M10089_1        | 1126 | 1.50E-04 | 34  |
| TF    | Factor: TEF-3:E2A; motif: NCAGSTGNGWATGYN           | TF:M08438          | 4948 | 1.50E-04 | 91  |
| TF    | Factor: Sox-4; motif: NYCTTTGTYYYN                  | TF:M10069          | 6179 | 1.50E-04 | 107 |
| TF    | Factor: EAR2; motif: YGNNCTTTGNCCTK                 | TF:M01728          | 5407 | 1.60E-04 | 97  |
| TF    | Factor: AP-1; motif: NTGACTCAN                      | TF:M00925          | 2147 | 1.60E-04 | 51  |
| TF    | Factor: AP-4; motif: AWCAGCTGWT; match class: 1     | TF:M11208_1        | 3285 | 1.60E-04 | 68  |
| TF    | Factor: NR1B1:RXR-ALPHA; motif: RRGGTCANNNNRRGGTCA  | TF:M08964          | 6106 | 1.60E-04 | 106 |
| TF    | Factor: NR3C1; motif: RRGAAACATWMYGTICTRN           | TF:M02219          | 5643 | 1.60E-04 | 100 |
| TF    | Factor: Ngn-2; motif: RACATATGTY; match class: 1    | TF:M11132_1        | 664  | 1.70E-04 | 25  |
| TF    | Factor: Smad2; motif: TGTCTGNCACT; match class: 1   | TF:M09656_1        | 1022 | 1.70E-04 | 32  |
| TF    | Factor: HOXC11; motif: NGYMATWAANN                  | TF:M10816          | 4292 | 1.70E-04 | 82  |
| TF    | Factor: Msx-2; motif: NNNGACYAATTAGYNNNT            | TF:M01393          | 7307 | 1.70E-04 | 121 |
| GO:BP | granulocyte migration                               | GO:0097530         | 123  | 1.80E-04 | 11  |
| GO:MF | NAD+ nucleosidase activity                          | GO:0003953         | 28   | 1.80E-04 | 6   |
| REAC  | Diseases associated with the TLR signaling cascade  | REAC:R-HSA-5602358 | 28   | 1.80E-04 | 6   |
| REAC  | Diseases of Immune System                           | REAC:R-HSA-5260271 | 28   | 1.80E-04 | 6   |
| TF    | Factor: SREBP-1; motif: NNGTGGGGTGAN                | TF:M04632          | 4149 | 1.80E-04 | 80  |
| TF    | Factor: C/EBP; motif: NNATTGCNNAANN                 | TF:M00190          | 4665 | 1.80E-04 | 87  |
| TF    | Factor: PEA3; motif: ACAGGAAGGAAGTN                 | TF:M11429          | 4815 | 1.80E-04 | 89  |
| TF    | Factor: POU3F2; motif: NTATGCWAATKAG                | TF:M11909          | 4151 | 1.80E-04 | 80  |
| TF    | Factor: TFAP4; motif: AWCAGCTGWT; match class: 1    | TF:M04192_1        | 3506 | 1.80E-04 | 71  |
| TF    | Factor: POU3F1; motif: RNYBCATTGCATTWCAA            | TF:M03842          | 4299 | 1.80E-04 | 82  |
| GO:BP | superoxide anion generation                         | GO:0042554         | 36   | 1.90E-04 | 7   |

|       |  |                   |      |          |     |
|-------|--|-------------------|------|----------|-----|
| REAC  | Signal Transduction  | REAC:R-HSA-162582 | 2365 | 1.90E-04 | 52  |
| TF    | Factor: LRH-1; motif: TGACCTTGRNYCAAGGTCA                  | TF:M11830         | 6126 | 1.90E-04 | 106 |
| TF    | Factor: PU.1; motif: NNNNYYYACTTCCCTTTY; match class: 1    | TF:M01172_1       | 484  | 1.90E-04 | 21  |
| TF    | Factor: DLX6; motif: NWRNGYAAWYA                           | TF:M12595         | 3231 | 1.90E-04 | 67  |
| TF    | Factor: RORA; motif: CCYTGNCCTN                            | TF:M12659         | 6920 | 1.90E-04 | 116 |
| TF    | Factor: HOXC-8; motif: NNNNNGTAATTANNNT; match class: 1    | TF:M01321_1       | 3583 | 1.90E-04 | 72  |
| TF    | Factor: ESRRA; motif: CAAGGTCANNYSAAAGGTCA; match class: 1 | TF:M04458_1       | 3797 | 1.90E-04 | 75  |
| TF    | Factor: POU3F2; motif: TAATKAGNNNNTAATKA; match class: 1   | TF:M11908_1       | 975  | 1.90E-04 | 31  |
| TF    | Factor: AML1; motif: TGTGGTK                               | TF:M01658         | 3726 | 1.90E-04 | 74  |
| GO:BP | positive regulation of cell migration                      | GO:0030335        | 496  | 2.00E-04 | 21  |
| GO:BP | negative regulation of myeloid leukocyte mediated immunity | GO:0002887        | 12   | 2.00E-04 | 5   |
| GO:BP | neutrophil degranulation                                   | GO:0043312        | 12   | 2.00E-04 | 5   |
| KEGG  | Toxoplasmosis  | KEGG:05145        | 108  | 2.00E-04 | 9   |
| TF    | Factor: C-JUN:FRA-1; motif: NNATGACTCATNN                  | TF:M08938         | 3094 | 2.00E-04 | 65  |
| TF    | Factor: C/EBPdelta; motif: NTTGCNCMAYN                     | TF:M09882         | 1725 | 2.00E-04 | 44  |
| GO:BP | regulation of phosphorylation                              | GO:0042325        | 1159 | 2.10E-04 | 34  |
| REAC  | Signaling by Interleukins                                  | REAC:R-HSA-449147 | 411  | 2.10E-04 | 18  |
| TF    | Factor: DLX2; motif: AMSMCTGACKG                           | TF:M08873         | 6450 | 2.10E-04 | 110 |
| TF    | Factor: NeuroD-2; motif: RMCATATGKY; match class: 1        | TF:M01287_1       | 1666 | 2.10E-04 | 43  |
| GO:BP | homeostatic process  | GO:0042592        | 1631 | 2.20E-04 | 42  |
| REAC  | GPCR downstream signalling                                 | REAC:R-HSA-388396 | 549  | 2.20E-04 | 21  |
| TF    | Factor: VDR; motif: RRGGTCANNRGRKTCA                       | TF:M09671         | 7096 | 2.20E-04 | 118 |
| TF    | Factor: RARA; motif: AGGTCANNYAAAGGTCA                     | TF:M08019         | 4689 | 2.20E-04 | 87  |
| TF    | Factor: ZNF684; motif: MAAGGGTGGACTGT; match class: 1      | TF:M10550_1       | 8324 | 2.20E-04 | 133 |
| REAC  | Phosphorylation of CD3 and TCR zeta chains                 | REAC:R-HSA-202427 | 16   | 2.30E-04 | 5   |

|       |  |                   |       |          |     |
|-------|--|-------------------|-------|----------|-----|
| TF    | Factor: SREBP-1; motif: RTCACCCAY                                | TF:M07405         | 5912  | 2.30E-04 | 103 |
| TF    | Factor: E2A; motif: CACCTGNY                                     | TF:M00973         | 4692  | 2.30E-04 | 87  |
| TF    | Factor: Sohlh2; motif: NNCACGTGNN                                | TF:M11075         | 10531 | 2.30E-04 | 159 |
| GO:BP | regulation of myeloid cell differentiation                       | GO:0045637        | 187   | 2.40E-04 | 13  |
| GO:BP | negative regulation of endopeptidase activity                    | GO:0010951        | 187   | 2.40E-04 | 13  |
| GO:BP | antigen processing and presentation of exogenous peptide antigen | GO:0002478        | 55    | 2.40E-04 | 8   |
| GO:BP | B cell receptor signaling pathway                                | GO:0050853        | 55    | 2.40E-04 | 8   |
| REAC  | Toll-like Receptor Cascades                                      | REAC:R-HSA-168898 | 148   | 2.40E-04 | 11  |
| GO:BP | killing of cells of another organism                             | GO:0031640        | 23    | 2.50E-04 | 6   |
| TF    | Factor: VDR; motif: NRRGTTCA                                     | TF:M08979         | 3966  | 2.50E-04 | 77  |
| TF    | Factor: PMX2B; motif: NNNAATTAATTAANNNG                          | TF:M01356         | 2639  | 2.50E-04 | 58  |
| GO:BP | positive regulation of cellular protein metabolic process        | GO:0032270        | 1284  | 2.60E-04 | 36  |
| TF    | Factor: NFATc1; motif: NATGGAAANWNANTTYCMN                       | TF:M04051         | 4704  | 2.60E-04 | 87  |
| TF    | Factor: POU2F1; motif: NWTATGCWAATN                              | TF:M04070         | 2180  | 2.60E-04 | 51  |
| TF    | Factor: IRF-7; motif: AAGWGAA; match class: 1                    | TF:M01884_1       | 3752  | 2.60E-04 | 74  |
| TF    | Factor: Ets; motif: ANNCACTTCCTG                                 | TF:M00771         | 3397  | 2.60E-04 | 69  |
| GO:BP | lysosome localization  | GO:0032418        | 77    | 2.70E-04 | 9   |
| GO:BP | vacuolar localization  | GO:1990849        | 77    | 2.70E-04 | 9   |
| TF    | Factor: TFIIIB; motif: YTNTMTGMSN                                | TF:M08904         | 5698  | 2.70E-04 | 100 |
| TF    | Factor: GR; motif: RGWACATWATGWCY                                | TF:M11847         | 4559  | 2.70E-04 | 85  |
| TF    | Factor: BRN1; motif: NANNTATGCATAATNNA                           | TF:M01324         | 4046  | 2.70E-04 | 78  |
| TF    | Factor: HoxA5; motif: RTCATTAN                                   | TF:M10704         | 4413  | 2.70E-04 | 83  |
| TF    | Factor: Sox-10; motif: AACAATRGNCYATTGTT; match class: 1         | TF:M11632_1       | 3758  | 2.70E-04 | 74  |
| GO:BP | T cell migration   | GO:0072678        | 56    | 2.80E-04 | 8   |
| GO:BP | positive regulation of phosphorylation                           | GO:0042327        | 746   | 2.80E-04 | 26  |
| TF    | Factor: MafG; motif: CMATGACTCAGCAGA; match class: 1             | TF:M07048_1       | 1269  | 2.80E-04 | 36  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: HOXB2; motif: NNTMATTANN                         | TF:M04347   | 2782 | 2.80E-04 | 60  |
| TF    | Factor: Fra-2; motif: TGASTCANCN                         | TF:M03870   | 3056 | 2.80E-04 | 64  |
| TF    | Factor: Sox-10; motif: AACAATGGNCCATTGTT; match class: 1 | TF:M11633_1 | 2648 | 2.80E-04 | 58  |
| TF    | Factor: HoxA5; motif: RTCATTAN                           | TF:M10707   | 2383 | 2.90E-04 | 54  |
| TF    | Factor: NR1B1; motif: NRGGTCANRRGGTCAN                   | TF:M11792   | 4126 | 2.90E-04 | 79  |
| TF    | Factor: Ngn-2; motif: RACATATGTY                         | TF:M11134   | 1215 | 3.00E-04 | 35  |
| TF    | Factor: c-Fos; motif: ACTCACCA                           | TF:M04802   | 6417 | 3.00E-04 | 109 |
| TF    | Factor: LKLF; motif: GGGTGGKSN                           | TF:M07261   | 8865 | 3.00E-04 | 139 |
| TF    | Factor: Foxm1; motif: NTGTTTTRT                          | TF:M07255   | 4796 | 3.00E-04 | 88  |
| TF    | Factor: TBX2; motif: TCACACCWN                           | TF:M08831   | 1049 | 3.00E-04 | 32  |
| GO:BP | negative regulation of cell adhesion                     | GO:0007162  | 261  | 3.10E-04 | 15  |
| GO:BP | regulation of peptidase activity                         | GO:0052547  | 379  | 3.10E-04 | 18  |
| TF    | Factor: Oct-4; motif: YWTTSTNATGCAAAT                    | TF:M01125   | 1629 | 3.10E-04 | 42  |
| GO:BP | response to interferon-gamma                             | GO:0034341  | 130  | 3.20E-04 | 11  |
| GO:MF | complement binding                                       | GO:0001848  | 17   | 3.20E-04 | 5   |
| TF    | Factor: Erm:E2A; motif: CASGTGNNNCGGAAGNN                | TF:M08571   | 9890 | 3.20E-04 | 151 |
| TF    | Factor: CART1; motif: NGNNYAATTARTNNNN; match class: 1   | TF:M01362_1 | 2860 | 3.20E-04 | 61  |
| GO:MF | identical protein binding                                | GO:0042802  | 1948 | 3.30E-04 | 45  |
| TF    | Factor: POU2F1:PEA3; motif: ACCGGATATGCAN                | TF:M08402   | 6988 | 3.30E-04 | 116 |
| GO:BP | regulation of protein phosphorylation                    | GO:0001932  | 1017 | 3.40E-04 | 31  |
| GO:BP | myeloid leukocyte differentiation                        | GO:0002573  | 193  | 3.40E-04 | 13  |
| TF    | Factor: Zic1; motif: KGGGTGGTC                           | TF:M00448   | 9729 | 3.40E-04 | 149 |
| GO:BP | interleukin-1 production                                 | GO:0032612  | 104  | 3.50E-04 | 10  |
| GO:BP | regulation of interleukin-1 production                   | GO:0032652  | 104  | 3.50E-04 | 10  |
| KEGG  | Antigen processing and presentation                      | KEGG:04612  | 62   | 3.50E-04 | 7   |

|       |   |                   |      |          |     |
|-------|---|-------------------|------|----------|-----|
| TF    | Factor: C/EBPdelta; motif: NRTTGCGYAAYN                     | TF:M11321         | 4812 | 3.50E-04 | 88  |
| TF    | Factor: JUND:C-FOS; motif: NNATGAGTCATNN                    | TF:M08933         | 3998 | 3.50E-04 | 77  |
| TF    | Factor: SMAD; motif: TNGNCAGACWN; match class: 1            | TF:M00974_1       | 594  | 3.50E-04 | 23  |
| TF    | Factor: NF-E2; motif: TGCTGAGTCAY                           | TF:M00037         | 5577 | 3.60E-04 | 98  |
| TF    | Factor: Sox-4; motif: NNNNNAATTGTTNNNNN                     | TF:M02909         | 3641 | 3.60E-04 | 72  |
| TF    | Factor: VDR; motif: NRRGGTCANNGRGKCA                        | TF:M10106         | 6125 | 3.60E-04 | 105 |
| GO:BP | negative regulation of peptidase activity                   | GO:0010466        | 194  | 3.70E-04 | 13  |
| GO:BP | response to oxygen-containing compound                      | GO:1901700        | 1480 | 3.70E-04 | 39  |
| GO:MF | MHC class II receptor activity                              | GO:0032395        | 8    | 3.70E-04 | 4   |
| TF    | Factor: Oct3; motif: NNWTATGYWAATKANN                       | TF:M11935         | 2402 | 3.70E-04 | 54  |
| TF    | Factor: Ngn-2; motif: RMCATATGY                             | TF:M11133         | 1170 | 3.70E-04 | 34  |
| GO:BP | regulation of myeloid leukocyte differentiation             | GO:0002761        | 105  | 3.80E-04 | 10  |
| REAC  | Peptide ligand-binding receptors                            | REAC:R-HSA-375276 | 155  | 3.80E-04 | 11  |
| TF    | Factor: Sox-30; motif: NRACAATG                             | TF:M11640         | 794  | 3.80E-04 | 27  |
| GO:BP | positive regulation of cell motility                        | GO:2000147        | 516  | 3.90E-04 | 21  |
| TF    | Factor: TBX15; motif: NAGGTGTGAN                            | TF:M12039         | 2145 | 3.90E-04 | 50  |
| TF    | Factor: Smad4; motif: NWTCTGNCACT                           | TF:M10061         | 3223 | 3.90E-04 | 66  |
| GO:BP | regulation of gene expression                               | GO:0010468        | 4415 | 4.00E-04 | 82  |
| TF    | Factor: Oct-1; motif: MKVATTTGCATATT                        | TF:M00161         | 2408 | 4.00E-04 | 54  |
| GO:BP | positive regulation of protein metabolic process            | GO:0051247        | 1367 | 4.10E-04 | 37  |
| GO:BP | response to fungus  | GO:0009620        | 40   | 4.10E-04 | 7   |
| TF    | Factor: JUN; motif: NRTGACTCA                               | TF:M12589         | 3227 | 4.10E-04 | 66  |
| TF    | Factor: Oct3; motif: NYWTTSWTATGCAAAT; match class: 1       | TF:M09646_1       | 1119 | 4.10E-04 | 33  |
| TF    | Factor: GKLf; motif: CCTCCYN; match class: 1                | TF:M01835_1       | 9081 | 4.20E-04 | 141 |
| GO:BP | positive regulation of toll-like receptor signaling pathway | GO:0034123        | 25   | 4.30E-04 | 6   |
| GO:BP | alpha-beta T cell activation                                | GO:0046631        | 134  | 4.30E-04 | 11  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: POU2F1; motif: ANKNRWATGSAAWYAW            | TF:M10033   | 3948 | 4.40E-04 | 76  |
| TF    | Factor: NF-1C; motif: TTGGCANN                     | TF:M07300   | 5371 | 4.40E-04 | 95  |
| TF    | Factor: MYB; motif: NNCAACTGNN                     | TF:M09813   | 4688 | 4.50E-04 | 86  |
| TF    | Factor: TCF-3; motif: CTTTGA; match class: 1       | TF:M03858_1 | 4541 | 4.60E-04 | 84  |
| TF    | Factor: TCF-7; motif: TCAAAG; match class: 1       | TF:M00805_1 | 4541 | 4.60E-04 | 84  |
| TF    | Factor: Fra-1; motif: NNNTGAGTCAYN                 | TF:M09922   | 3807 | 4.60E-04 | 74  |
| TF    | Factor: POU2F1:HOXB13; motif: NGMATATACCAATAAA     | TF:M08405   | 3168 | 4.60E-04 | 65  |
| TF    | Factor: Lhx8; motif: TGATTG                        | TF:M07476   | 7600 | 4.70E-04 | 123 |
| TF    | Factor: HOXD1; motif: NATYCAKCAN                   | TF:M12625   | 4694 | 4.70E-04 | 86  |
| TF    | Factor: MIBP1; motif: WNWCCCCAGCTR                 | TF:M03878   | 2488 | 4.80E-04 | 55  |
| TF    | Factor: AP-4; motif: YCAGCTGNKN                    | TF:M10097   | 5226 | 4.80E-04 | 93  |
| GO:BP | cellular component organization                    | GO:0016043  | 6205 | 4.90E-04 | 105 |
| TF    | Factor: SREBP-1; motif: KATCACCCAC                 | TF:M00221   | 6557 | 4.90E-04 | 110 |
| TF    | Factor: E2F2; motif: AAAAATGGCGCCAAAAG             | TF:M03958   | 9442 | 4.90E-04 | 145 |
| TF    | Factor: ATF3; motif: GRTGACKCA                     | TF:M12582   | 6319 | 4.90E-04 | 107 |
| GO:BP | positive regulation of response to biotic stimulus | GO:0002833  | 167  | 5.10E-04 | 12  |
| GO:BP | regulation of chemotaxis                           | GO:0050920  | 200  | 5.20E-04 | 13  |
| TF    | Factor: MAFA; motif: TCAGCAN                       | TF:M01709   | 5314 | 5.30E-04 | 94  |
| TF    | Factor: HNF3alpha; motif: TRTTTGYTYWN              | TF:M00724   | 2167 | 5.30E-04 | 50  |
| TF    | Factor: AP4; motif: NMNCAGCTGGN                    | TF:M12580   | 5085 | 5.30E-04 | 91  |
| TF    | Factor: Sox-10; motif: NACAATRNNNNYATTGTN          | TF:M11635   | 5086 | 5.40E-04 | 91  |
| GO:BP | regulation of lymphocyte differentiation           | GO:0045619  | 168  | 5.50E-04 | 12  |
| GO:BP | positive regulation of chemokine production        | GO:0032722  | 61   | 5.50E-04 | 8   |
| TF    | Factor: TIF2; motif: ANANAGAWAAGN                  | TF:M09849   | 2975 | 5.50E-04 | 62  |
| TF    | Factor: STAT5A; motif: NAWTTCYNGGAANYN             | TF:M00457   | 3468 | 5.70E-04 | 69  |
| TF    | Factor: ER-alpha; motif: AGGTCASMNTGACCY           | TF:M09909   | 5943 | 5.70E-04 | 102 |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| GO:BP | chemokine production                                      | GO:0032602  | 84   | 5.80E-04 | 9   |
| GO:BP | regulation of chemokine production                        | GO:0032642  | 84   | 5.80E-04 | 9   |
| GO:BP | positive regulation of cellular component movement        | GO:0051272  | 529  | 5.80E-04 | 21  |
| TF    | Factor: NR1B2; motif: RAGGTCRTGACCTY                      | TF:M11800   | 3188 | 5.80E-04 | 65  |
| TF    | Factor: Sox-17; motif: NCCATTGTNNN                        | TF:M10066   | 2239 | 5.80E-04 | 51  |
| GO:BP | negative regulation of T cell activation                  | GO:0050868  | 110  | 6.00E-04 | 10  |
| GO:BP | positive regulation of locomotion                         | GO:0040017  | 530  | 6.00E-04 | 21  |
| TF    | Factor: Sox-8; motif: NNAACAATRN                          | TF:M11628   | 1082 | 6.00E-04 | 32  |
| TF    | Factor: Hoxa9; motif: NTTAAWTAMA                          | TF:M07457   | 3906 | 6.00E-04 | 75  |
| TF    | Factor: GR; motif: AGAACAN; match class: 1                | TF:M07355_1 | 813  | 6.10E-04 | 27  |
| TF    | Factor: VDR:RXR-ALPHA; motif: NRRGTCANNNGGTTCCNN          | TF:M08980   | 9219 | 6.10E-04 | 142 |
| TF    | Factor: C/EBPepsilon; motif: HAANMTTKCNWMAC               | TF:M01868   | 2507 | 6.10E-04 | 55  |
| GO:BP | negative regulation of cell-cell adhesion                 | GO:0022408  | 170  | 6.20E-04 | 12  |
| GO:BP | antigen processing and presentation of exogenous antigen  | GO:0019884  | 62   | 6.30E-04 | 8   |
| TF    | Factor: MRF4; motif: CASCTGC; match class: 1              | TF:M03831_1 | 2377 | 6.40E-04 | 53  |
| TF    | Factor: HTF4; motif: CASCTGB; match class: 1              | TF:M02018_1 | 2377 | 6.40E-04 | 53  |
| TF    | Factor: JunB; motif: TGACTION                             | TF:M03551   | 3551 | 6.40E-04 | 70  |
| TF    | Factor: AP1; motif: TGACTION                              | TF:M02280   | 3553 | 6.50E-04 | 70  |
| KEGG  | Fc gamma R-mediated phagocytosis                          | KEGG:04666  | 95   | 6.60E-04 | 8   |
| GO:BP | axon ensheathment   | GO:0008366  | 140  | 6.70E-04 | 11  |
| GO:BP | ensheathment of neurons                                   | GO:0007272  | 140  | 6.70E-04 | 11  |
| GO:CC | ficolin-1-rich granule membrane                           | GO:0101003  | 55   | 6.80E-04 | 7   |
| TF    | Factor: Pitx3; motif: GATTANA                             | TF:M07057   | 1864 | 6.80E-04 | 45  |
| TF    | Factor: POU3F2; motif: TAATKAGNNNNTAATKA                  | TF:M11908   | 2993 | 6.80E-04 | 62  |
| GO:BP | regulation of inflammatory response to antigenic stimulus | GO:0002861  | 43   | 6.90E-04 | 7   |
| TF    | Factor: Dlx-5; motif: NNRGYAATTRNYKNNN; match class: 1    | TF:M01388_1 | 4735 | 6.90E-04 | 86  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: Tst-1; motif: NNKGAATTAVAVTDN            | TF:M00133   | 4735 | 6.90E-04 | 86  |
| GO:BP | positive regulation of secretion                 | GO:0051047  | 278  | 7.00E-04 | 15  |
| TF    | Factor: Erm; motif: RSAGGAAGGAAGTN               | TF:M11423   | 4288 | 7.00E-04 | 80  |
| TF    | Factor: AP-1; motif: NTGASTCAG; match class: 1   | TF:M00199_1 | 3560 | 7.10E-04 | 70  |
| GO:BP | NIK/NF-kappaB signaling                          | GO:0038061  | 141  | 7.20E-04 | 11  |
| GO:BP | regulation of response to biotic stimulus        | GO:0002831  | 318  | 7.20E-04 | 16  |
| TF    | Factor: MTF-1; motif: GTGTGCANMACTTTGCGCAC       | TF:M01242   | 3492 | 7.30E-04 | 69  |
| TF    | Factor: AP-4:Dlx-3; motif: NCAGCTGNNNNNGTAATKR   | TF:M08671   | 3638 | 7.50E-04 | 71  |
| TF    | Factor: ZNFPT1; motif: YCNNCNCWGCCNY             | TF:M12721   | 8164 | 7.80E-04 | 129 |
| TF    | Factor: ZNF586; motif: CAGGCCYRGAGG              | TF:M10491   | 1230 | 7.80E-04 | 177 |
| TF    | Factor: AML3; motif: NWAACCACRAAAACCACRAN        | TF:M11999   | 5905 | 7.90E-04 | 101 |
| GO:BP | positive regulation of NIK/NF-kappaB signaling   | GO:1901224  | 64   | 8.10E-04 | 8   |
| TF    | Factor: HOXA4; motif: RTMATTAN                   | TF:M10716   | 3290 | 8.30E-04 | 66  |
| TF    | Factor: HDAC1; motif: KGCARGGTC                  | TF:M07041   | 1116 | 8.30E-04 | 164 |
| TF    | Factor: Ngn-2; motif: RACATATGTY; match class: 1 | TF:M11131_1 | 624  | 8.40E-04 | 23  |
| TF    | Factor: gsh-1; motif: NTMATNRN; match class: 1   | TF:M10750_1 | 3221 | 8.40E-04 | 65  |
| GO:CC | plasma membrane raft                             | GO:0044853  | 108  | 8.60E-04 | 9   |
| TF    | Factor: Lhx2; motif: WATTAN                      | TF:M07047   | 9102 | 8.70E-04 | 140 |
| GO:BP | regulation of superoxide metabolic process       | GO:0090322  | 28   | 8.80E-04 | 6   |
| TF    | Factor: Fra-1; motif: NRTGACTCATN                | TF:M09615   | 3439 | 8.90E-04 | 68  |
| TF    | Factor: Tbx3; motif: AGGTGTNR                    | TF:M08786   | 3157 | 9.00E-04 | 64  |
| GO:BP | regulation of leukocyte mediated cytotoxicity    | GO:0001910  | 65   | 9.10E-04 | 8   |
| GO:BP | second-messenger-mediated signaling              | GO:0019932  | 284  | 9.10E-04 | 15  |
| TF    | Factor: PEA3; motif: NTCGTAAATGCA                | TF:M11431   | 9024 | 9.10E-04 | 139 |
| TF    | Factor: LCOR; motif: CMAAGKNCANN                 | TF:M12628   | 2949 | 9.10E-04 | 61  |
| TF    | Factor: FOSL1; motif: NNATGACTCATNN              | TF:M12518   | 3875 | 9.20E-04 | 74  |

|       |   |                   |       |          |     |
|-------|---|-------------------|-------|----------|-----|
| TF    | Factor: SP2; motif: NNRCCAATSRGNRNSNGSN             | TF:M12668         | 10569 | 9.20E-04 | 157 |
| GO:BP | blood vessel development                            | GO:0001568        | 641   | 9.30E-04 | 23  |
| TF    | Factor: POU3F1; motif: NTAATKWATGCNN                | TF:M11929         | 5613  | 9.40E-04 | 97  |
| TF    | Factor: NFATc3; motif: NTTTCCRYGGAAN                | TF:M11988         | 6242  | 9.40E-04 | 105 |
| GO:BP | positive regulation of T cell proliferation         | GO:0042102        | 89    | 9.50E-04 | 9   |
| GO:BP | regulation of regulated secretory pathway           | GO:1903305        | 145   | 9.50E-04 | 11  |
| TF    | Factor: Oct-2; motif: NTATGCWAATN; match class: 1   | TF:M11896_1       | 993   | 9.50E-04 | 30  |
| TF    | Factor: Fra-2; motif: RTGACTCANN                    | TF:M09616         | 3952  | 9.60E-04 | 75  |
| TF    | Factor: SREBP-1; motif: NSNNTCACNCCANN              | TF:M01173         | 4099  | 9.60E-04 | 77  |
| TF    | Factor: six4; motif: NCGTATCRNN                     | TF:M11025         | 5538  | 9.60E-04 | 96  |
| TF    | Factor: Spi-B; motif: NAAWNGGAAGTN                  | TF:M11377         | 399   | 9.60E-04 | 18  |
| GO:BP | antigen processing and presentation                 | GO:0019882        | 116   | 9.80E-04 | 10  |
| TF    | Factor: Tal-1; motif: CTCCTMTCTSY                   | TF:M01591         | 1889  | 9.80E-04 | 45  |
| TF    | Factor: Sox-9; motif: AANGNNNCWTTGTYY               | TF:M10070         | 2212  | 9.80E-04 | 50  |
| GO:BP | movement of cell or subcellular component           | GO:0006928        | 1918  | 1.00E-03 | 45  |
| GO:MF | pattern recognition receptor activity               | GO:0038187        | 21    | 1.00E-03 | 5   |
| GO:MF | amyloid-beta binding                                | GO:0001540        | 81    | 1.00E-03 | 8   |
| REAC  | Initial triggering of complement                    | REAC:R-HSA-166663 | 21    | 1.00E-03 | 5   |
| TF    | Factor: MTF-1; motif: NTTTTGCACACGGCNYN             | TF:M12279         | 5776  | 1.00E-03 | 99  |
| TF    | Factor: Sox-10; motif: CWTTGTN                      | TF:M01131         | 7621  | 1.00E-03 | 122 |
| TF    | Factor: Smad1; motif: NGGCAGACN                     | TF:M03845         | 3958  | 1.00E-03 | 75  |
| TF    | Factor: POU3F2; motif: ATGMATWWATTCAT               | TF:M00463         | 2550  | 1.00E-03 | 55  |
| GO:BP | positive regulation of protein modification process | GO:0031401        | 906   | 1.10E-03 | 28  |
| GO:BP | anatomical structure morphogenesis                  | GO:0009653        | 2447  | 1.10E-03 | 53  |
| GO:BP | toll-like receptor 2 signaling pathway              | GO:0034134        | 16    | 1.10E-03 | 5   |
| GO:BP | detection of other organism                         | GO:0098543        | 16    | 1.10E-03 | 5   |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:CC | ficolin-1-rich granule                                       | GO:0101002  | 175   | 1.10E-03 | 11  |
| GO:CC | receptor complex   | GO:0043235  | 376   | 1.10E-03 | 16  |
| TF    | Factor: NFE2L1; motif: NNNATGACTCAGCANW; match class: 1      | TF:M12499_1 | 2824  | 1.10E-03 | 59  |
| TF    | Factor: Smad4; motif: TGTCTGN                                | TF:M01889   | 4482  | 1.10E-03 | 82  |
| TF    | Factor: POU1F1; motif: AWTATGCWAATKAG                        | TF:M04069   | 2623  | 1.10E-03 | 56  |
| GO:BP | positive regulation of vasculature development               | GO:1904018  | 148   | 1.20E-03 | 11  |
| GO:BP | positive regulation of angiogenesis                          | GO:0045766  | 148   | 1.20E-03 | 11  |
| GO:BP | positive regulation of cellular metabolic process            | GO:0031325  | 2936  | 1.20E-03 | 60  |
| GO:MF | peptidase regulator activity                                 | GO:0061134  | 174   | 1.20E-03 | 11  |
| TF    | Factor: OC-2; motif: TCAATA                                  | TF:M02112   | 6190  | 1.20E-03 | 104 |
| TF    | Factor: CRX; motif: YTAATC; match class: 1                   | TF:M01712_1 | 4120  | 1.20E-03 | 77  |
| TF    | Factor: ER-alpha; motif: AGGTCACNGTGACCT                     | TF:M01801   | 2834  | 1.20E-03 | 59  |
| TF    | Factor: GR; motif: RGWACATWAYGTWCY                           | TF:M11846   | 5101  | 1.20E-03 | 90  |
| TF    | Factor: Fra-2; motif: NNRTGAGTCAYN                           | TF:M09923   | 3611  | 1.20E-03 | 70  |
| TF    | Factor: Oct3; motif: WTATGCGCATAW                            | TF:M11934   | 8394  | 1.20E-03 | 131 |
| TF    | Factor: TEF-3/C/EBPbeta; motif: RTTGCGYAAAYNNNNNGGAATGY      | TF:M08626   | 5958  | 1.20E-03 | 101 |
| TF    | Factor: STAT3; motif: NTTYKGGGAN                             | TF:M07229   | 3185  | 1.20E-03 | 64  |
| TF    | Factor: PPARALPHA:RXR-ALPHA; motif: AWNTRGGTNAAGGTCAN        | TF:M08960   | 10094 | 1.20E-03 | 151 |
| TF    | Factor: AP-4; motif: ANCATATGNT; match class: 1              | TF:M11211_1 | 1841  | 1.20E-03 | 44  |
| TF    | Factor: Sox-9; motif: NAACAATRN                              | TF:M04004   | 897   | 1.20E-03 | 28  |
| GO:BP | defense response to Gram-negative bacterium                  | GO:0050829  | 47    | 1.30E-03 | 7   |
| GO:BP | negative regulation of leukocyte cell-cell adhesion          | GO:1903038  | 120   | 1.30E-03 | 10  |
| TF    | Factor: CEBPD; motif: NNTTGCACAAYNN                          | TF:M12567   | 1780  | 1.30E-03 | 43  |
| TF    | Factor: BCL-6; motif: NYGCTTTCKAGGAANN                       | TF:M12341   | 5187  | 1.30E-03 | 91  |
| TF    | Factor: CDP:HOXA13; motif: ATCGATYAYSYCRATAA; match class: 1 | TF:M08201_1 | 2433  | 1.30E-03 | 53  |
| TF    | Factor: Pax-2; motif: CAYSCCTSAGT                            | TF:M03839   | 4355  | 1.30E-03 | 80  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| TF    | Factor: Dlx-5; motif: NNRGYAATRNYKNNN                                  | TF:M01388   | 6366  | 1.30E-03 | 106 |
| GO:BP | defense response to fungus   | GO:0050832  | 30    | 1.40E-03 | 6   |
| TF    | Factor: TCF-3; motif: NCTTTGWTNTKYW                                    | TF:M01594   | 3987  | 1.40E-03 | 75  |
| TF    | Factor: VDR; motif: RRTGNMCTNNTGAMCCNYNT; match class: 1               | TF:M00966_1 | 2778  | 1.40E-03 | 58  |
| TF    | Factor: TR4; motif: ACCCCGS; match class: 1                            | TF:M04934_1 | 13946 | 1.40E-03 | 194 |
| TF    | Factor: POU2F1; motif: HOXB13; motif: NGMATATACCAATAAA; match class: 1 | TF:M08405_1 | 744   | 1.40E-03 | 25  |
| TF    | Factor: Oct-2; motif: NNNATTATGCAN                                     | TF:M11897   | 3920  | 1.40E-03 | 74  |
| GO:BP | positive regulation of myeloid leukocyte differentiation               | GO:0002763  | 48    | 1.50E-03 | 7   |
| TF    | Factor: HEY1; motif: NYYYATCTNN  | TF:M12614   | 4742  | 1.50E-03 | 85  |
| TF    | Factor: NFATc1; motif: TTTCCATGGAAAN                                   | TF:M04053   | 7187  | 1.50E-03 | 116 |
| TF    | Factor: TGIF; motif: TGACAGS   | TF:M10101   | 4444  | 1.50E-03 | 81  |
| TF    | Factor: LF-A1; motif: GGGSTCWR   | TF:M00646   | 11261 | 1.50E-03 | 164 |
| TF    | Factor: Six-2; motif: NCGTATCRNN                                       | TF:M11031   | 7846  | 1.50E-03 | 124 |
| GO:CC | lytic vacuole membrane   | GO:0098852  | 387   | 1.60E-03 | 16  |
| GO:CC | lysosomal membrane   | GO:0005765  | 387   | 1.60E-03 | 16  |
| TF    | Factor: MITF; motif: CATGTGM   | TF:M02099   | 2582  | 1.60E-03 | 55  |
| TF    | Factor: Fli-1; motif: NNRGGMAGGAAGRRRGR; match class: 1                | TF:M09920_1 | 2997  | 1.60E-03 | 61  |
| TF    | Factor: ER-alpha; motif: TGACCYN                                       | TF:M03547   | 4003  | 1.60E-03 | 75  |
| TF    | Factor: SPIC; motif: NAAAAGMGGAAAGTA                                   | TF:M03996   | 550   | 1.60E-03 | 21  |
| TF    | Factor: SOX13; motif: NNACAATGGNN                                      | TF:M09787   | 550   | 1.60E-03 | 21  |
| TF    | Factor: Pax-3; motif: TCGTACRCITTHM                                    | TF:M00360   | 10921 | 1.60E-03 | 160 |
| GO:BP | regulation of NIK/NF-kappaB signaling                                  | GO:1901222  | 95    | 1.70E-03 | 9   |
| GO:BP | negative regulation of inflammatory response to antigenic stimulus     | GO:0002862  | 31    | 1.70E-03 | 6   |
| TF    | Factor: Gscl; motif: NTAATCCN  | TF:M10924   | 5762  | 1.70E-03 | 98  |
| TF    | Factor: Msx-2; motif: TAATTAN  | TF:M07425   | 3073  | 1.70E-03 | 62  |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| TF    | Factor: AP-2gamma; motif: NNNNSCCYCAGGSCN           | TF:M07137          | 1078 | 1.70E-03 | 31  |
| TF    | Factor: oct-2; motif: NNWNATGCAAATNN                | TF:M03836          | 3147 | 1.70E-03 | 63  |
| GO:BP | response to bacterial lipoprotein                   | GO:0032493         | 8    | 1.80E-03 | 4   |
| GO:BP | positive regulation of lymphocyte proliferation     | GO:0050671         | 124  | 1.80E-03 | 10  |
| TF    | Factor: C-JUN:FRA-2; motif: NNRTGAGTCAYN            | TF:M08940          | 3007 | 1.80E-03 | 61  |
| TF    | Factor: DEC1; motif: NCNCACRTGNCS                   | TF:M08870          | 6965 | 1.80E-03 | 113 |
| TF    | Factor: ZNF394; motif: NRARWRGAANNAMWGNAAK          | TF:M10147          | 4537 | 1.80E-03 | 82  |
| TF    | Factor: HSF1; motif: GAANNTTCTRGAN; match class: 1  | TF:M02017_1        | 462  | 1.80E-03 | 19  |
| REAC  | Interleukin-10 signaling                            | REAC:R-HSA-6783783 | 41   | 1.90E-03 | 6   |
| TF    | Factor: Ngn-2; motif: RACATATGTY; match class: 1    | TF:M11134_1        | 970  | 1.90E-03 | 29  |
| TF    | Factor: CP2; motif: NNNCCAGNCNN                     | TF:M07602          | 9815 | 1.90E-03 | 147 |
| TF    | Factor: ipf1; motif: RTCATTAN                       | TF:M10745          | 2599 | 1.90E-03 | 55  |
| TF    | Factor: HB9; motif: NTCRTTAN                        | TF:M10569          | 2599 | 1.90E-03 | 55  |
| GO:BP | macrophage migration                                | GO:1905517         | 50   | 2.00E-03 | 7   |
| GO:BP | vasculature development                             | GO:0001944         | 671  | 2.00E-03 | 23  |
| GO:BP | cellular response to mechanical stimulus            | GO:0071260         | 72   | 2.00E-03 | 8   |
| GO:BP | regulation of apoptotic process                     | GO:0042981         | 1281 | 2.00E-03 | 34  |
| GO:BP | dendritic cell migration                            | GO:0036336         | 32   | 2.00E-03 | 6   |
| GO:MF | lipopolysaccharide binding                          | GO:0001530         | 24   | 2.00E-03 | 5   |
| TF    | Factor: HNF-4alpha; motif: AGTCCAAR                 | TF:M04903          | 5939 | 2.00E-03 | 100 |
| TF    | Factor: LBX2; motif: CTNRANSTAATTA                  | TF:M04383          | 6738 | 2.00E-03 | 110 |
| TF    | Factor: ELF3; motif: NNCCACTTCTGNN; match class: 1  | TF:M12544_1        | 334  | 2.00E-03 | 16  |
| TF    | Factor: GR; motif: RGNACANMNTGTNCY                  | TF:M09941          | 4931 | 2.00E-03 | 87  |
| TF    | Factor: TWIST; motif: CACCTGG                       | TF:M03582          | 7309 | 2.00E-03 | 117 |
| TF    | Factor: HOXB4; motif: NTMATTAN                      | TF:M10720          | 1500 | 2.00E-03 | 38  |
| TF    | Factor: c-Ets-2; motif: NNCTTCCTNNN; match class: 1 | TF:M07379_1        | 294  | 2.00E-03 | 15  |

|       |  |             |           |          |     |
|-------|--|-------------|-----------|----------|-----|
| GO:BP | positive regulation of mononuclear cell proliferation                | GO:0032946  | 126       | 2.10E-03 | 10  |
| GO:BP | negative regulation of cell death                                    | GO:0060548  | 884       | 2.10E-03 | 27  |
| GO:CC | luminal side of endoplasmic reticulum membrane                       | GO:0098553  | 25        | 2.10E-03 | 5   |
| GO:CC | integral component of luminal side of endoplasmic reticulum membrane | GO:0071556  | 25        | 2.10E-03 | 5   |
| TF    | Factor: nerf; motif: YRNCAGGAAGYRGSTBDS; match class: 1              | TF:M00531_1 | 1624      | 2.10E-03 | 40  |
| TF    | Factor: JUNB:C-FOS; motif: NATGAGTCATNN                              | TF:M08925   | 2882      | 2.10E-03 | 59  |
| TF    | Factor: c-Jun; motif: NRTGAGTCAYN                                    | TF:M09965   | 3738      | 2.10E-03 | 71  |
| TF    | Factor: c-Jun; motif: NATGASTCATN                                    | TF:M11264   | 3593      | 2.10E-03 | 69  |
| TF    | Factor: ipf1; motif: RNWCATTAAANWN                                   | TF:M01255   | 3449      | 2.10E-03 | 67  |
| TF    | Factor: SRY; motif: AACAAATNNNCATTGTT; match class: 1                | TF:M04556_1 | 5013      | 2.10E-03 | 88  |
| TF    | Factor: ERF:pitx1; motif: NNCGGAWGNNNRGNNTA                          | TF:M08692   | 4709      | 2.10E-03 | 84  |
| TF    | Factor: HOXA7; motif: GYMATTAN                                       | TF:M10690   | 8983      | 2.10E-03 | 137 |
| GO:BP | cellular component organization or biogenesis                        | GO:0071840  | 6398      | 2.20E-03 | 105 |
| TF    | Factor: CDP:T-bet; motif: NTCACACNYRATCRATM                          | TF:M08203   | 5093      | 2.20E-03 | 89  |
| TF    | Factor: JunB; motif: NRRTGASTCAK                                     | TF:M07103   | 2010      | 2.20E-03 | 46  |
| TF    | Factor: RelB:p50; motif: RGAAANTCCCYNNHGC                            | TF:M03882   | 3891      | 2.20E-03 | 73  |
| TF    | Factor: NFATc3; motif: NNTTCCRYGGAAAN; match class: 1                | TF:M11988_1 | 5797      | 2.20E-03 | 98  |
| TF    | Factor: HOXC-8; motif: NNNNGTAATTANNNT                               | TF:M01321   | 4639      | 2.20E-03 | 83  |
| GO:BP | apoptotic cell clearance   | GO:0043277  | 51        | 2.30E-03 | 7   |
| GO:BP | positive regulation of MAPK cascade                                  | GO:0043410  | 435       | 2.30E-03 | 18  |
| GO:BP | neutrophil migration   | GO:1990266  | 99        | 2.40E-03 | 9   |
| TF    | Factor: NR1H4; motif: NNAATGACCNN                                    | TF:M09777   | 3246      | 2.40E-03 | 64  |
| TF    | Factor: Pax-5; motif: BCNNNRNGCANBGNTGNRTAGCSGC HNB                  | TF:M00143   | 1019<br>9 | 2.40E-03 | 151 |
| TF    | Factor: C/EBPbeta; motif: ATTGCGYAAT                                 | TF:M07413   | 2826      | 2.40E-03 | 58  |
| TF    | Factor: NFATc2; motif: TTTTCCATGGAAAA                                | TF:M11985   | 4876      | 2.40E-03 | 86  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: ZXDL; motif: NGGGGWS                                | TF:M05775   | 6205 | 2.40E-03 | 103 |
| GO:BP | negative regulation of B cell activation                    | GO:0050869  | 33   | 2.50E-03 | 6   |
| GO:BP | vertebrate eye-specific patterning                          | GO:0150064  | 3    | 2.50E-03 | 3   |
| GO:BP | response to triacyl bacterial lipopeptide                   | GO:0071725  | 3    | 2.50E-03 | 3   |
| GO:BP | cellular response to triacyl bacterial lipopeptide          | GO:0071727  | 3    | 2.50E-03 | 3   |
| GO:BP | regulation of peptidyl-tyrosine phosphorylation             | GO:0050730  | 230  | 2.50E-03 | 13  |
| TF    | Factor: Msx-1; motif: CNGTAWNTG                             | TF:M00394   | 7584 | 2.50E-03 | 120 |
| TF    | Factor: MATH1; motif: NCASCTGGYN                            | TF:M01716   | 665  | 2.50E-03 | 23  |
| TF    | Factor: ER71:C/EBPdelta; motif: NNCGGAWRTRRCGYAAN           | TF:M08246   | 7178 | 2.50E-03 | 115 |
| GO:BP | granulocyte chemotaxis                                      | GO:0071621  | 100  | 2.60E-03 | 9   |
| GO:BP | negative regulation of immune effector process              | GO:0002698  | 100  | 2.60E-03 | 9   |
| TF    | Factor: NKX2B; motif: CACTTNA                               | TF:M02109   | 8588 | 2.60E-03 | 132 |
| TF    | Factor: BRCA1:USF2; motif: KTNNGTTG                         | TF:M01082   | 6054 | 2.60E-03 | 101 |
| TF    | Factor: YY1; motif: NGCCATYTTKGRCNWWNNGTGCK; match class: 1 | TF:M12276_1 | 2903 | 2.60E-03 | 59  |
| TF    | Factor: JunD; motif: NATGASTCATS; match class: 1            | TF:M11268_1 | 1455 | 2.60E-03 | 37  |
| TF    | Factor: Oct-4; motif: ATTGWSWTGCWAAWN; match class: 1       | TF:M01124_1 | 1335 | 2.70E-03 | 35  |
| TF    | Factor: C/EBPalpha; motif: NNNTTNNGCAANN; match class: 1    | TF:M01866_1 | 771  | 2.70E-03 | 25  |
| TF    | Factor: ipf1; motif: NNRNTAATTAGYNCAN                       | TF:M01438   | 2697 | 2.70E-03 | 56  |
| TF    | Factor: c-Fos; motif: RTGAGTCAYNN                           | TF:M09617   | 2224 | 2.70E-03 | 49  |
| GO:BP | ion transport   | GO:0006811  | 1420 | 2.80E-03 | 36  |
| TF    | Factor: HOXB5; motif: NNYMATTANN; match class: 1            | TF:M04349_1 | 3333 | 2.80E-03 | 65  |
| TF    | Factor: RARA; motif: GAGGTCAAAAGGTCAAkk                     | TF:M08018   | 3915 | 2.80E-03 | 73  |
| TF    | Factor: AR; motif: GNCCNNNTGTTCTN                           | TF:M01996   | 2495 | 2.80E-03 | 53  |
| TF    | Factor: HOXB5; motif: GTCATTAN                              | TF:M10701   | 4817 | 2.80E-03 | 85  |
| TF    | Factor: znf136; motif: CAAGAATWCATAYCCAG; match class: 1    | TF:M10535_1 | 2029 | 2.80E-03 | 46  |

|       |   |                   |           |          |     |
|-------|---|-------------------|-----------|----------|-----|
| KEGG  | Epstein-Barr virus infection                              | KEGG:05169        | 188       | 2.90E-03 | 10  |
| GO:BP | B cell differentiation                                    | GO:0030183        | 131       | 3.00E-03 | 10  |
| GO:BP | positive regulation of lymphocyte differentiation         | GO:0045621        | 102       | 3.00E-03 | 9   |
| TF    | Factor: CLOCK; motif: CNGNCACGTGNNMM                      | TF:M09884         | 7117      | 3.00E-03 | 114 |
| TF    | Factor: HFH2; motif: NNWAYRTAACW                          | TF:M11555         | 3923      | 3.00E-03 | 73  |
| TF    | Factor: ZNF436; motif: TCCTCCAGGAAGCCY; match class: 1    | TF:M10477_1       | 7782      | 3.10E-03 | 122 |
| GO:BP | cellular chemical homeostasis                             | GO:0055082        | 741       | 3.20E-03 | 24  |
| TF    | Factor: HOXD12;Elk-1; motif: NRNCGGAAGTCGTAAAN            | TF:M08359         | 5293      | 3.20E-03 | 91  |
| TF    | Factor: GABP-alpha; motif: AACCGGAAR                      | TF:M04748         | 1418<br>1 | 3.20E-03 | 195 |
| TF    | Factor: RAR-gamma; motif: RGGTCANNNTGNCNNNN               | TF:M10045         | 6400      | 3.20E-03 | 105 |
| TF    | Factor: LRH-1; motif: TGACCTTGRNYCAAGGTCA; match class: 1 | TF:M11830_1       | 5296      | 3.20E-03 | 91  |
| TF    | Factor: Blimp-1; motif: RRGNGAAAGRANNN                    | TF:M10526         | 1974      | 3.20E-03 | 45  |
| KEGG  | Influenza A   | KEGG:05164        | 153       | 3.30E-03 | 9   |
| TF    | Factor: HSF1; motif: TCYAGAAANTTC                         | TF:M07259         | 4006      | 3.30E-03 | 74  |
| TF    | Factor: HOXC4; motif: RTCRTTAN                            | TF:M10718         | 2239      | 3.30E-03 | 49  |
| TF    | Factor: AR; motif: AGWACATNWTGTCT                         | TF:M00447         | 3496      | 3.40E-03 | 67  |
| TF    | Factor: RORbeta; motif: TGACCYA; match class: 1           | TF:M01722_1       | 944       | 3.40E-03 | 28  |
| TF    | Factor: VSX1; motif: NGCYAATTRNN                          | TF:M04450         | 5852      | 3.40E-03 | 98  |
| TF    | Factor: HOXA10; motif: TTATNNYWN                          | TF:M07257         | 2998      | 3.50E-03 | 60  |
| TF    | Factor: POU3F1; motif: NTAATKWATGCNN; match class: 1      | TF:M11929_1       | 1472      | 3.50E-03 | 37  |
| TF    | Factor: NFATc4; motif: NRYGGAAANW                         | TF:M11995         | 578       | 3.50E-03 | 21  |
| TF    | Factor: p73; motif: NNRCAGYCCARRCWGTC                     | TF:M10025         | 5463      | 3.50E-03 | 93  |
| TF    | Factor: Pbx; motif: GATTGATKGNNS                          | TF:M00998         | 4313      | 3.50E-03 | 78  |
| GO:MF | opsonin binding   | GO:0001846        | 13        | 3.60E-03 | 4   |
| REAC  | Translocation of ZAP-70 to Immunological synapse          | REAC:R-HSA-202430 | 13        | 3.60E-03 | 4   |
| TF    | Factor: SREBP; motif: NNNNYCACNCCANN                      | TF:M01168         | 5699      | 3.60E-03 | 96  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: C-JUN:FOSB; motif: NATGACTCAY                     | TF:M08936   | 2723 | 3.60E-03 | 56  |
| TF    | Factor: AP-4; motif: NNCAGCTGNN                           | TF:M11212   | 2517 | 3.60E-03 | 53  |
| TF    | Factor: Isl2; motif: YTAAGTG                              | TF:M02082   | 6418 | 3.70E-03 | 105 |
| TF    | Factor: Sox-9; motif: MACARWGNNNYCNTTNNW                  | TF:M08838   | 3505 | 3.70E-03 | 67  |
| TF    | Factor: Pax-2; motif: NNNNGTCANGNRTKANNNN; match class: 1 | TF:M00098_1 | 1663 | 3.70E-03 | 40  |
| TF    | Factor: Freac-3; motif: NNNNNGTAATAAACA                   | TF:M00291   | 4394 | 3.70E-03 | 79  |
| TF    | Factor: GATA-3; motif: AGATAACGATCW                       | TF:M12192   | 3947 | 3.80E-03 | 73  |
| TF    | Factor: Fli-1; motif: MGGAAGT; match class: 1             | TF:M07382_1 | 1237 | 3.80E-03 | 33  |
| TF    | Factor: C-ets-1; motif: AGGAAGN; match class: 1           | TF:M01870_1 | 1237 | 3.80E-03 | 33  |
| TF    | Factor: SPI1; motif: AGGAAGT; match class: 1              | TF:M02278_1 | 1237 | 3.80E-03 | 33  |
| TF    | Factor: PEA3; motif: AGGAAGT; match class: 1              | TF:M03579_1 | 1237 | 3.80E-03 | 33  |
| GO:MF | endopeptidase inhibitor activity                          | GO:0004866  | 127  | 3.90E-03 | 9   |
| TF    | Factor: Nkx2-3; motif: NNCGTTRWS                          | TF:M10638   | 9672 | 3.90E-03 | 144 |
| TF    | Factor: COUP-TF1; motif: GRGGKSARAGGTCAGNG                | TF:M09886   | 4855 | 3.90E-03 | 85  |
| TF    | Factor: HMGYI; motif: NNKKNAWTTTNYTNN; match class: 1     | TF:M01010_1 | 2523 | 3.90E-03 | 53  |
| TF    | Factor: c-Myb; motif: NNNNCMGTTNNN                        | TF:M07299   | 3223 | 3.90E-03 | 63  |
| TF    | Factor: HOXA13; motif: ATAAMA; match class: 1             | TF:M01292_1 | 6832 | 3.90E-03 | 110 |
| GO:BP | positive regulation of leukocyte proliferation            | GO:0070665  | 135  | 4.00E-03 | 10  |
| GO:BP | regulation of reactive oxygen species metabolic process   | GO:2000377  | 135  | 4.00E-03 | 10  |
| GO:BP | viral entry into host cell                                | GO:0046718  | 135  | 4.00E-03 | 10  |
| TF    | Factor: HSF1; motif: GAANTTCTRGNAN                        | TF:M02017   | 3440 | 4.00E-03 | 66  |
| TF    | Factor: Sox-2; motif: NNCCTTTGTNYYN; match class: 1       | TF:M10067_1 | 1065 | 4.00E-03 | 30  |
| TF    | Factor: GATA-1; motif: MNAGATAANR                         | TF:M00347   | 3733 | 4.00E-03 | 70  |
| TF    | Factor: DMRT5; motif: NNNNGWTACANT                        | TF:M11513   | 1733 | 4.10E-03 | 41  |
| TF    | Factor: Sox-9; motif: NNNACAATRG; match class: 1          | TF:M11626_1 | 1241 | 4.10E-03 | 33  |
| TF    | Factor: SPIB; motif: NAAAAGMGGAAGTN                       | TF:M03995   | 634  | 4.10E-03 | 22  |



|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| GO:BP | neutrophil chemotaxis   | GO:0030593         | 79   | 4.20E-03 | 8   |
| GO:BP | negative regulation of proteolysis                              | GO:0045861         | 280  | 4.20E-03 | 14  |
| GO:BP | positive regulation of interleukin-12 production                | GO:0032735         | 36   | 4.20E-03 | 6   |
| TF    | Factor: ERF; FOXO1A; motif: RTMAACAGGAARNS; match class: 1      | TF:M08241_1        | 1671 | 4.20E-03 | 40  |
| TF    | Factor: RXRA; motif: RRGTCATGACCYY; match class: 1              | TF:M04490_1        | 3016 | 4.20E-03 | 60  |
| GO:BP | cation transport  | GO:0006812         | 1088 | 4.30E-03 | 30  |
| TF    | Factor: elf5; motif: AANRAGGAAGTR                               | TF:M11388          | 537  | 4.30E-03 | 20  |
| TF    | Factor: Oct-2; motif: NNNATTGTCATRT                             | TF:M07120          | 3962 | 4.30E-03 | 73  |
| TF    | Factor: Sox-10; motif: NACAATRNNNYATTGTN; match class: 1        | TF:M11635_1        | 4716 | 4.40E-03 | 83  |
| TF    | Factor: MZF-1; motif: KNGNKAGGGGNA                              | TF:M00084          | 5964 | 4.40E-03 | 99  |
| TF    | Factor: Brn-3c; motif: NNTTATTAATKANKNC                         | TF:M01408          | 3964 | 4.40E-03 | 73  |
| GO:MF | glycosaminoglycan binding                                       | GO:0005539         | 200  | 4.50E-03 | 11  |
| REAC  | Disease   | REAC:R-HSA-1643685 | 1493 | 4.50E-03 | 35  |
| TF    | Factor: Hoxa9; motif: NTTAAWTAMA; match class: 1                | TF:M07457_1        | 1366 | 4.50E-03 | 35  |
| TF    | Factor: ipf1; motif: CATTAR; match class: 1                     | TF:M01275_1        | 2742 | 4.50E-03 | 56  |
| TF    | Factor: DPF2; motif: NYCACYTCCYCNYYCY                           | TF:M09760          | 7424 | 4.50E-03 | 117 |
| REAC  | Generation of second messenger molecules                        | REAC:R-HSA-202433  | 28   | 4.60E-03 | 5   |
| TF    | Factor: RARA; motif: AGGTCAANNARAGGTCA                          | TF:M04483          | 3600 | 4.60E-03 | 68  |
| TF    | Factor: LRH-1; motif: TCAAGGTCRYGACCTTGR                        | TF:M11828          | 9272 | 4.60E-03 | 139 |
| TF    | Factor: AP-4; Max; motif: NCAGCTGNNNNNNNCACGTGN; match class: 1 | TF:M08674_1        | 4802 | 4.70E-03 | 84  |
| GO:BP | myelination   | GO:0042552         | 138  | 4.80E-03 | 10  |
| KEGG  | Toll-like receptor signaling pathway                            | KEGG:04620         | 92   | 4.80E-03 | 7   |
| KEGG  | Th17 cell differentiation                                       | KEGG:04659         | 92   | 4.80E-03 | 7   |
| TF    | Factor: ALX3; motif: NNYAATTANN                                 | TF:M04279          | 3243 | 4.80E-03 | 63  |
| GO:BP | negative regulation of metabolic process                        | GO:0009892         | 2853 | 4.90E-03 | 57  |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| TF    | Factor: E2F2; motif: AAAATGGCGCCATTTT                   | TF:M04517          | 8014 | 4.90E-03 | 124 |
| TF    | Factor: FOX; motif: KWTTGTTRTTT                         | TF:M00809          | 3102 | 4.90E-03 | 61  |
| TF    | Factor: YB-1; motif: CCAMTCNGMR                         | TF:M03805          | 8857 | 4.90E-03 | 134 |
| GO:BP | gliogenesis   | GO:0042063         | 284  | 5.00E-03 | 14  |
| GO:BP | amyloid-beta clearance                                  | GO:0097242         | 37   | 5.00E-03 | 6   |
| TF    | Factor: FOXM1; motif: NAGASTGATTA; match class: 1       | TF:M04611_1        | 2751 | 5.00E-03 | 56  |
| GO:BP | protein phosphorylation                                 | GO:0006468         | 1459 | 5.10E-03 | 36  |
| GO:MF | lipopeptide binding                                     | GO:0071723         | 5    | 5.10E-03 | 3   |
| GO:MF | complement component C3b binding                        | GO:0001851         | 5    | 5.10E-03 | 3   |
| KEGG  | Acute myeloid leukemia                                  | KEGG:05221         | 64   | 5.10E-03 | 6   |
| KEGG  | Rap1 signaling pathway                                  | KEGG:04015         | 201  | 5.10E-03 | 10  |
| TF    | Factor: CDP; motif: TRATCRATAN                          | TF:M03952          | 3537 | 5.10E-03 | 67  |
| TF    | Factor: islet1; motif: SCAMTTAN                         | TF:M11012          | 5352 | 5.10E-03 | 91  |
| TF    | Factor: GATA-3; motif: MGATAASATCT                      | TF:M12195          | 3177 | 5.10E-03 | 62  |
| TF    | Factor: ER-beta; motif: GTCANASTGRCCYNR; match class: 1 | TF:M01875_1        | 1196 | 5.20E-03 | 32  |
| GO:CC | secretory granule lumen                                 | GO:0034774         | 289  | 5.30E-03 | 13  |
| GO:MF | peptidase inhibitor activity                            | GO:0030414         | 132  | 5.30E-03 | 9   |
| TF    | Factor: HOXA4; motif: RYCATTRN                          | TF:M08771          | 2345 | 5.30E-03 | 50  |
| REAC  | Antigen processing-Cross presentation                   | REAC:R-HSA-1236975 | 101  | 5.50E-03 | 8   |
| TF    | Factor: Fra-2; motif: NRRTGASTCAB                       | TF:M07092          | 2621 | 5.50E-03 | 54  |
| TF    | Factor: CEBPD; motif: NRTTGCNCAAYN                      | TF:M12587          | 2484 | 5.50E-03 | 52  |
| GO:BP | positive regulation of mononuclear cell migration       | GO:0071677         | 58   | 5.60E-03 | 7   |
| GO:MF | antigen binding   | GO:0003823         | 49   | 5.60E-03 | 6   |
| TF    | Factor: Sox-3; motif: SNNACAATRK                        | TF:M11617          | 3258 | 5.60E-03 | 63  |
| TF    | Factor: OSR2; motif: NGCTACTGNN                         | TF:M12051          | 2148 | 5.60E-03 | 47  |
| GO:BP | regulation of protein modification process              | GO:0031399         | 1404 | 5.70E-03 | 35  |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:CC | cytoplasmic vesicle lumen                                      | GO:0060205  | 291   | 5.70E-03 | 13  |
| TF    | Factor: SUHW1; motif: TCTCTCCAGTRTGAATTCTCTGAT; match class: 1 | TF:M10541_1 | 1442  | 5.70E-03 | 36  |
| GO:BP | positive regulation of ERK1 and ERK2 cascade                   | GO:0070374  | 174   | 5.80E-03 | 11  |
| GO:BP | regulation of proteolysis                                      | GO:0030162  | 662   | 5.80E-03 | 22  |
| KEGG  | Alcoholic liver disease  | KEGG:04936  | 128   | 5.80E-03 | 8   |
| TF    | Factor: HOXA7; motif: GYMATTAN; match class: 1                 | TF:M10690_1 | 4980  | 5.80E-03 | 86  |
| GO:BP | entry into host  | GO:0044409  | 141   | 5.90E-03 | 10  |
| GO:BP | regulation of macrophage migration                             | GO:1905521  | 38    | 5.90E-03 | 6   |
| TF    | Factor: ESE-1; motif: NNANVAGGAAGTNN                           | TF:M09902   | 2697  | 5.90E-03 | 55  |
| GO:CC | coated vesicle membrane  | GO:0030662  | 172   | 6.00E-03 | 10  |
| GO:CC | phagocytic vesicle membrane                                    | GO:0030670  | 76    | 6.00E-03 | 7   |
| TF    | Factor: T3R-beta; motif: NTGACCTNRNYNAGGTCAN                   | TF:M11820   | 4448  | 6.00E-03 | 79  |
| TF    | Factor: TCF-1; motif: ASATCAAAG                                | TF:M11602   | 5688  | 6.00E-03 | 95  |
| GO:CC | vesicle lumen  | GO:0031983  | 293   | 6.10E-03 | 13  |
| TF    | Factor: p300; motif: ACNTCCG                                   | TF:M04826   | 15885 | 6.10E-03 | 212 |
| TF    | Factor: SPI1; motif: NGRGGAAGTN; match class: 1                | TF:M02078_1 | 321   | 6.10E-03 | 15  |
| TF    | Factor: MOX1; motif: NTCRTTAN                                  | TF:M10761   | 2561  | 6.10E-03 | 53  |
| GO:BP | cellular response to interferon-gamma                          | GO:0071346  | 111   | 6.20E-03 | 9   |
| GO:BP | MyD88-dependent toll-like receptor signaling pathway           | GO:0002755  | 22    | 6.20E-03 | 5   |
| TF    | Factor: GABPA; motif: NNCACCTTCCTGTNN                          | TF:M12494   | 1762  | 6.20E-03 | 41  |
| TF    | Factor: GATA-3; motif: ANAGATMWWA                              | TF:M00351   | 2155  | 6.20E-03 | 47  |
| TF    | Factor: POU5F1; motif: NNATGCAAANN                             | TF:M09782   | 2982  | 6.20E-03 | 59  |
| TF    | Factor: p53; motif: NGRCWTGYCY; match class: 1                 | TF:M00272_1 | 974   | 6.20E-03 | 28  |
| TF    | Factor: CTF/NF1; motif: TTGGCN; match class: 1                 | TF:M02050_1 | 3413  | 6.20E-03 | 65  |
| GO:BP | negative regulation of leukocyte mediated immunity             | GO:0002704  | 59    | 6.30E-03 | 7   |
| GO:BP | regulation of interleukin-2 production                         | GO:0032663  | 59    | 6.30E-03 | 7   |

|       |   |             |       |          |     |
|-------|---|-------------|-------|----------|-----|
| GO:BP | interleukin-2 production  | GO:0032623  | 59    | 6.30E-03 | 7   |
| GO:MF | hydrolase activity, hydrolyzing N-glycosyl compounds            | GO:0016799  | 50    | 6.30E-03 | 6   |
| TF    | Factor: YB-1; motif: NNNNCCAATNN                                | TF:M03862   | 7885  | 6.30E-03 | 122 |
| TF    | Factor: RARA; motif: AGGTCAANNARAGGTCA; match class: 1          | TF:M04483_1 | 502   | 6.30E-03 | 19  |
| TF    | Factor: Pit-1; motif: NTAATGAKATGCRN                            | TF:M11950   | 4913  | 6.30E-03 | 85  |
| TF    | Factor: Sox-4; motif: NYCTTTGTYYYN; match class: 1              | TF:M10069_1 | 1449  | 6.30E-03 | 36  |
| TF    | Factor: CDP-SRF; motif: NCCWTAYAAGGTMNKRATCRATN; match class: 1 | TF:M08520_1 | 3199  | 6.40E-03 | 62  |
| GO:CC | luminal side of membrane  | GO:0098576  | 31    | 6.50E-03 | 5   |
| GO:BP | cellular homeostasis  | GO:0019725  | 828   | 6.60E-03 | 25  |
| GO:BP | positive regulation of leukocyte chemotaxis                     | GO:0002690  | 84    | 6.60E-03 | 8   |
| TF    | Factor: ESE-1; motif: NTGTGCGGATGCN                             | TF:M11385   | 10801 | 6.60E-03 | 156 |
| TF    | Factor: STAT1; motif: NNTTTCYNGGAARNNNNNNNNN                    | TF:M01260   | 1832  | 6.70E-03 | 42  |
| TF    | Factor: THAP1; motif: YTGCCCNNA; match class: 1                 | TF:M07407_1 | 3639  | 6.70E-03 | 68  |
| TF    | Factor: RAR-gamma; motif: NRRGTCAAAAAGGTCAN                     | TF:M11804   | 2639  | 6.70E-03 | 54  |
| TF    | Factor: CSX; motif: NCCACTTRAN                                  | TF:M10640   | 5466  | 6.70E-03 | 92  |
| GO:BP | response to abiotic stimulus                                    | GO:0009628  | 1055  | 6.80E-03 | 29  |
| TF    | Factor: Nkx2-3; motif: NSCACTTNNC                               | TF:M10634   | 1641  | 6.80E-03 | 39  |
| GO:BP | viral life cycle  | GO:0019058  | 292   | 6.90E-03 | 14  |
| TF    | Factor: AP-2alpha; motif: NTNSCCTGRGGSNAN                       | TF:M09590   | 4694  | 6.90E-03 | 82  |
| TF    | Factor: T3R-beta; motif: NRRGGTCRTGACCCYNN                      | TF:M11817   | 4694  | 6.90E-03 | 82  |
| TF    | Factor: RUSH-1alpha; motif: NNMCVTNKNN                          | TF:M01107   | 2573  | 7.00E-03 | 53  |
| GO:BP | superoxide metabolic process                                    | GO:0006801  | 60    | 7.10E-03 | 7   |
| GO:BP | inflammatory response to antigenic stimulus                     | GO:0002437  | 60    | 7.10E-03 | 7   |
| GO:CC | vacuolar membrane   | GO:0005774  | 436   | 7.10E-03 | 16  |
| TF    | Factor: PBX2; motif: TGANTGACAGN                                | TF:M09736   | 4240  | 7.10E-03 | 76  |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| TF    | Factor: MZF-1; motif: TGGGGAR; match class: 1          | TF:M01733_1 | 4394 | 7.20E-03 | 78  |
| TF    | Factor: SOX2; motif: NNACAATGGNN                       | TF:M12505   | 1396 | 7.20E-03 | 35  |
| TF    | Factor: Dlx-5; motif: AATTAN; match class: 1           | TF:M03546_1 | 4779 | 7.40E-03 | 83  |
| TF    | Factor: DR11; motif: AATTAA; match class: 1            | TF:M01654_1 | 4779 | 7.40E-03 | 83  |
| TF    | Factor: Hoxa9; motif: NCGGYCATWAAAWTANW                | TF:M01351   | 1712 | 7.50E-03 | 40  |
| TF    | Factor: E2A; motif: NRMCASCTGCNNN                      | TF:M02088   | 2511 | 7.60E-03 | 52  |
| TF    | Factor: POU6F1; motif: NTAATGAKATGNNN                  | TF:M11958   | 2239 | 7.60E-03 | 48  |
| GO:BP | regulation of cellular localization                    | GO:0060341  | 781  | 7.80E-03 | 24  |
| TF    | Factor: GATA-4; motif: NNGATAASNN                      | TF:M12207   | 2377 | 7.80E-03 | 50  |
| GO:BP | membrane raft organization                             | GO:0031579  | 23   | 7.90E-03 | 5   |
| TF    | Factor: Pax-4; motif: WNNNYTAATARYNSNN                 | TF:M01385   | 2724 | 8.00E-03 | 55  |
| TF    | Factor: ESE-1; motif: ACCGGAAGTANNNNNNAAWAA            | TF:M11383   | 3150 | 8.10E-03 | 61  |
| TF    | Factor: GATA-6; motif: NGATAACGATCN                    | TF:M12209   | 1717 | 8.10E-03 | 40  |
| TF    | Factor: POU2F2; motif: NTATGCWAATN                     | TF:M04072   | 1912 | 8.10E-03 | 43  |
| TF    | Factor: IRF-1; motif: TTCACTT                          | TF:M00747   | 4332 | 8.10E-03 | 77  |
| GO:BP | phosphorylation  | GO:0016310  | 1744 | 8.20E-03 | 40  |
| TF    | Factor: AP-4; motif: NNCAGCTGNN; match class: 1        | TF:M11212_1 | 2449 | 8.20E-03 | 51  |
| TF    | Factor: JUND; motif: NNATGACTCATNN                     | TF:M12524   | 3514 | 8.20E-03 | 66  |
| TF    | Factor: CDX-2; motif: TTTATN                           | TF:M02087   | 8261 | 8.20E-03 | 126 |
| GO:MF | cell adhesion molecule binding                         | GO:0050839  | 535  | 8.30E-03 | 18  |
| TF    | Factor: Ngn-2; motif: RACATATGTC                       | TF:M04183   | 822  | 8.40E-03 | 25  |
| TF    | Factor: Prx2; motif: TYAWAKTAA                         | TF:M02115   | 2870 | 8.50E-03 | 57  |
| TF    | Factor: POU3F3; motif: WTNAATAWKNAW                    | TF:M04082   | 2941 | 8.50E-03 | 58  |
| TF    | Factor: GR; motif: NNNNNNCNNTNTGTNCTNN; match class: 1 | TF:M00192_1 | 1531 | 8.60E-03 | 37  |
| GO:BP | MAPK cascade   | GO:0000165  | 732  | 8.70E-03 | 23  |
| GO:BP | positive regulation of alpha-beta T cell activation    | GO:0046635  | 62   | 8.80E-03 | 7   |

|       |   |                    |      |          |     |
|-------|---|--------------------|------|----------|-----|
| GO:BP | regulation of ERK1 and ERK2 cascade                                   | GO:0070372         | 258  | 9.00E-03 | 13  |
| GO:BP | tube morphogenesis  | GO:0035239         | 788  | 9.00E-03 | 24  |
| GO:CC | plasma membrane region  | GO:0098590         | 1176 | 9.00E-03 | 29  |
| GO:MF | endopeptidase regulator activity                                      | GO:0061135         | 141  | 9.00E-03 | 9   |
| TF    | Factor: Dlx-7; motif: NTCRTTAN  | TF:M10600          | 6220 | 9.00E-03 | 101 |
| REAC  | DAP12 interactions  | REAC:R-HSA-2172127 | 32   | 9.10E-03 | 5   |
| TF    | Factor: FRA-2; motif: RTGANTCA  | TF:M08914          | 3234 | 9.10E-03 | 62  |
| TF    | Factor: Pit-1; motif: NTAATTTATKCGY                                   | TF:M11949          | 4653 | 9.30E-03 | 81  |
| GO:BP | positive regulation of pattern recognition receptor signaling pathway | GO:0062208         | 41   | 9.40E-03 | 6   |
| GO:BP | positive regulation of myeloid cell differentiation                   | GO:0045639         | 88   | 9.40E-03 | 8   |
| GO:BP | positive regulation of T cell differentiation                         | GO:0045582         | 88   | 9.40E-03 | 8   |
| TF    | Factor: Oct-2; motif: ATTTGCA   | TF:M04715          | 5273 | 9.40E-03 | 89  |
| TF    | Factor: NFATc1; motif: TTTTCCATGGAAAN; match class: 1                 | TF:M04053_1        | 4962 | 9.40E-03 | 85  |
| TF    | Factor: TEF-3/C/EBPdelta; motif: RGWATGYNRTRCGYAAAY                   | TF:M08413          | 5118 | 9.40E-03 | 87  |
| GO:CC | extracellular matrix  | GO:0031012         | 497  | 9.60E-03 | 17  |
| TF    | Factor: GATA-3; motif: MGATAACGATCT                                   | TF:M12194          | 2811 | 9.60E-03 | 56  |
| TF    | Factor: BCL-6; motif: WRCTTCKAGGRAT                                   | TF:M01185          | 5120 | 9.60E-03 | 87  |
| TF    | Factor: c-Fos; motif: NNTGASTCATN                                     | TF:M07090          | 3604 | 9.60E-03 | 67  |
| TF    | Factor: HOXD12;Elk-1; motif: NRNCGGAAGTCGTAAAN; match class: 1        | TF:M08359_1        | 997  | 9.70E-03 | 28  |
| TF    | Factor: MyoD; motif: YGNCAGSTGTYN                                     | TF:M11185          | 997  | 9.70E-03 | 28  |
| TF    | Factor: GATA-1; motif: NTGNNNNNNNSAGATAAGR                            | TF:M09621          | 4581 | 9.70E-03 | 80  |
| GO:BP | positive regulation of interferon-gamma production                    | GO:0032729         | 63   | 9.80E-03 | 7   |
| TF    | Factor: GATA-4; motif: AGATAAN  | TF:M03549          | 3977 | 9.80E-03 | 72  |
| TF    | Factor: SOX; motif: CTCTTTGTTANGA                                     | TF:M01014          | 4278 | 9.80E-03 | 76  |
| TF    | Factor: c-Myb; motif: NNNAACKGNNN                                     | TF:M01821          | 3242 | 9.80E-03 | 62  |

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|-------|--|-------------|------|----------|-----|
| GO:BP | regulation of monocyte chemotaxis                            | GO:0090025  | 24   | 9.90E-03 | 5   |
| GO:CC | external encapsulating structure                             | GO:0030312  | 498  | 9.90E-03 | 17  |
| GO:BP | positive regulation of microglial cell mediated cytotoxicity | GO:1904151  | 4    | 1.00E-02 | 3   |
| GO:BP | positive regulation of neutrophil degranulation              | GO:0043315  | 4    | 1.00E-02 | 3   |
| GO:BP | interleukin-3-mediated signaling pathway                     | GO:0038156  | 4    | 1.00E-02 | 3   |
| GO:BP | chemical homeostasis   | GO:0048878  | 1078 | 1.00E-02 | 29  |
| GO:BP | regulation of alpha-beta T cell activation                   | GO:0046634  | 89   | 1.00E-02 | 8   |
| TF    | Factor: RARA; motif: ARGGTCAAAGGTCA                          | TF:M04481   | 2675 | 1.00E-02 | 54  |
| TF    | Factor: FOXJ2; motif: NNTGTTGTAAYAN; match class: 1          | TF:M11585_1 | 1057 | 1.00E-02 | 29  |
| TF    | Factor: ipf1; motif: NVSTAATTAC; match class: 1              | TF:M01235_1 | 1295 | 1.00E-02 | 33  |
| TF    | Factor: NKX3A; motif: NTNAAGTGNTTN                           | TF:M10009   | 3102 | 1.00E-02 | 60  |
| TF    | Factor: FAC1; motif: NNNCAMAACRNA; match class: 1            | TF:M00456_1 | 2264 | 1.00E-02 | 48  |
| GO:BP | negative regulation of programmed cell death                 | GO:0043069  | 799  | 1.10E-02 | 24  |
| GO:BP | regulation of cellular metabolic process                     | GO:0031323  | 5347 | 1.10E-02 | 89  |
| GO:MF | molecular function regulator                                 | GO:0098772  | 1692 | 1.10E-02 | 37  |
| KEGG  | Natural killer cell mediated cytotoxicity                    | KEGG:04650  | 105  | 1.10E-02 | 7   |
| TF    | Factor: AR; motif: GGTACANNRTGTTCT                           | TF:M00481   | 4286 | 1.10E-02 | 76  |
| TF    | Factor: HNRPUL1; motif: NCNCAGN; match class: 1              | TF:M09746_1 | 6727 | 1.10E-02 | 107 |
| TF    | Factor: HOXC4; motif: NTMATTAN                               | TF:M10717   | 2962 | 1.10E-02 | 58  |
| TF    | Factor: Oct3; motif: NATGCAANNN                              | TF:M01307   | 3322 | 1.10E-02 | 63  |
| TF    | Factor: ZNF775; motif: RGRGAGAAGN                            | TF:M12720   | 3038 | 1.10E-02 | 59  |
| TF    | Factor: Oct3; motif: WTATGCGCATAW; match class: 1            | TF:M11934_1 | 7810 | 1.10E-02 | 120 |
| GO:BP | movement in host environment                                 | GO:0052126  | 152  | 1.20E-02 | 10  |
| GO:BP | lymphocyte migration   | GO:0072676  | 91   | 1.20E-02 | 8   |
| GO:BP | dendritic cell antigen processing and presentation           | GO:0002468  | 12   | 1.20E-02 | 4   |
| GO:BP | negative regulation of leukocyte migration                   | GO:0002686  | 43   | 1.20E-02 | 6   |

|       |  |                    |      |          |     |
|-------|--|--------------------|------|----------|-----|
| GO:CC | endosome membrane  | GO:0010008         | 507  | 1.20E-02 | 17  |
| REAC  | Interferon Signaling   | REAC:R-HSA-913531  | 182  | 1.20E-02 | 10  |
| REAC  | PD-1 signaling   | REAC:R-HSA-389948  | 17   | 1.20E-02 | 4   |
| REAC  | Leishmania infection   | REAC:R-HSA-9658195 | 223  | 1.20E-02 | 11  |
| TF    | Factor: ZABC1; motif: ATTCNCAC; match class: 1                   | TF:M01306_1        | 2342 | 1.20E-02 | 49  |
| TF    | Factor: NF-1B; motif: KCCAGANWN                                  | TF:M08825          | 4990 | 1.20E-02 | 85  |
| TF    | Factor: Msx-1; motif: WNGNAATTANV                                | TF:M08822          | 5618 | 1.20E-02 | 93  |
| TF    | Factor: FOXO1A; motif: NNNYTGTTTNCN                              | TF:M09931          | 5699 | 1.20E-02 | 94  |
| TF    | Factor: STAT6; motif: NNYTTCCY                                   | TF:M00500          | 4076 | 1.20E-02 | 73  |
| TF    | Factor: RAR-gamma; motif: RAGGTCATGACCTY                         | TF:M11807          | 1747 | 1.20E-02 | 40  |
| TF    | Factor: ZNF586; motif: CAGGCCYRGAGG; match class: 1              | TF:M10491_1        | 6912 | 1.20E-02 | 109 |
| GO:BP | central nervous system development                               | GO:0007417         | 974  | 1.30E-02 | 27  |
| GO:BP | positive regulation of reactive oxygen species metabolic process | GO:2000379         | 66   | 1.30E-02 | 7   |
| GO:CC | clathrin-coated vesicle  | GO:0030136         | 188  | 1.30E-02 | 10  |
| GO:MF | carboxylic acid binding  | GO:0031406         | 147  | 1.30E-02 | 9   |
| KEGG  | Malaria  | KEGG:05144         | 48   | 1.30E-02 | 5   |
| KEGG  | Leukocyte transendothelial migration                             | KEGG:04670         | 108  | 1.30E-02 | 7   |
| TF    | Factor: DMBX1; motif: NNGGATTANN                                 | TF:M04305          | 4383 | 1.30E-02 | 77  |
| TF    | Factor: Cdx-2; motif: BNNATAAANRN                                | TF:M01659          | 1188 | 1.30E-02 | 31  |
| TF    | Factor: MafB; motif: TGCTGASTNNN                                 | TF:M09978          | 2768 | 1.30E-02 | 55  |
| TF    | Factor: Oct-2; motif: NNNTATGCAAATNNNN                           | TF:M01368          | 1947 | 1.30E-02 | 43  |
| TF    | Factor: Spi-B; motif: NNGGAAGYN                                  | TF:M02076          | 258  | 1.30E-02 | 13  |
| TF    | Factor: Smad2; Smad3; Smad4; motif: NTGTCTGNACCT                 | TF:M07126          | 3639 | 1.30E-02 | 67  |
| TF    | Factor: UNCX; motif: NYAATTAN                                    | TF:M04443          | 2702 | 1.30E-02 | 54  |
| GO:BP | calcium-mediated signaling                                       | GO:0019722         | 191  | 1.40E-02 | 11  |
| GO:BP | positive regulation of leukocyte mediated cytotoxicity           | GO:0001912         | 44   | 1.40E-02 | 6   |

|       |  |             |      |          |     |
|-------|--|-------------|------|----------|-----|
| GO:BP | monocyte chemotaxis                                      | GO:0002548  | 44   | 1.40E-02 | 6   |
| TF    | Factor: ESR1; motif: NNNNMAGGTACCCCTGACCY                | TF:M02261   | 4090 | 1.40E-02 | 73  |
| TF    | Factor: STAT5B; motif: NAWTTCYNGGAAWWTN                  | TF:M00459   | 2634 | 1.40E-02 | 53  |
| TF    | Factor: Oct-1; motif: NNNNWTATGCAAATNTNNN                | TF:M00135   | 1692 | 1.40E-02 | 39  |
| TF    | Factor: MLR1; motif: NTGNMCYYTGNNCYN                     | TF:M12637   | 3795 | 1.40E-02 | 69  |
| TF    | Factor: VDR:RXR; motif: GGGTCAWNGRGTTC                   | TF:M01202   | 3426 | 1.40E-02 | 64  |
| TF    | Factor: HNF-3alpha; motif: CNYTAAGTAAACAAAN              | TF:M11570   | 3064 | 1.40E-02 | 59  |
| TF    | Factor: CP2; motif: GCHCDAMCCAG                          | TF:M00072   | 7846 | 1.40E-02 | 120 |
| TF    | Factor: T-bet; motif: NAGGTGTGAA                         | TF:M12019   | 483  | 1.40E-02 | 18  |
| GO:BP | positive regulation of leukocyte degranulation           | GO:0043302  | 26   | 1.50E-02 | 5   |
| GO:BP | metal ion transport                                      | GO:0030001  | 813  | 1.50E-02 | 24  |
| GO:MF | lipoprotein particle receptor activity                   | GO:0030228  | 18   | 1.50E-02 | 4   |
| GO:MF | cytokine receptor activity                               | GO:0004896  | 85   | 1.50E-02 | 7   |
| TF    | Factor: POU3F1; motif: WTGMATAAWTNA                      | TF:M04077   | 2294 | 1.50E-02 | 48  |
| TF    | Factor: Fli-1:C/EBPbeta; motif: RNCGGAWRTTGGCAAY         | TF:M08281   | 6613 | 1.50E-02 | 105 |
| TF    | Factor: FOXL2; motif: TWAKACWAMTTT                       | TF:M03548   | 3875 | 1.50E-02 | 70  |
| TF    | Factor: C-FOS:C-JUN; motif: ATGAGTCAYN                   | TF:M08942   | 2715 | 1.50E-02 | 54  |
| GO:BP | regulation of tissue remodeling                          | GO:0034103  | 68   | 1.60E-02 | 7   |
| TF    | Factor: FXR:RXR-ALPHA; motif: NAGKTCATTGACCYN            | TF:M08954   | 5497 | 1.60E-02 | 91  |
| TF    | Factor: POU3F2; motif: TTATGYTAAT                        | TF:M00464   | 2716 | 1.60E-02 | 54  |
| TF    | Factor: C/EBPalpha; motif: NRRTGTGCAAYNN; match class: 1 | TF:M09596_1 | 852  | 1.60E-02 | 25  |
| TF    | Factor: MEIS1A:HOXA9; motif: TGACAGKTTTAYGA              | TF:M00420   | 4639 | 1.60E-02 | 80  |
| TF    | Factor: nanog; motif: NYYWTTGWNATGCAAAT                  | TF:M09996   | 1141 | 1.60E-02 | 30  |
| TF    | Factor: Ncx; motif: NAATNAATTAATAANWW; match class: 1    | TF:M01420_1 | 1701 | 1.60E-02 | 39  |
| TF    | Factor: MAFB; motif: NTCAGCN; match class: 1             | TF:M08888_1 | 2789 | 1.60E-02 | 55  |
| TF    | Factor: c-Ets-2; motif: NNNRGAARNRRR                     | TF:M09912   | 4412 | 1.60E-02 | 77  |

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|-------|---|-------------------|------|----------|-----|
| TF    | Factor: JunD; motif: NRTGACGTCATS                           | TF:M11270         | 7948 | 1.60E-02 | 121 |
| TF    | Factor: Sox-3; motif: NNAACAATRN                            | TF:M11616         | 393  | 1.60E-02 | 16  |
| TF    | Factor: RARA; motif: ARRGGTCANSNGAGGTCA                     | TF:M04482         | 3221 | 1.60E-02 | 61  |
| TF    | Factor: HPX42B; motif: NNYNATTANN                           | TF:M10681         | 2033 | 1.60E-02 | 44  |
| TF    | Factor: AP-4; motif: WGARYCAGCTGYGGNCNK                     | TF:M00005         | 4645 | 1.60E-02 | 80  |
| GO:BP | regulation of DNA-binding transcription factor activity     | GO:0051090        | 406  | 1.70E-02 | 16  |
| GO:BP | negative regulation of mast cell activation                 | GO:0033004        | 13   | 1.70E-02 | 4   |
| REAC  | Costimulation by the CD28 family                            | REAC:R-HSA-388841 | 59   | 1.70E-02 | 6   |
| TF    | Factor: POU3F2; motif: WTATGCWAATKAG                        | TF:M11904         | 2582 | 1.70E-02 | 52  |
| TF    | Factor: ZNF644; motif: TCCWGCCTCTSN; match class: 1         | TF:M09737_1       | 1577 | 1.70E-02 | 37  |
| TF    | Factor: Tal-1; motif: TCCAKCTGNY                            | TF:M00993         | 1642 | 1.70E-02 | 38  |
| TF    | Factor: OC-2; motif: TCAATA; match class: 1                 | TF:M02112_1       | 1837 | 1.70E-02 | 41  |
| TF    | Factor: NFATc1; motif: TTCCAYWRTGGAAA; match class: 1       | TF:M04052_1       | 3299 | 1.70E-02 | 62  |
| TF    | Factor: PRDM16; motif: KGGTCATRACCM; match class: 1         | TF:M05946_1       | 1838 | 1.70E-02 | 41  |
| TF    | Factor: COUP-TF; motif: TGAMCTTTGMMCYT                      | TF:M00158         | 1904 | 1.70E-02 | 42  |
| TF    | Factor: Oct-1; motif: TATGCAAATN                            | TF:M00342         | 2446 | 1.70E-02 | 50  |
| TF    | Factor: NR1B2; motif: NTGACCY; match class: 1               | TF:M02111_1       | 2939 | 1.70E-02 | 57  |
| GO:BP | cellular extravasation                                      | GO:0045123        | 69   | 1.80E-02 | 7   |
| KEGG  | Th1 and Th2 cell differentiation                            | KEGG:04658        | 80   | 1.80E-02 | 6   |
| REAC  | Activation of C3 and C5                                     | REAC:R-HSA-174577 | 7    | 1.80E-02 | 3   |
| TF    | Factor: GEMIN3; motif: NCWGGRRRRGRGNGNG                     | TF:M09727         | 7710 | 1.80E-02 | 118 |
| TF    | Factor: Fra-1; motif: RRTGASTCAKN                           | TF:M07091         | 1454 | 1.80E-02 | 35  |
| TF    | Factor: TTF-1; motif: CTTGASN                               | TF:M03891         | 3013 | 1.80E-02 | 58  |
| TF    | Factor: PPARgamma; motif: NWSTRGGKSARAGGKCA; match class: 1 | TF:M10038_1       | 1269 | 1.80E-02 | 32  |
| TF    | Factor: CP2/LBP-1c/LSF; motif: GCTGGNTNGNCCYNG              | TF:M00947         | 7463 | 1.80E-02 | 115 |

|       |  |                    |      |          |     |
|-------|--|--------------------|------|----------|-----|
| TF    | Factor: CIZ; motif: TTTTNNNNNNNNNNNNNAAAAA; match class: 1 | TF:M12070_1        | 2108 | 1.80E-02 | 45  |
| TF    | Factor: HOXA2; motif: RTCRTTAR                             | TF:M10736          | 1583 | 1.80E-02 | 37  |
| TF    | Factor: Oct3; motif: CYWTTSWNATGCAAAT; match class: 1      | TF:M10036_1        | 696  | 1.80E-02 | 22  |
| GO:BP | positive regulation of chemotaxis                          | GO:0050921         | 127  | 1.90E-02 | 9   |
| GO:BP | response to mechanical stimulus                            | GO:0009612         | 197  | 1.90E-02 | 11  |
| GO:BP | ERK1 and ERK2 cascade                                      | GO:0070371         | 277  | 1.90E-02 | 13  |
| TF    | Factor: HNF-3beta; motif: NTRTTTRYT                        | TF:M02014          | 2179 | 1.90E-02 | 46  |
| TF    | Factor: HOXA6; motif: NGYMATTANN                           | TF:M10696          | 4053 | 1.90E-02 | 72  |
| GO:BP | activation of innate immune response                       | GO:0002218         | 70   | 2.00E-02 | 7   |
| GO:CC | apical plasma membrane                                     | GO:0016324         | 328  | 2.00E-02 | 13  |
| TF    | Factor: STAT3; motif: NTTCCYGAAN                           | TF:M09664          | 4899 | 2.00E-02 | 83  |
| TF    | Factor: NURR1:RXR-ALPHA; motif: NRGGTCRTTGACCYN            | TF:M08957          | 9681 | 2.00E-02 | 141 |
| TF    | Factor: CDP; motif: NNNNWGWYMAATR                          | TF:M04610          | 3683 | 2.00E-02 | 67  |
| TF    | Factor: Pit-1; motif: NNWWATTCAT                           | TF:M03559          | 4362 | 2.00E-02 | 76  |
| TF    | Factor: PPARGAMMA; motif: NWNTRGGTYANN                     | TF:M08961          | 4518 | 2.00E-02 | 78  |
| REAC  | FCGR3A-mediated IL10 synthesis                             | REAC:R-HSA-9664323 | 38   | 2.10E-02 | 5   |
| TF    | Factor: SPIB; motif: NNCTACTTCTCTTTN; match class: 1       | TF:M12498_1        | 123  | 2.10E-02 | 9   |
| TF    | Factor: PMX2B; motif: NNNAATTAATTAANNNG; match class: 1    | TF:M01356_1        | 1722 | 2.10E-02 | 39  |
| TF    | Factor: Erm; motif: NRRSAGGAARNGRN; match class: 1         | TF:M09916_1        | 1466 | 2.10E-02 | 35  |
| TF    | Factor: Pbx; motif: NKTGATTGACRKS                          | TF:M01967          | 4369 | 2.10E-02 | 76  |
| TF    | Factor: Prop-1; motif: TAATTNNRTTA                         | TF:M10928          | 1404 | 2.10E-02 | 34  |
| GO:BP | regulation of MAPK cascade                                 | GO:0043408         | 613  | 2.20E-02 | 20  |
| GO:BP | Fc receptor signaling pathway                              | GO:0038093         | 71   | 2.20E-02 | 7   |
| GO:BP | regulation of B cell differentiation                       | GO:0045577         | 28   | 2.20E-02 | 5   |
| TF    | Factor: HNF-3alpha; motif: YTRWGTMAATATTRCWYWN             | TF:M11571          | 3470 | 2.20E-02 | 64  |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: c-MYB; motif: NNNNGCAGTTN                                   | TF:M00773   | 2962 | 2.20E-02 | 57  |
| TF    | Factor: COUPTF; motif: NNNNNTGACCYTTGNMCNYNGMN                      | TF:M01036   | 3252 | 2.20E-02 | 61  |
| TF    | Factor: JunD; motif: RTGACGTC                                       | TF:M04681   | 4994 | 2.20E-02 | 84  |
| TF    | Factor: HOXB2:Sox-20; motif: ACAATRSNNNNNNNATYA                     | TF:M08719   | 1470 | 2.20E-02 | 35  |
| TF    | Factor: FOXP3; motif: NNNVAAACANWD                                  | TF:M07419   | 5230 | 2.20E-02 | 87  |
| TF    | Factor: Sox-14; motif: NNNACAATGN                                   | TF:M11618   | 927  | 2.20E-02 | 26  |
| GO:BP | regulation of adaptive immune response                              | GO:0002819  | 164  | 2.30E-02 | 10  |
| GO:BP | leukocyte mediated cytotoxicity                                     | GO:0001909  | 99   | 2.30E-02 | 8   |
| TF    | Factor: JUNB:FOSB; motif: NRTGASTCAT                                | TF:M08920   | 2610 | 2.30E-02 | 52  |
| TF    | Factor: LUMAN; motif: CYCAGCYCY                                     | TF:M09729   | 9533 | 2.30E-02 | 139 |
| TF    | Factor: PLZF; motif: ACTKTANNTN                                     | TF:M04625   | 5075 | 2.30E-02 | 85  |
| TF    | Factor: TBR2; motif: NAGGTGTGAN                                     | TF:M12017   | 1044 | 2.30E-02 | 28  |
| TF    | Factor: AP-2rep; motif: CAGTGGG; match class: 1                     | TF:M00468_1 | 1409 | 2.30E-02 | 34  |
| TF    | Factor: TEF-3; motif: GNTATTTTT; match class: 1                     | TF:M07270_1 | 3552 | 2.30E-02 | 65  |
| TF    | Factor: LHX2; motif: NNYTAATTRNNN                                   | TF:M09976   | 1928 | 2.30E-02 | 42  |
| TF    | Factor: HTF4; motif: NCACCTGN                                       | TF:M11157   | 1601 | 2.30E-02 | 37  |
| GO:BP | production of molecular mediator involved in inflammatory response  | GO:0002532  | 72   | 2.40E-02 | 7   |
| GO:BP | detection of bacterium  | GO:0016045  | 14   | 2.40E-02 | 4   |
| GO:BP | negative regulation of leukocyte degranulation                      | GO:0043301  | 14   | 2.40E-02 | 4   |
| TF    | Factor: Tal-1; motif: CAGATGG                                       | TF:M03804   | 4459 | 2.40E-02 | 77  |
| TF    | Factor: C/EBP; motif: NNATTGCNNAANN; match class: 1                 | TF:M00190_1 | 1046 | 2.40E-02 | 28  |
| TF    | Factor: BCL-6; motif: NNCTTTCYAGGAA                                 | TF:M09874   | 2405 | 2.40E-02 | 49  |
| TF    | Factor: Fra-1; motif: NATGASTCAYM                                   | TF:M11284   | 2615 | 2.40E-02 | 52  |
| TF    | Factor: TTF-1; motif: NNNCAAGNRNN                                   | TF:M00794   | 4005 | 2.40E-02 | 71  |
| TF    | Factor: C/EBPgamma:Elf-1; motif: TKRCGHAATWSCGGAAGT; match class: 1 | TF:M08676_1 | 2065 | 2.40E-02 | 44  |
| TF    | Factor: CP2; motif: NTGNCTGGNN                                      | TF:M03868   | 4006 | 2.40E-02 | 71  |

|       |   |             |           |          |     |
|-------|---|-------------|-----------|----------|-----|
| GO:BP | positive regulation of complement activation                | GO:0045917  | 5         | 2.50E-02 | 3   |
| GO:BP | detection of bacterial lipoprotein                          | GO:0042494  | 5         | 2.50E-02 | 3   |
| GO:BP | microglial cell activation involved in immune response      | GO:0002282  | 5         | 2.50E-02 | 3   |
| GO:BP | positive regulation of neutrophil activation                | GO:1902565  | 5         | 2.50E-02 | 3   |
| GO:BP | positive regulation of peptidyl-tyrosine phosphorylation    | GO:0050731  | 166       | 2.50E-02 | 10  |
| GO:CC | actin cytoskeleton  | GO:0015629  | 484       | 2.50E-02 | 16  |
| TF    | Factor: HSF1; motif: GAANNTTCTNGN                           | TF:M07459   | 2902      | 2.50E-02 | 56  |
| TF    | Factor: T3R-beta; motif: NTGACCTNACGTGACCTYA                | TF:M11821   | 2134      | 2.50E-02 | 45  |
| TF    | Factor: NR1B2; motif: NAAAGGTCAN                            | TF:M11798   | 2760      | 2.50E-02 | 54  |
| TF    | Factor: JUND:FRA-1; motif: NRTGACTCAN                       | TF:M08929   | 1290      | 2.50E-02 | 32  |
| TF    | Factor: c-Ets-2; motif: NACCGAAGYRCTTCCGGTN; match class: 1 | TF:M11417_1 | 1273<br>4 | 2.50E-02 | 175 |
| TF    | Factor: LHX3; motif: ATTAAW; match class: 1                 | TF:M02097_1 | 5323      | 2.50E-02 | 88  |
| TF    | Factor: IRF-4; motif: RGGAASWGR; match class: 1             | TF:M04818_1 | 2691      | 2.50E-02 | 53  |
| TF    | Factor: MyoD; motif: CGNCAGSTGTTN                           | TF:M11183   | 3049      | 2.50E-02 | 58  |
| GO:BP | negative regulation of apoptotic process                    | GO:0043066  | 783       | 2.60E-02 | 23  |
| GO:BP | membrane organization                                       | GO:0061024  | 728       | 2.60E-02 | 22  |
| GO:BP | regulation of exocytosis                                    | GO:0017157  | 204       | 2.60E-02 | 11  |
| GO:BP | regulation of glial cell differentiation                    | GO:0045685  | 73        | 2.60E-02 | 7   |
| GO:CC | intracellular anatomical structure                          | GO:0005622  | 1426<br>9 | 2.60E-02 | 187 |
| TF    | Factor: Pbx-1; motif: ATCAATCAW                             | TF:M00096   | 2137      | 2.60E-02 | 45  |
| TF    | Factor: Oct-1; motif: NNGAATATKCANNNN                       | TF:M00136   | 3417      | 2.60E-02 | 63  |
| TF    | Factor: AREB6; motif: NNYYACCTGWVT                          | TF:M00412   | 3939      | 2.60E-02 | 70  |
| GO:BP | biological process involved in symbiotic interaction        | GO:0044403  | 244       | 2.70E-02 | 12  |
| GO:BP | negative regulation of macromolecule metabolic process      | GO:0010605  | 2662      | 2.70E-02 | 52  |
| TF    | Factor: TEF-1; motif: ACATTCCWSNN                           | TF:M07340   | 3273      | 2.70E-02 | 61  |
| TF    | Factor: GATA-3; motif: WGATAASN                             | TF:M08918   | 3568      | 2.70E-02 | 65  |

|       |  |                   |           |          |     |
|-------|--|-------------------|-----------|----------|-----|
| TF    | Factor: GATA3; motif: NGATAANN                             | TF:M03997         | 3568      | 2.70E-02 | 65  |
| TF    | Factor: HNF4alpha; motif: VTGAACCTTGMMB                    | TF:M00638         | 2348      | 2.70E-02 | 48  |
| TF    | Factor: ipf1; motif: TSNYCATANNNNNC                        | TF:M01013         | 2348      | 2.70E-02 | 48  |
| TF    | Factor: NRL; motif: NNNNTGCTGAC                            | TF:M04224         | 3869      | 2.70E-02 | 69  |
| TF    | Factor: SREBP-2; motif: ATCACMCCAY                         | TF:M11084         | 2770      | 2.70E-02 | 54  |
| GO:BP | biological process involved in interaction with host       | GO:0051701        | 168       | 2.80E-02 | 10  |
| GO:MF | CD4 receptor binding                                       | GO:0042609        | 8         | 2.80E-02 | 3   |
| GO:MF | inhibitory MHC class I receptor activity                   | GO:0032396        | 8         | 2.80E-02 | 3   |
| TF    | Factor: NR3C1; motif: NRGWACAYNRGTWCYN; match class: 1     | TF:M04476_1       | 4480      | 2.80E-02 | 77  |
| TF    | Factor: AR; motif: NGNACANNNTGTTCYNN                       | TF:M09589         | 4327      | 2.80E-02 | 75  |
| TF    | Factor: HSF1; motif: NTTCTRGAANNTTCY                       | TF:M07100         | 2844      | 2.80E-02 | 55  |
| TF    | Factor: CIZ; motif: TTTTNNNNNNNNNNNNNAAAAA                 | TF:M12070         | 2146      | 2.80E-02 | 45  |
| GO:BP | actin cytoskeleton organization                            | GO:0030036        | 680       | 2.90E-02 | 21  |
| REAC  | Toll Like Receptor 4 (TLR4) Cascade                        | REAC:R-HSA-166016 | 127       | 2.90E-02 | 8   |
| TF    | Factor: POU2F1:Elk-1; motif: ACCGGAWATGCAW                 | TF:M08398         | 7041      | 2.90E-02 | 109 |
| TF    | Factor: TAL1:GATA1; motif: NTTATCWNNNNNNNNNCAG             | TF:M07230         | 2991      | 2.90E-02 | 57  |
| TF    | Factor: ETF; motif: CCCCGCCCCYN                            | TF:M07039         | 1487<br>7 | 2.90E-02 | 198 |
| GO:BP | reactive oxygen species metabolic process                  | GO:0072593        | 207       | 3.00E-02 | 11  |
| TF    | Factor: NFATc2; motif: TTTTCCATGGAAA; match class: 1       | TF:M11985_1       | 3803      | 3.00E-02 | 68  |
| TF    | Factor: c-Ets; motif: KRCAGGAARTRNKT; match class: 1       | TF:M00340_1       | 718       | 3.00E-02 | 22  |
| TF    | Factor: CP2; motif: NNNNCCAGNCNN; match class: 1           | TF:M07602_1       | 4106      | 3.00E-02 | 72  |
| TF    | Factor: BCL-11A; motif: NAAAGAGGAAGTGARAN; match class: 1  | TF:M09595_1       | 413       | 3.00E-02 | 16  |
| TF    | Factor: CDP; motif: NNATYGATYN                             | TF:M11508         | 3068      | 3.00E-02 | 58  |
| GO:BP | positive regulation of nitrogen compound metabolic process | GO:0051173        | 2747      | 3.10E-02 | 53  |
| GO:BP | mature B cell differentiation                              | GO:0002335        | 30        | 3.10E-02 | 5   |

|       |  |             |       |          |     |
|-------|--|-------------|-------|----------|-----|
| GO:CC | apical part of cell                                  | GO:0045177  | 391   | 3.10E-02 | 14  |
| TF    | Factor: FXR:RXR-alpha; motif: CAAGGTSAWTAACC         | TF:M00631   | 2924  | 3.10E-02 | 56  |
| TF    | Factor: beta-catenin; motif: CTTTGATN                | TF:M07599   | 6721  | 3.10E-02 | 105 |
| TF    | Factor: Cdx-2; motif: NYMATAANN                      | TF:M10850   | 2154  | 3.10E-02 | 45  |
| TF    | Factor: POU4F3; motif: CTAATYW                       | TF:M07061   | 5993  | 3.10E-02 | 96  |
| TF    | Factor: TFF-1; motif: NNANCCACTTGAMNTT               | TF:M01312   | 4653  | 3.20E-02 | 79  |
| TF    | Factor: SRY; motif: AAACWAM; match class: 1          | TF:M00148_1 | 3665  | 3.30E-02 | 66  |
| TF    | Factor: C/EBPbeta; motif: NATTGCRYAAYN               | TF:M09597   | 2506  | 3.30E-02 | 50  |
| KEGG  | Human T-cell leukemia virus 1 infection              | KEGG:05166  | 208   | 3.40E-02 | 9   |
| TF    | Factor: ESR1; motif: STGACCTN                        | TF:M12602   | 2862  | 3.40E-02 | 55  |
| TF    | Factor: JunB; motif: NNNTGAGTCAY                     | TF:M09631   | 1628  | 3.40E-02 | 37  |
| TF    | Factor: HOXA5; motif: ANGNTAATTANCNNAN               | TF:M01452   | 3008  | 3.40E-02 | 57  |
| GO:BP | detection of stimulus                                | GO:0051606  | 337   | 3.50E-02 | 14  |
| GO:BP | negative regulation of hydrolase activity            | GO:0051346  | 293   | 3.50E-02 | 13  |
| TF    | Factor: Oct-1; motif: CWNATKWSATRYN                  | TF:M00162   | 2937  | 3.50E-02 | 56  |
| TF    | Factor: GATA-6; motif: WGATAACGATCW                  | TF:M12208   | 3449  | 3.50E-02 | 63  |
| TF    | Factor: AML2; motif: CCRACCAAYDN                     | TF:M01854   | 2372  | 3.50E-02 | 48  |
| TF    | Factor: NKX2-2; motif: NNNCCACTCAANN; match class: 1 | TF:M12456_1 | 2512  | 3.50E-02 | 50  |
| TF    | Factor: ZNF7; motif: NCYYTGYCWNCWCTTR                | TF:M12716   | 2166  | 3.60E-02 | 45  |
| GO:BP | cellular component disassembly                       | GO:0022411  | 432   | 3.70E-02 | 16  |
| GO:BP | Fc-gamma receptor signaling pathway                  | GO:0038094  | 31    | 3.70E-02 | 5   |
| TF    | Factor: HOXD4; motif: NYMATTAN                       | TF:M10712   | 3380  | 3.70E-02 | 62  |
| TF    | Factor: c-Ets-2; motif: NACCGGAAGYRCTTCCGGTN         | TF:M11417   | 12989 | 3.70E-02 | 177 |
| GO:BP | regeneration   | GO:0031099  | 174   | 3.80E-02 | 10  |
| TF    | Factor: NeuroD; motif: NNSCWGCTGNSY                  | TF:M01288   | 4210  | 3.80E-02 | 73  |
| TF    | Factor: PUR1; motif: GGGNCAGNN                       | TF:M01721   | 8254  | 3.80E-02 | 123 |

|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| TF    | Factor: NF-kappaB; motif: NGGGGAMTTCCNN                   | TF:M00194   | 2103 | 3.80E-02 | 44  |
| TF    | Factor: AP-4:Fl-1; motif: RSCGGAWRCAGSTGN                 | TF:M08445   | 8339 | 3.80E-02 | 124 |
| TF    | Factor: Sall1; motif: NGGTCCCKRGKRA                       | TF:M05467   | 3757 | 3.80E-02 | 67  |
| TF    | Factor: GR; motif: RGWACATWATGTWCY; match class: 1        | TF:M11847_1 | 3311 | 3.80E-02 | 61  |
| GO:BP | regulation of interleukin-10 production                   | GO:0032653  | 52   | 3.90E-02 | 6   |
| GO:BP | interleukin-10 production                                 | GO:0032613  | 52   | 3.90E-02 | 6   |
| GO:BP | negative regulation of developmental process              | GO:0051093  | 804  | 3.90E-02 | 23  |
| TF    | Factor: Brachyury; motif: NTNNCANNNNRGTGTGAANN            | TF:M09878   | 3240 | 3.90E-02 | 60  |
| TF    | Factor: HPX42B; motif: NNYAATTANN                         | TF:M10679   | 1770 | 3.90E-02 | 39  |
| TF    | Factor: Smad3; motif: NGNCAGACASNN; match class: 1        | TF:M01888_1 | 571  | 3.90E-02 | 19  |
| TF    | Factor: OCT-2; motif: ATGMATATGCWAAT                      | TF:M08836   | 2950 | 3.90E-02 | 56  |
| TF    | Factor: ipf1; motif: NVSTAATTAC                           | TF:M01235   | 2878 | 3.90E-02 | 55  |
| GO:BP | positive regulation of secretion by cell                  | GO:1903532  | 254  | 4.00E-02 | 12  |
| TF    | Factor: Brn-4; motif: NATTATGCAWGN                        | TF:M11921   | 1076 | 4.00E-02 | 28  |
| TF    | Factor: SF-1; motif: NYYCAAGGYCA                          | TF:M10084   | 3390 | 4.00E-02 | 62  |
| TF    | Factor: GSC2; motif: NNTAATCCNN                           | TF:M04325   | 3097 | 4.00E-02 | 58  |
| GO:MF | peptide antigen binding                                   | GO:0042605  | 23   | 4.10E-02 | 4   |
| GO:MF | polysaccharide binding                                    | GO:0030247  | 23   | 4.10E-02 | 4   |
| GO:BP | negative regulation of cell migration                     | GO:0030336  | 255  | 4.20E-02 | 12  |
| GO:CC | Fc-epsilon receptor I complex                             | GO:0032998  | 2    | 4.20E-02 | 2   |
| GO:CC | Fc receptor complex                                       | GO:0032997  | 2    | 4.20E-02 | 2   |
| GO:CC | integrin alphaL-beta2 complex                             | GO:0034687  | 2    | 4.20E-02 | 2   |
| GO:CC | integrin alphaM-beta2 complex                             | GO:0034688  | 2    | 4.20E-02 | 2   |
| GO:CC | Toll-like receptor 1-Toll-like receptor 2 protein complex | GO:0035354  | 2    | 4.20E-02 | 2   |
| GO:CC | macrophage migration inhibitory factor receptor complex   | GO:0035692  | 2    | 4.20E-02 | 2   |
| GO:MF | complement receptor activity                              | GO:0004875  | 9    | 4.20E-02 | 3   |



|       |   |             |      |          |     |
|-------|---|-------------|------|----------|-----|
| GO:MF | T cell receptor binding                                     | GO:0042608  | 9    | 4.20E-02 | 3   |
| TF    | Factor: SPI1; motif: NNNAAAGAGGAAGTGANNNN; match class: 1   | TF:M12497_1 | 134  | 4.20E-02 | 9   |
| TF    | Factor: FOXP1; motif: TNTGTTTMY                             | TF:M09933   | 4223 | 4.20E-02 | 73  |
| TF    | Factor: NF-1B; motif: KCCAGANWN; match class: 1             | TF:M08825_1 | 903  | 4.20E-02 | 25  |
| TF    | Factor: VDR; motif: GGGKNARNRRGGWSA                         | TF:M00444   | 9297 | 4.20E-02 | 135 |
| GO:BP | positive regulation of humoral immune response              | GO:0002922  | 16   | 4.30E-02 | 4   |
| GO:BP | regulation of T cell differentiation                        | GO:0045580  | 141  | 4.30E-02 | 9   |
| KEGG  | Fc epsilon RI signaling pathway                             | KEGG:04664  | 62   | 4.30E-02 | 5   |
| TF    | Factor: HNF3; motif: NNNNNTRTTTRYTYWNKN                     | TF:M01012   | 1910 | 4.30E-02 | 41  |
| TF    | Factor: Six-1; motif: CTCARRTTWCN                           | TF:M07466   | 2887 | 4.30E-02 | 55  |
| GO:BP | neutrophil mediated immunity                                | GO:0002446  | 32   | 4.40E-02 | 5   |
| GO:BP | positive regulation of cell death                           | GO:0010942  | 539  | 4.40E-02 | 18  |
| GO:MF | scavenger receptor activity                                 | GO:0005044  | 44   | 4.40E-02 | 5   |
| TF    | Factor: HOXA5; motif: ANGNTAATTANCNNAN; match class: 1      | TF:M01452_1 | 1143 | 4.40E-02 | 29  |
| TF    | Factor: HNF-3alpha; motif: NNYTAWGTAAACAAAN; match class: 1 | TF:M11568_1 | 170  | 4.40E-02 | 10  |
| TF    | Factor: CTCF; motif: ACCAGGKGGC                             | TF:M04727   | 5802 | 4.40E-02 | 93  |
| GO:BP | cellular response to external stimulus                      | GO:0071496  | 300  | 4.50E-02 | 13  |
| GO:BP | peptidyl-tyrosine phosphorylation                           | GO:0018108  | 345  | 4.50E-02 | 14  |
| KEGG  | Chagas disease  | KEGG:05142  | 95   | 4.50E-02 | 6   |
| TF    | Factor: Tbx20; motif: SGAGGTGTGAGGSGR                       | TF:M07474   | 3181 | 4.50E-02 | 59  |
| TF    | Factor: CDP; motif: ATCGATNNNNNNATCRAT                      | TF:M03951   | 3255 | 4.50E-02 | 60  |
| TF    | Factor: msc; motif: NRACAGCTGTYN                            | TF:M11145   | 1024 | 4.50E-02 | 27  |
| TF    | Factor: HOXB6; motif: NTAATKRC                              | TF:M10691   | 4386 | 4.50E-02 | 75  |
| TF    | Factor: NFATc2; motif: TTTTCCA; match class: 1              | TF:M02265_1 | 1650 | 4.50E-02 | 37  |
| TF    | Factor: MZF1; motif: NNAATCCCCANNN                          | TF:M12493   | 1330 | 4.50E-02 | 32  |
| GO:BP | integrin-mediated signaling pathway                         | GO:0007229  | 109  | 4.60E-02 | 8   |

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|-------|---|-------------|------|----------|----|
| KEGG  | Herpes simplex virus 1 infection                              | KEGG:05168  | 471  | 4.60E-02 | 14 |
| KEGG  | Viral protein interaction with cytokine and cytokine receptor | KEGG:04061  | 63   | 4.60E-02 | 5  |
| TF    | Factor: IRF-3; motif: GCNGTTTCCWGGAAACNGAAAC                  | TF:M11674   | 3929 | 4.60E-02 | 69 |
| TF    | Factor: POU2F1; motif: ANKNRWATGSAAWYAW; match class: 1       | TF:M10033_1 | 794  | 4.60E-02 | 23 |
| TF    | Factor: AR; motif: ARGAAACANNNTGTNC                           | TF:M07204   | 4006 | 4.60E-02 | 70 |
| GO:BP | phosphate-containing compound metabolic process               | GO:0006796  | 2574 | 4.70E-02 | 50 |
| GO:MF | virus receptor activity                                       | GO:0001618  | 71   | 4.70E-02 | 6  |
| TF    | Factor: CDX2; motif: NNGCAATAAANN                             | TF:M12513   | 2609 | 4.70E-02 | 51 |
| TF    | Factor: POU2F3; motif: NNAYGCTNATS                            | TF:M11903   | 1395 | 4.70E-02 | 33 |
| TF    | Factor: ZBRK1; motif: NGNNNGGTNAWAAAARRGCNG; match class: 1   | TF:M10468_1 | 3933 | 4.70E-02 | 69 |
| GO:BP | interleukin-12 production                                     | GO:0032615  | 54   | 4.80E-02 | 6  |
| GO:BP | regulation of interleukin-12 production                       | GO:0032655  | 54   | 4.80E-02 | 6  |
| TF    | Factor: Kaiso; motif: NTCCTGCNAN                              | TF:M01119   | 3633 | 4.80E-02 | 65 |
| TF    | Factor: POU3F2; motif: NWTGCATAAWTTA                          | TF:M04078   | 3189 | 4.80E-02 | 59 |
| TF    | Factor: EMX1; motif: NNTAATKANN                               | TF:M07988   | 2898 | 4.80E-02 | 55 |
| GO:BP | regulation of innate immune response                          | GO:0045088  | 218  | 4.90E-02 | 11 |
| GO:BP | positive regulation of lipoprotein particle clearance         | GO:0010986  | 6    | 4.90E-02 | 3  |
| GO:BP | membrane raft distribution                                    | GO:0031580  | 6    | 4.90E-02 | 3  |
| GO:BP | cellular response to bacterial lipoprotein                    | GO:0071220  | 6    | 4.90E-02 | 3  |
| GO:BP | response to bacterial lipopeptide                             | GO:0070339  | 6    | 4.90E-02 | 3  |
| GO:BP | cellular response to bacterial lipopeptide                    | GO:0071221  | 6    | 4.90E-02 | 3  |
| TF    | Factor: Blimp-1; motif: NAGKGAAAGTGN                          | TF:M12243   | 1721 | 4.90E-02 | 38 |
| TF    | Factor: Pit-1; motif: NMTCATAAWTATWNMNA; match class: 1       | TF:M00802_1 | 797  | 4.90E-02 | 23 |
| TF    | Factor: HSF2; motif: NGAANNWTCK                               | TF:M00147   | 4941 | 4.90E-02 | 82 |
| CORUM | C1q complex   | CORUM:6418  | 2    | 5.00E-02 | 2  |

|       |  |            |     |          |    |
|-------|--|------------|-----|----------|----|
| CORUM | TLR1-TLR2 complex                      | CORUM:7048 | 2   | 5.00E-02 | 2  |
| CORUM | TLR1-TLR2-lipoprotein complex          | CORUM:7049 | 2   | 5.00E-02 | 2  |
| GO:BP | peptidyl-tyrosine modification         | GO:0018212 | 348 | 5.00E-02 | 14 |
| GO:MF | arachidonate 5-lipoxygenase activity   | GO:0004051 | 2   | 5.00E-02 | 2  |
| GO:MF | chemokine (C-C motif) ligand 5 binding | GO:0071791 | 2   | 5.00E-02 | 2  |
| GO:MF | IgM binding                            | GO:0001791 | 2   | 5.00E-02 | 2  |

*Table A34. KCL BrainBank enrichment for Cluster 3 with gProfiler2. Term size refers to the number of genes in the term, with the intersection size denoting the number of genes in the dataset found in the term. GO:BP – Gene Ontology Biological Process, GO:CC – Gene Ontology Cellular Components, GO:MF – Gene Ontology Molecular Function, KEGG: Kyoto Encyclopaedia of Genes and Genomes, REAC: Reactome.*

| Dataset          | Sample ID        | Cluster One | Cluster Two | Cluster Three |
|------------------|------------------|-------------|-------------|---------------|
| TargetALS (case) | CGND.HRA.00217   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00359   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.02228   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.02233   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00223   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00366   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00587   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00615   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00089.2 | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.01517   | 0.0000      | 0.0000      | 1.0000        |
| TargetALS (case) | CGND.HRA.00604   | 0.0000      | 0.0002      | 0.9998        |
| TargetALS (case) | CGND.HRA.01574   | 0.0002      | 0.0000      | 0.9998        |
| TargetALS (case) | CGND.HRA.02239   | 0.0000      | 0.0002      | 0.9998        |
| TargetALS (case) | CGND.HRA.01403   | 0.0001      | 0.0003      | 0.9996        |
| TargetALS (case) | CGND.HRA.02227   | 0.0005      | 0.0001      | 0.9995        |
| TargetALS (case) | CGND.HRA.00225   | 0.0006      | 0.0000      | 0.9994        |
| TargetALS (case) | CGND.HRA.00083   | 0.0003      | 0.0010      | 0.9987        |
| TargetALS (case) | CGND.HRA.01586.2 | 0.0002      | 0.0020      | 0.9978        |
| TargetALS (case) | CGND.HRA.00334   | 0.0018      | 0.0012      | 0.9970        |
| TargetALS (case) | CGND.HRA.00603   | 0.0021      | 0.0022      | 0.9957        |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.02427 | 0.0416 | 0.0015 | 0.9569 |
| TargetALS (case) | CGND.HRA.01511 | 0.0011 | 0.0436 | 0.9553 |
| TargetALS (case) | CGND.HRA.00215 | 0.0719 | 0.0007 | 0.9275 |
| TargetALS (case) | CGND.HRA.01635 | 0.0811 | 0.0038 | 0.9151 |
| TargetALS (case) | CGND.HRA.02252 | 0.1130 | 0.0007 | 0.8863 |
| TargetALS (case) | CGND.HRA.00394 | 0.1197 | 0.0005 | 0.8797 |
| TargetALS (case) | CGND.HRA.00733 | 0.1476 | 0.0007 | 0.8516 |
| TargetALS (case) | CGND.HRA.01424 | 0.1467 | 0.0203 | 0.8330 |
| TargetALS (case) | CGND.HRA.00664 | 0.1718 | 0.0005 | 0.8276 |
| TargetALS (case) | CGND.HRA.00312 | 0.0120 | 0.1679 | 0.8201 |
| TargetALS (case) | CGND.HRA.00393 | 0.1993 | 0.0001 | 0.8006 |
| TargetALS (case) | CGND.HRA.00222 | 0.0027 | 0.2104 | 0.7869 |
| TargetALS (case) | CGND.HRA.00561 | 0.2119 | 0.0067 | 0.7814 |
| TargetALS (case) | CGND.HRA.00663 | 0.2177 | 0.0063 | 0.7760 |
| TargetALS (case) | CGND.HRA.02428 | 0.2436 | 0.0001 | 0.7563 |
| TargetALS (case) | CGND.HRA.00631 | 0.2443 | 0.0002 | 0.7555 |
| TargetALS (case) | CGND.HRA.01568 | 0.2543 | 0.0052 | 0.7405 |
| TargetALS (case) | CGND.HRA.01575 | 0.2639 | 0.0018 | 0.7343 |
| TargetALS (case) | CGND.HRA.00599 | 0.0026 | 0.2822 | 0.7152 |
| TargetALS (case) | CGND.HRA.01500 | 0.3084 | 0.0000 | 0.6916 |
| TargetALS (case) | CGND.HRA.00586 | 0.2600 | 0.1167 | 0.6233 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.01407 | 0.2472 | 0.1868 | 0.5661 |
| TargetALS (case) | CGND.HRA.00624 | 0.3666 | 0.1009 | 0.5325 |
| TargetALS (case) | CGND.HRA.00582 | 0.6016 | 0.0000 | 0.3984 |
| TargetALS (case) | CGND.HRA.00313 | 0.0619 | 0.6137 | 0.3245 |
| TargetALS (case) | CGND.HRA.00462 | 0.6421 | 0.0475 | 0.3104 |
| TargetALS (case) | CGND.HRA.00748 | 0.6507 | 0.0950 | 0.2543 |
| TargetALS (case) | CGND.HRA.02240 | 0.4191 | 0.3825 | 0.1984 |
| TargetALS (case) | CGND.HRA.00430 | 0.8144 | 0.0005 | 0.1851 |
| TargetALS (case) | CGND.HRA.00374 | 0.8247 | 0.0004 | 0.1749 |
| TargetALS (case) | CGND.HRA.01320 | 0.7792 | 0.0472 | 0.1736 |
| TargetALS (case) | CGND.HRA.00424 | 0.8274 | 0.0068 | 0.1659 |
| TargetALS (case) | CGND.HRA.01398 | 0.8417 | 0.0018 | 0.1565 |
| TargetALS (case) | CGND.HRA.00435 | 0.8915 | 0.0001 | 0.1084 |
| TargetALS (case) | CGND.HRA.00488 | 0.8930 | 0.0000 | 0.1069 |
| TargetALS (case) | CGND.HRA.00095 | 0.9025 | 0.0001 | 0.0974 |
| TargetALS (case) | CGND.HRA.00461 | 0.9128 | 0.0044 | 0.0827 |
| TargetALS (case) | CGND.HRA.01174 | 0.8919 | 0.0260 | 0.0821 |
| TargetALS (case) | CGND.HRA.00226 | 0.9246 | 0.0086 | 0.0669 |
| TargetALS (case) | CGND.HRA.01482 | 0.8987 | 0.0351 | 0.0662 |
| TargetALS (case) | CGND.HRA.00250 | 0.0262 | 0.9138 | 0.0600 |
| TargetALS (case) | CGND.HRA.00429 | 0.8988 | 0.0464 | 0.0548 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.01518 | 0.9474 | 0.0001 | 0.0525 |
| TargetALS (case) | CGND.HRA.00563 | 0.0014 | 0.9507 | 0.0480 |
| TargetALS (case) | CGND.HRA.01415 | 0.9531 | 0.0000 | 0.0469 |
| TargetALS (case) | CGND.HRA.00423 | 0.9591 | 0.0011 | 0.0399 |
| TargetALS (case) | CGND.HRA.01394 | 0.9610 | 0.0002 | 0.0388 |
| TargetALS (case) | CGND.HRA.02489 | 0.9662 | 0.0001 | 0.0336 |
| TargetALS (case) | CGND.HRA.00285 | 0.4111 | 0.5641 | 0.0248 |
| TargetALS (case) | CGND.HRA.01636 | 0.9683 | 0.0093 | 0.0224 |
| TargetALS (case) | CGND.HRA.00065 | 0.5498 | 0.4288 | 0.0215 |
| TargetALS (case) | CGND.HRA.01428 | 0.9009 | 0.0795 | 0.0196 |
| TargetALS (case) | CGND.HRA.00358 | 0.9682 | 0.0141 | 0.0177 |
| TargetALS (case) | CGND.HRA.00747 | 0.6360 | 0.3518 | 0.0122 |
| TargetALS (case) | CGND.HRA.01175 | 0.9114 | 0.0801 | 0.0085 |
| TargetALS (case) | CGND.HRA.02526 | 0.1310 | 0.8624 | 0.0066 |
| TargetALS (case) | CGND.HRA.00342 | 0.1379 | 0.8581 | 0.0040 |
| TargetALS (case) | CGND.HRA.01569 | 0.9959 | 0.0004 | 0.0036 |
| TargetALS (case) | CGND.HRA.00220 | 0.9943 | 0.0024 | 0.0033 |
| TargetALS (case) | CGND.HRA.00732 | 0.9952 | 0.0021 | 0.0026 |
| TargetALS (case) | CGND.HRA.01493 | 0.9968 | 0.0006 | 0.0026 |
| TargetALS (case) | CGND.HRA.00335 | 0.9191 | 0.0794 | 0.0015 |
| TargetALS (case) | CGND.HRA.00367 | 0.4251 | 0.5735 | 0.0014 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.00574 | 0.9234 | 0.0756 | 0.0010 |
| TargetALS (case) | CGND.HRA.02905 | 0.9988 | 0.0002 | 0.0010 |
| TargetALS (case) | CGND.HRA.00061 | 0.9860 | 0.0131 | 0.0008 |
| TargetALS (case) | CGND.HRA.02904 | 0.9989 | 0.0005 | 0.0007 |
| TargetALS (case) | CGND.HRA.00343 | 0.0080 | 0.9915 | 0.0005 |
| TargetALS (case) | CGND.HRA.01321 | 0.9953 | 0.0042 | 0.0005 |
| TargetALS (case) | CGND.HRA.01512 | 0.0669 | 0.9327 | 0.0004 |
| TargetALS (case) | CGND.HRA.00351 | 0.9935 | 0.0061 | 0.0004 |
| TargetALS (case) | CGND.HRA.00087 | 0.4071 | 0.5927 | 0.0003 |
| TargetALS (case) | CGND.HRA.02170 | 0.0031 | 0.9966 | 0.0003 |
| TargetALS (case) | CGND.HRA.02739 | 0.9997 | 0.0001 | 0.0003 |
| TargetALS (case) | CGND.HRA.00600 | 0.5374 | 0.4624 | 0.0003 |
| TargetALS (case) | CGND.HRA.02251 | 0.9327 | 0.0671 | 0.0002 |
| TargetALS (case) | CGND.HRA.00350 | 0.9997 | 0.0000 | 0.0002 |
| TargetALS (case) | CGND.HRA.01429 | 0.9998 | 0.0000 | 0.0002 |
| TargetALS (case) | CGND.HRA.00436 | 0.9979 | 0.0020 | 0.0002 |
| TargetALS (case) | CGND.HRA.00373 | 0.9998 | 0.0000 | 0.0002 |
| TargetALS (case) | CGND.HRA.01557 | 0.9998 | 0.0000 | 0.0001 |
| TargetALS (case) | CGND.HRA.00616 | 0.0934 | 0.9064 | 0.0001 |
| TargetALS (case) | CGND.HRA.01481 | 0.0434 | 0.9565 | 0.0001 |
| TargetALS (case) | CGND.HRA.00581 | 0.9998 | 0.0001 | 0.0001 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.00638 | 0.9845 | 0.0154 | 0.0001 |
| TargetALS (case) | CGND.HRA.01280 | 0.9998 | 0.0001 | 0.0001 |
| TargetALS (case) | CGND.HRA.00147 | 0.9999 | 0.0000 | 0.0001 |
| TargetALS (case) | CGND.HRA.00678 | 0.0362 | 0.9638 | 0.0001 |
| TargetALS (case) | CGND.HRA.00219 | 0.9998 | 0.0001 | 0.0001 |
| TargetALS (case) | CGND.HRA.01587 | 0.9694 | 0.0305 | 0.0001 |
| TargetALS (case) | CGND.HRA.00556 | 0.8843 | 0.1157 | 0.0000 |
| TargetALS (case) | CGND.HRA.01414 | 0.9999 | 0.0001 | 0.0000 |
| TargetALS (case) | CGND.HRA.02221 | 0.9999 | 0.0001 | 0.0000 |
| TargetALS (case) | CGND.HRA.00059 | 0.0050 | 0.9950 | 0.0000 |
| TargetALS (case) | CGND.HRA.02234 | 0.9999 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00252 | 0.8953 | 0.1047 | 0.0000 |
| TargetALS (case) | CGND.HRA.00575 | 0.9996 | 0.0004 | 0.0000 |
| TargetALS (case) | CGND.HRA.02171 | 0.0015 | 0.9985 | 0.0000 |
| TargetALS (case) | CGND.HRA.01629 | 0.9992 | 0.0008 | 0.0000 |
| TargetALS (case) | CGND.HRA.01279 | 0.9998 | 0.0002 | 0.0000 |
| TargetALS (case) | CGND.HRA.00134 | 0.9952 | 0.0048 | 0.0000 |
| TargetALS (case) | CGND.HRA.00055 | 0.0000 | 1.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00677 | 0.0533 | 0.9467 | 0.0000 |
| TargetALS (case) | CGND.HRA.00489 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00562 | 0.9936 | 0.0064 | 0.0000 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.00284 | 0.0321 | 0.9678 | 0.0000 |
| TargetALS (case) | CGND.HRA.02222 | 0.9996 | 0.0004 | 0.0000 |
| TargetALS (case) | CGND.HRA.02490 | 0.9999 | 0.0001 | 0.0000 |
| TargetALS (case) | CGND.HRA.01399 | 0.9806 | 0.0194 | 0.0000 |
| TargetALS (case) | CGND.HRA.02246 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00564 | 0.0000 | 1.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.02914 | 0.9964 | 0.0036 | 0.0000 |
| TargetALS (case) | CGND.HRA.01532 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01528 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01531 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00193 | 0.4984 | 0.5016 | 0.0000 |
| TargetALS (case) | CGND.HRA.00093 | 0.7809 | 0.2191 | 0.0000 |
| TargetALS (case) | CGND.HRA.00557 | 0.9959 | 0.0041 | 0.0000 |
| TargetALS (case) | CGND.HRA.02520 | 0.9962 | 0.0038 | 0.0000 |
| TargetALS (case) | CGND.HRA.02150 | 0.9999 | 0.0001 | 0.0000 |
| TargetALS (case) | CGND.HRA.00321 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00066 | 0.0000 | 1.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01505 | 0.0000 | 1.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01628 | 0.0003 | 0.9997 | 0.0000 |
| TargetALS (case) | CGND.HRA.00249 | 0.0008 | 0.9992 | 0.0000 |
| TargetALS (case) | CGND.HRA.00216 | 0.0313 | 0.9687 | 0.0000 |

|                  |                |        |        |        |
|------------------|----------------|--------|--------|--------|
| TargetALS (case) | CGND.HRA.01384 | 0.0592 | 0.9408 | 0.0000 |
| TargetALS (case) | CGND.HRA.01506 | 0.4441 | 0.5559 | 0.0000 |
| TargetALS (case) | CGND.HRA.02644 | 0.8966 | 0.1034 | 0.0000 |
| TargetALS (case) | CGND.HRA.00633 | 0.9712 | 0.0288 | 0.0000 |
| TargetALS (case) | CGND.HRA.00068 | 0.9762 | 0.0238 | 0.0000 |
| TargetALS (case) | CGND.HRA.00096 | 0.9858 | 0.0142 | 0.0000 |
| TargetALS (case) | CGND.HRA.02915 | 0.9919 | 0.0081 | 0.0000 |
| TargetALS (case) | CGND.HRA.01425 | 0.9973 | 0.0027 | 0.0000 |
| TargetALS (case) | CGND.HRA.00637 | 0.9976 | 0.0024 | 0.0000 |
| TargetALS (case) | CGND.HRA.01499 | 0.9986 | 0.0014 | 0.0000 |
| TargetALS (case) | CGND.HRA.01494 | 0.9988 | 0.0012 | 0.0000 |
| TargetALS (case) | CGND.HRA.01540 | 0.9992 | 0.0008 | 0.0000 |
| TargetALS (case) | CGND.HRA.02151 | 0.9998 | 0.0002 | 0.0000 |
| TargetALS (case) | CGND.HRA.00221 | 0.9999 | 0.0001 | 0.0000 |
| TargetALS (case) | CGND.HRA.01539 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01387 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.02740 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01524 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.01527 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.00320 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (case) | CGND.HRA.02245 | 1.0000 | 0.0000 | 0.0000 |

|                     |                |        |        |        |
|---------------------|----------------|--------|--------|--------|
| TargetALS (case)    | CGND.HRA.01386 | 1.0000 | 0.0000 | 0.0000 |
| TargetALS (control) | CGND.HRA.00063 | 0.0000 | 0.9944 | 0.0056 |
| TargetALS (control) | CGND.HRA.00091 | 0.9079 | 0.0280 | 0.0641 |
| TargetALS (control) | CGND.HRA.00218 | 0.2764 | 0.0001 | 0.7235 |
| TargetALS (control) | CGND.HRA.00224 | 0.0069 | 0.0000 | 0.9930 |
| TargetALS (control) | CGND.HRA.00467 | 0.2592 | 0.7275 | 0.0132 |
| TargetALS (control) | CGND.HRA.00477 | 0.9947 | 0.0048 | 0.0006 |
| TargetALS (control) | CGND.HRA.00478 | 0.8574 | 0.0023 | 0.1403 |
| TargetALS (control) | CGND.HRA.00590 | 0.9981 | 0.0018 | 0.0001 |
| TargetALS (control) | CGND.HRA.00594 | 0.4474 | 0.1307 | 0.4218 |
| TargetALS (control) | CGND.HRA.00595 | 0.8086 | 0.1777 | 0.0137 |
| TargetALS (control) | CGND.HRA.00596 | 0.9981 | 0.0019 | 0.0000 |
| TargetALS (control) | CGND.HRA.00644 | 0.3218 | 0.2746 | 0.4037 |
| TargetALS (control) | CGND.HRA.00646 | 0.0001 | 0.9987 | 0.0012 |
| TargetALS (control) | CGND.HRA.00647 | 0.0001 | 0.9923 | 0.0075 |
| TargetALS (control) | CGND.HRA.00658 | 0.9899 | 0.0100 | 0.0001 |
| TargetALS (control) | CGND.HRA.00659 | 0.9729 | 0.0263 | 0.0008 |
| TargetALS (control) | CGND.HRA.00660 | 0.9860 | 0.0022 | 0.0118 |
| TargetALS (control) | CGND.HRA.00661 | 0.9743 | 0.0216 | 0.0041 |
| TargetALS (control) | CGND.HRA.01180 | 0.9971 | 0.0003 | 0.0026 |
| TargetALS (control) | CGND.HRA.01181 | 0.9997 | 0.0001 | 0.0002 |

|                     |                |        |        |        |
|---------------------|----------------|--------|--------|--------|
| TargetALS (control) | CGND.HRA.01186 | 0.7127 | 0.2868 | 0.0005 |
| TargetALS (control) | CGND.HRA.01187 | 0.5971 | 0.4027 | 0.0002 |
| TargetALS (control) | CGND.HRA.01312 | 0.9721 | 0.0097 | 0.0183 |
| TargetALS (control) | CGND.HRA.01313 | 0.0024 | 0.0001 | 0.9975 |
| TargetALS (control) | CGND.HRA.01380 | 0.9882 | 0.0118 | 0.0001 |
| TargetALS (control) | CGND.HRA.01381 | 0.9931 | 0.0069 | 0.0000 |
| TargetALS (control) | CGND.HRA.01977 | 0.9998 | 0.0002 | 0.0000 |
| TargetALS (control) | CGND.HRA.01978 | 0.9919 | 0.0026 | 0.0055 |
| TargetALS (control) | CGND.HRA.02176 | 0.9999 | 0.0000 | 0.0001 |
| TargetALS (control) | CGND.HRA.02177 | 0.9996 | 0.0001 | 0.0003 |
| TargetALS (control) | CGND.HRA.02496 | 0.8171 | 0.0112 | 0.1717 |
| TargetALS (control) | CGND.HRA.02497 | 0.3176 | 0.0015 | 0.6809 |
| TargetALS (control) | CGND.HRA.02792 | 0.0886 | 0.0099 | 0.9015 |
| TargetALS (control) | CGND.HRA.02793 | 0.9527 | 0.0211 | 0.0262 |
| van Rheenen (case)  | GSM3077801     | 0.0037 | 0.0024 | 0.9939 |
| van Rheenen (case)  | GSM3078181     | 0.0107 | 0.0018 | 0.9876 |
| van Rheenen (case)  | GSM3078009     | 0.0150 | 0.0018 | 0.9831 |
| van Rheenen (case)  | GSM3078360     | 0.0188 | 0.0010 | 0.9803 |
| van Rheenen (case)  | GSM3078171     | 0.0511 | 0.0002 | 0.9487 |
| van Rheenen (case)  | GSM3077825     | 0.0360 | 0.0288 | 0.9352 |
| van Rheenen (case)  | GSM3077701     | 0.0591 | 0.0198 | 0.9211 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3077063 | 0.1036 | 0.0030 | 0.8934 |
| van Rheenen (case) | GSM3078169 | 0.1080 | 0.0013 | 0.8907 |
| van Rheenen (case) | GSM3077787 | 0.0056 | 0.1042 | 0.8902 |
| van Rheenen (case) | GSM3078387 | 0.1374 | 0.0108 | 0.8518 |
| van Rheenen (case) | GSM3078247 | 0.1339 | 0.0664 | 0.7997 |
| van Rheenen (case) | GSM3076775 | 0.1991 | 0.0080 | 0.7928 |
| van Rheenen (case) | GSM3078232 | 0.2814 | 0.0144 | 0.7042 |
| van Rheenen (case) | GSM3077663 | 0.1590 | 0.1394 | 0.7016 |
| van Rheenen (case) | GSM3076586 | 0.2931 | 0.0233 | 0.6836 |
| van Rheenen (case) | GSM3077792 | 0.2797 | 0.0523 | 0.6680 |
| van Rheenen (case) | GSM3078154 | 0.3290 | 0.0082 | 0.6628 |
| van Rheenen (case) | GSM3080153 | 0.3518 | 0.0010 | 0.6472 |
| van Rheenen (case) | GSM3080115 | 0.4577 | 0.0039 | 0.5384 |
| van Rheenen (case) | GSM3078258 | 0.4350 | 0.0283 | 0.5368 |
| van Rheenen (case) | GSM3079919 | 0.0362 | 0.4376 | 0.5263 |
| van Rheenen (case) | GSM3080127 | 0.1154 | 0.3588 | 0.5259 |
| van Rheenen (case) | GSM3080144 | 0.4786 | 0.0081 | 0.5134 |
| van Rheenen (case) | GSM3078304 | 0.4159 | 0.0740 | 0.5101 |
| van Rheenen (case) | GSM3079992 | 0.4114 | 0.0884 | 0.5002 |
| van Rheenen (case) | GSM3077141 | 0.5054 | 0.0002 | 0.4944 |
| van Rheenen (case) | GSM3078166 | 0.4804 | 0.0259 | 0.4938 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080102 | 0.5332 | 0.0107 | 0.4561 |
| van Rheenen (case) | GSM3077843 | 0.3086 | 0.2372 | 0.4542 |
| van Rheenen (case) | GSM3080108 | 0.4893 | 0.0700 | 0.4408 |
| van Rheenen (case) | GSM3078230 | 0.2677 | 0.2919 | 0.4404 |
| van Rheenen (case) | GSM3080109 | 0.5049 | 0.0624 | 0.4327 |
| van Rheenen (case) | GSM3076867 | 0.5569 | 0.0507 | 0.3924 |
| van Rheenen (case) | GSM3078011 | 0.6374 | 0.0000 | 0.3626 |
| van Rheenen (case) | GSM3080135 | 0.5016 | 0.1420 | 0.3565 |
| van Rheenen (case) | GSM3078242 | 0.6667 | 0.0023 | 0.3310 |
| van Rheenen (case) | GSM3079864 | 0.3975 | 0.2825 | 0.3200 |
| van Rheenen (case) | GSM3078176 | 0.5652 | 0.1214 | 0.3134 |
| van Rheenen (case) | GSM3078139 | 0.6918 | 0.0003 | 0.3080 |
| van Rheenen (case) | GSM3077827 | 0.6977 | 0.0024 | 0.3000 |
| van Rheenen (case) | GSM3080180 | 0.7062 | 0.0028 | 0.2910 |
| van Rheenen (case) | GSM3078335 | 0.1420 | 0.5710 | 0.2870 |
| van Rheenen (case) | GSM3077807 | 0.7227 | 0.0079 | 0.2694 |
| van Rheenen (case) | GSM3077061 | 0.7338 | 0.0186 | 0.2477 |
| van Rheenen (case) | GSM3078250 | 0.7408 | 0.0188 | 0.2404 |
| van Rheenen (case) | GSM3076821 | 0.7602 | 0.0032 | 0.2366 |
| van Rheenen (case) | GSM3076602 | 0.7629 | 0.0289 | 0.2082 |
| van Rheenen (case) | GSM3079763 | 0.6445 | 0.1476 | 0.2079 |



|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080105 | 0.7899 | 0.0029 | 0.2073 |
| van Rheenen (case) | GSM3080141 | 0.2733 | 0.5210 | 0.2057 |
| van Rheenen (case) | GSM3077366 | 0.5752 | 0.2264 | 0.1984 |
| van Rheenen (case) | GSM3080130 | 0.5239 | 0.2788 | 0.1974 |
| van Rheenen (case) | GSM3079849 | 0.7195 | 0.0884 | 0.1922 |
| van Rheenen (case) | GSM3076702 | 0.5332 | 0.2762 | 0.1906 |
| van Rheenen (case) | GSM3077804 | 0.8160 | 0.0133 | 0.1707 |
| van Rheenen (case) | GSM3080113 | 0.8291 | 0.0046 | 0.1663 |
| van Rheenen (case) | GSM3077426 | 0.5327 | 0.3012 | 0.1661 |
| van Rheenen (case) | GSM3079859 | 0.7555 | 0.0785 | 0.1660 |
| van Rheenen (case) | GSM3079993 | 0.7902 | 0.0457 | 0.1642 |
| van Rheenen (case) | GSM3079876 | 0.1340 | 0.7032 | 0.1628 |
| van Rheenen (case) | GSM3077975 | 0.0310 | 0.8099 | 0.1592 |
| van Rheenen (case) | GSM3076893 | 0.8184 | 0.0228 | 0.1587 |
| van Rheenen (case) | GSM3076994 | 0.8415 | 0.0023 | 0.1563 |
| van Rheenen (case) | GSM3078188 | 0.2632 | 0.5806 | 0.1562 |
| van Rheenen (case) | GSM3077704 | 0.8419 | 0.0067 | 0.1514 |
| van Rheenen (case) | GSM3078499 | 0.8579 | 0.0045 | 0.1376 |
| van Rheenen (case) | GSM3079913 | 0.4348 | 0.4279 | 0.1373 |
| van Rheenen (case) | GSM3077098 | 0.8612 | 0.0106 | 0.1282 |
| van Rheenen (case) | GSM3076832 | 0.8278 | 0.0469 | 0.1253 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3077227 | 0.8487 | 0.0262 | 0.1251 |
| van Rheenen (case) | GSM3076704 | 0.8709 | 0.0045 | 0.1245 |
| van Rheenen (case) | GSM3078234 | 0.8703 | 0.0156 | 0.1141 |
| van Rheenen (case) | GSM3079758 | 0.7136 | 0.1724 | 0.1140 |
| van Rheenen (case) | GSM3076647 | 0.8495 | 0.0412 | 0.1092 |
| van Rheenen (case) | GSM3080160 | 0.8175 | 0.0779 | 0.1047 |
| van Rheenen (case) | GSM3079841 | 0.1158 | 0.7811 | 0.1031 |
| van Rheenen (case) | GSM3078503 | 0.8965 | 0.0005 | 0.1029 |
| van Rheenen (case) | GSM3079890 | 0.7220 | 0.1789 | 0.0991 |
| van Rheenen (case) | GSM3078425 | 0.1305 | 0.7716 | 0.0979 |
| van Rheenen (case) | GSM3079851 | 0.9000 | 0.0034 | 0.0966 |
| van Rheenen (case) | GSM3078237 | 0.7455 | 0.1584 | 0.0961 |
| van Rheenen (case) | GSM3077112 | 0.8704 | 0.0337 | 0.0959 |
| van Rheenen (case) | GSM3078444 | 0.1233 | 0.7815 | 0.0952 |
| van Rheenen (case) | GSM3079891 | 0.8039 | 0.1015 | 0.0946 |
| van Rheenen (case) | GSM3080168 | 0.2405 | 0.6682 | 0.0914 |
| van Rheenen (case) | GSM3076842 | 0.9093 | 0.0044 | 0.0862 |
| van Rheenen (case) | GSM3076622 | 0.9121 | 0.0017 | 0.0862 |
| van Rheenen (case) | GSM3078497 | 0.8650 | 0.0496 | 0.0855 |
| van Rheenen (case) | GSM3077625 | 0.7189 | 0.1976 | 0.0835 |
| van Rheenen (case) | GSM3077364 | 0.8432 | 0.0746 | 0.0822 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079996 | 0.8422 | 0.0765 | 0.0813 |
| van Rheenen (case) | GSM3078038 | 0.0025 | 0.9208 | 0.0767 |
| van Rheenen (case) | GSM3077934 | 0.2723 | 0.6522 | 0.0755 |
| van Rheenen (case) | GSM3077114 | 0.9118 | 0.0156 | 0.0726 |
| van Rheenen (case) | GSM3077441 | 0.9111 | 0.0170 | 0.0719 |
| van Rheenen (case) | GSM3076729 | 0.9306 | 0.0000 | 0.0694 |
| van Rheenen (case) | GSM3079961 | 0.6985 | 0.2361 | 0.0654 |
| van Rheenen (case) | GSM3080134 | 0.8637 | 0.0712 | 0.0651 |
| van Rheenen (case) | GSM3076681 | 0.4997 | 0.4375 | 0.0629 |
| van Rheenen (case) | GSM3079920 | 0.9151 | 0.0224 | 0.0625 |
| van Rheenen (case) | GSM3078252 | 0.6968 | 0.2450 | 0.0582 |
| van Rheenen (case) | GSM3076901 | 0.9417 | 0.0004 | 0.0579 |
| van Rheenen (case) | GSM3077266 | 0.9111 | 0.0323 | 0.0566 |
| van Rheenen (case) | GSM3079870 | 0.9272 | 0.0178 | 0.0550 |
| van Rheenen (case) | GSM3078227 | 0.9474 | 0.0010 | 0.0516 |
| van Rheenen (case) | GSM3080028 | 0.7241 | 0.2272 | 0.0487 |
| van Rheenen (case) | GSM3076955 | 0.9415 | 0.0099 | 0.0486 |
| van Rheenen (case) | GSM3080149 | 0.9115 | 0.0404 | 0.0481 |
| van Rheenen (case) | GSM3076865 | 0.9390 | 0.0138 | 0.0472 |
| van Rheenen (case) | GSM3079823 | 0.9274 | 0.0265 | 0.0461 |
| van Rheenen (case) | GSM3079772 | 0.9194 | 0.0347 | 0.0458 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3077724 | 0.9526 | 0.0020 | 0.0454 |
| van Rheenen (case) | GSM3078178 | 0.9510 | 0.0041 | 0.0450 |
| van Rheenen (case) | GSM3080111 | 0.8830 | 0.0728 | 0.0443 |
| van Rheenen (case) | GSM3079960 | 0.9224 | 0.0335 | 0.0441 |
| van Rheenen (case) | GSM3080003 | 0.0805 | 0.8763 | 0.0432 |
| van Rheenen (case) | GSM3078068 | 0.8844 | 0.0724 | 0.0432 |
| van Rheenen (case) | GSM3078502 | 0.9554 | 0.0015 | 0.0431 |
| van Rheenen (case) | GSM3079834 | 0.9415 | 0.0167 | 0.0418 |
| van Rheenen (case) | GSM3076916 | 0.8389 | 0.1200 | 0.0411 |
| van Rheenen (case) | GSM3076843 | 0.9582 | 0.0026 | 0.0392 |
| van Rheenen (case) | GSM3077641 | 0.0219 | 0.9400 | 0.0382 |
| van Rheenen (case) | GSM3077721 | 0.9399 | 0.0223 | 0.0378 |
| van Rheenen (case) | GSM3076607 | 0.8571 | 0.1065 | 0.0364 |
| van Rheenen (case) | GSM3080006 | 0.7604 | 0.2039 | 0.0357 |
| van Rheenen (case) | GSM3078036 | 0.7817 | 0.1831 | 0.0352 |
| van Rheenen (case) | GSM3077246 | 0.6869 | 0.2782 | 0.0349 |
| van Rheenen (case) | GSM3076662 | 0.9660 | 0.0000 | 0.0340 |
| van Rheenen (case) | GSM3076798 | 0.9655 | 0.0008 | 0.0337 |
| van Rheenen (case) | GSM3080148 | 0.9636 | 0.0032 | 0.0332 |
| van Rheenen (case) | GSM3079989 | 0.9468 | 0.0204 | 0.0328 |
| van Rheenen (case) | GSM3077165 | 0.9674 | 0.0001 | 0.0325 |

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|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080023 | 0.7293 | 0.2391 | 0.0316 |
| van Rheenen (case) | GSM3078510 | 0.9536 | 0.0155 | 0.0309 |
| van Rheenen (case) | GSM3077079 | 0.9684 | 0.0010 | 0.0306 |
| van Rheenen (case) | GSM3076794 | 0.9694 | 0.0000 | 0.0306 |
| van Rheenen (case) | GSM3077008 | 0.9706 | 0.0001 | 0.0293 |
| van Rheenen (case) | GSM3079925 | 0.8076 | 0.1635 | 0.0289 |
| van Rheenen (case) | GSM3076929 | 0.6708 | 0.3007 | 0.0286 |
| van Rheenen (case) | GSM3080034 | 0.9547 | 0.0181 | 0.0272 |
| van Rheenen (case) | GSM3079812 | 0.8256 | 0.1477 | 0.0267 |
| van Rheenen (case) | GSM3079945 | 0.8680 | 0.1057 | 0.0262 |
| van Rheenen (case) | GSM3079779 | 0.9657 | 0.0087 | 0.0256 |
| van Rheenen (case) | GSM3078190 | 0.1535 | 0.8209 | 0.0256 |
| van Rheenen (case) | GSM3080119 | 0.9248 | 0.0499 | 0.0253 |
| van Rheenen (case) | GSM3078013 | 0.8779 | 0.0969 | 0.0252 |
| van Rheenen (case) | GSM3076753 | 0.9385 | 0.0375 | 0.0240 |
| van Rheenen (case) | GSM3077172 | 0.9503 | 0.0276 | 0.0222 |
| van Rheenen (case) | GSM3076767 | 0.9206 | 0.0574 | 0.0220 |
| van Rheenen (case) | GSM3079832 | 0.8527 | 0.1259 | 0.0215 |
| van Rheenen (case) | GSM3080124 | 0.9691 | 0.0099 | 0.0211 |
| van Rheenen (case) | GSM3077623 | 0.9462 | 0.0328 | 0.0210 |
| van Rheenen (case) | GSM3079985 | 0.8774 | 0.1027 | 0.0199 |

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|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080099 | 0.9792 | 0.0018 | 0.0190 |
| van Rheenen (case) | GSM3079803 | 0.9728 | 0.0086 | 0.0186 |
| van Rheenen (case) | GSM3076974 | 0.9761 | 0.0057 | 0.0182 |
| van Rheenen (case) | GSM3077679 | 0.1911 | 0.7919 | 0.0170 |
| van Rheenen (case) | GSM3077822 | 0.0012 | 0.9820 | 0.0168 |
| van Rheenen (case) | GSM3077919 | 0.0234 | 0.9604 | 0.0163 |
| van Rheenen (case) | GSM3077276 | 0.9838 | 0.0001 | 0.0161 |
| van Rheenen (case) | GSM3079740 | 0.9261 | 0.0588 | 0.0152 |
| van Rheenen (case) | GSM3076997 | 0.9846 | 0.0003 | 0.0151 |
| van Rheenen (case) | GSM3077303 | 0.9854 | 0.0000 | 0.0146 |
| van Rheenen (case) | GSM3079957 | 0.9843 | 0.0014 | 0.0143 |
| van Rheenen (case) | GSM3077076 | 0.7126 | 0.2732 | 0.0142 |
| van Rheenen (case) | GSM3077930 | 0.9758 | 0.0101 | 0.0141 |
| van Rheenen (case) | GSM3079982 | 0.9856 | 0.0004 | 0.0140 |
| van Rheenen (case) | GSM3079988 | 0.5253 | 0.4610 | 0.0137 |
| van Rheenen (case) | GSM3080120 | 0.9850 | 0.0017 | 0.0134 |
| van Rheenen (case) | GSM3080077 | 0.9606 | 0.0261 | 0.0133 |
| van Rheenen (case) | GSM3079824 | 0.9755 | 0.0125 | 0.0121 |
| van Rheenen (case) | GSM3079770 | 0.8340 | 0.1541 | 0.0120 |
| van Rheenen (case) | GSM3080019 | 0.8969 | 0.0912 | 0.0119 |
| van Rheenen (case) | GSM3077224 | 0.9780 | 0.0104 | 0.0117 |

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|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3076972 | 0.9833 | 0.0050 | 0.0117 |
| van Rheenen (case) | GSM3077170 | 0.9864 | 0.0023 | 0.0113 |
| van Rheenen (case) | GSM3077568 | 0.9799 | 0.0089 | 0.0112 |
| van Rheenen (case) | GSM3080125 | 0.9866 | 0.0025 | 0.0109 |
| van Rheenen (case) | GSM3079783 | 0.9450 | 0.0443 | 0.0107 |
| van Rheenen (case) | GSM3079857 | 0.9804 | 0.0088 | 0.0107 |
| van Rheenen (case) | GSM3080027 | 0.8016 | 0.1877 | 0.0107 |
| van Rheenen (case) | GSM3076877 | 0.9890 | 0.0004 | 0.0107 |
| van Rheenen (case) | GSM3080020 | 0.9659 | 0.0237 | 0.0104 |
| van Rheenen (case) | GSM3078505 | 0.9883 | 0.0014 | 0.0103 |
| van Rheenen (case) | GSM3076911 | 0.9878 | 0.0021 | 0.0102 |
| van Rheenen (case) | GSM3076661 | 0.9889 | 0.0009 | 0.0102 |
| van Rheenen (case) | GSM3078192 | 0.5481 | 0.4417 | 0.0101 |
| van Rheenen (case) | GSM3078495 | 0.9876 | 0.0028 | 0.0096 |
| van Rheenen (case) | GSM3078507 | 0.9804 | 0.0101 | 0.0095 |
| van Rheenen (case) | GSM3079863 | 0.9845 | 0.0068 | 0.0087 |
| van Rheenen (case) | GSM3079885 | 0.8337 | 0.1582 | 0.0081 |
| van Rheenen (case) | GSM3077473 | 0.9803 | 0.0116 | 0.0081 |
| van Rheenen (case) | GSM3079843 | 0.9864 | 0.0055 | 0.0081 |
| van Rheenen (case) | GSM3079881 | 0.9879 | 0.0040 | 0.0081 |
| van Rheenen (case) | GSM3079975 | 0.7033 | 0.2887 | 0.0081 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079896 | 0.9147 | 0.0773 | 0.0080 |
| van Rheenen (case) | GSM3076813 | 0.9832 | 0.0088 | 0.0080 |
| van Rheenen (case) | GSM3079926 | 0.7025 | 0.2896 | 0.0080 |
| van Rheenen (case) | GSM3080002 | 0.9875 | 0.0046 | 0.0080 |
| van Rheenen (case) | GSM3077650 | 0.6291 | 0.3631 | 0.0078 |
| van Rheenen (case) | GSM3077383 | 0.9706 | 0.0216 | 0.0077 |
| van Rheenen (case) | GSM3077344 | 0.9633 | 0.0290 | 0.0077 |
| van Rheenen (case) | GSM3077579 | 0.9910 | 0.0014 | 0.0076 |
| van Rheenen (case) | GSM3077582 | 0.9895 | 0.0031 | 0.0074 |
| van Rheenen (case) | GSM3078041 | 0.8119 | 0.1808 | 0.0073 |
| van Rheenen (case) | GSM3080059 | 0.7123 | 0.2805 | 0.0072 |
| van Rheenen (case) | GSM3076693 | 0.9916 | 0.0013 | 0.0071 |
| van Rheenen (case) | GSM3078390 | 0.0007 | 0.9924 | 0.0069 |
| van Rheenen (case) | GSM3080103 | 0.9474 | 0.0457 | 0.0069 |
| van Rheenen (case) | GSM3079785 | 0.8231 | 0.1700 | 0.0068 |
| van Rheenen (case) | GSM3079978 | 0.6573 | 0.3366 | 0.0061 |
| van Rheenen (case) | GSM3079908 | 0.9885 | 0.0054 | 0.0060 |
| van Rheenen (case) | GSM3079964 | 0.9001 | 0.0938 | 0.0060 |
| van Rheenen (case) | GSM3079897 | 0.9902 | 0.0039 | 0.0059 |
| van Rheenen (case) | GSM3076619 | 0.9921 | 0.0021 | 0.0058 |
| van Rheenen (case) | GSM3080074 | 0.9860 | 0.0083 | 0.0057 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079931 | 0.4950 | 0.4994 | 0.0056 |
| van Rheenen (case) | GSM3077269 | 0.9887 | 0.0057 | 0.0056 |
| van Rheenen (case) | GSM3076927 | 0.9859 | 0.0086 | 0.0055 |
| van Rheenen (case) | GSM3076951 | 0.9925 | 0.0021 | 0.0054 |
| van Rheenen (case) | GSM3076669 | 0.9934 | 0.0014 | 0.0052 |
| van Rheenen (case) | GSM3079829 | 0.9953 | 0.0001 | 0.0047 |
| van Rheenen (case) | GSM3079871 | 0.9642 | 0.0314 | 0.0044 |
| van Rheenen (case) | GSM3079974 | 0.7226 | 0.2730 | 0.0044 |
| van Rheenen (case) | GSM3076845 | 0.9868 | 0.0089 | 0.0044 |
| van Rheenen (case) | GSM3079756 | 0.9952 | 0.0005 | 0.0044 |
| van Rheenen (case) | GSM3077492 | 0.9877 | 0.0080 | 0.0043 |
| van Rheenen (case) | GSM3080012 | 0.9945 | 0.0013 | 0.0043 |
| van Rheenen (case) | GSM3080041 | 0.8487 | 0.1474 | 0.0039 |
| van Rheenen (case) | GSM3079953 | 0.9797 | 0.0165 | 0.0038 |
| van Rheenen (case) | GSM3080009 | 0.9952 | 0.0010 | 0.0037 |
| van Rheenen (case) | GSM3077428 | 0.8404 | 0.1560 | 0.0036 |
| van Rheenen (case) | GSM3079965 | 0.9931 | 0.0034 | 0.0035 |
| van Rheenen (case) | GSM3079765 | 0.9952 | 0.0013 | 0.0035 |
| van Rheenen (case) | GSM3080022 | 0.9901 | 0.0064 | 0.0035 |
| van Rheenen (case) | GSM3077203 | 0.9962 | 0.0005 | 0.0034 |
| van Rheenen (case) | GSM3078244 | 0.0215 | 0.9752 | 0.0033 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080056 | 0.9804 | 0.0163 | 0.0033 |
| van Rheenen (case) | GSM3076718 | 0.9967 | 0.0001 | 0.0032 |
| van Rheenen (case) | GSM3080054 | 0.9885 | 0.0084 | 0.0031 |
| van Rheenen (case) | GSM3076812 | 0.9967 | 0.0001 | 0.0031 |
| van Rheenen (case) | GSM3080072 | 0.9907 | 0.0063 | 0.0030 |
| van Rheenen (case) | GSM3079995 | 0.9811 | 0.0159 | 0.0030 |
| van Rheenen (case) | GSM3077539 | 0.8783 | 0.1188 | 0.0030 |
| van Rheenen (case) | GSM3077330 | 0.9623 | 0.0348 | 0.0030 |
| van Rheenen (case) | GSM3077469 | 0.8905 | 0.1066 | 0.0029 |
| van Rheenen (case) | GSM3080044 | 0.8822 | 0.1150 | 0.0029 |
| van Rheenen (case) | GSM3080067 | 0.3584 | 0.6388 | 0.0029 |
| van Rheenen (case) | GSM3077143 | 0.9972 | 0.0000 | 0.0028 |
| van Rheenen (case) | GSM3077030 | 0.9964 | 0.0008 | 0.0028 |
| van Rheenen (case) | GSM3080084 | 0.9105 | 0.0868 | 0.0027 |
| van Rheenen (case) | GSM3080029 | 0.8285 | 0.1688 | 0.0027 |
| van Rheenen (case) | GSM3079930 | 0.5759 | 0.4214 | 0.0027 |
| van Rheenen (case) | GSM3079877 | 0.9972 | 0.0003 | 0.0025 |
| van Rheenen (case) | GSM3079902 | 0.9071 | 0.0904 | 0.0025 |
| van Rheenen (case) | GSM3076679 | 0.9968 | 0.0008 | 0.0024 |
| van Rheenen (case) | GSM3077300 | 0.9975 | 0.0001 | 0.0024 |
| van Rheenen (case) | GSM3076584 | 0.9707 | 0.0270 | 0.0023 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3078255 | 0.0000 | 0.9978 | 0.0022 |
| van Rheenen (case) | GSM3076598 | 0.9945 | 0.0034 | 0.0021 |
| van Rheenen (case) | GSM3076683 | 0.9924 | 0.0055 | 0.0021 |
| van Rheenen (case) | GSM3077352 | 0.9973 | 0.0006 | 0.0021 |
| van Rheenen (case) | GSM3077325 | 0.9224 | 0.0756 | 0.0020 |
| van Rheenen (case) | GSM3077682 | 0.9516 | 0.0464 | 0.0020 |
| van Rheenen (case) | GSM3076708 | 0.9950 | 0.0031 | 0.0020 |
| van Rheenen (case) | GSM3080080 | 0.1054 | 0.8927 | 0.0019 |
| van Rheenen (case) | GSM3080087 | 0.9959 | 0.0023 | 0.0018 |
| van Rheenen (case) | GSM3079950 | 0.7720 | 0.2262 | 0.0018 |
| van Rheenen (case) | GSM3079794 | 0.9973 | 0.0010 | 0.0018 |
| van Rheenen (case) | GSM3076854 | 0.9957 | 0.0026 | 0.0017 |
| van Rheenen (case) | GSM3079742 | 0.9861 | 0.0123 | 0.0016 |
| van Rheenen (case) | GSM3076847 | 0.9979 | 0.0005 | 0.0016 |
| van Rheenen (case) | GSM3076956 | 0.9913 | 0.0071 | 0.0016 |
| van Rheenen (case) | GSM3076849 | 0.9680 | 0.0304 | 0.0016 |
| van Rheenen (case) | GSM3079958 | 0.8023 | 0.1962 | 0.0016 |
| van Rheenen (case) | GSM3076991 | 0.9976 | 0.0008 | 0.0016 |
| van Rheenen (case) | GSM3076823 | 0.9969 | 0.0016 | 0.0015 |
| van Rheenen (case) | GSM3077380 | 0.9980 | 0.0005 | 0.0015 |
| van Rheenen (case) | GSM3080098 | 0.6251 | 0.3734 | 0.0015 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079838 | 0.9884 | 0.0101 | 0.0015 |
| van Rheenen (case) | GSM3080000 | 0.0936 | 0.9050 | 0.0014 |
| van Rheenen (case) | GSM3076933 | 0.9984 | 0.0002 | 0.0014 |
| van Rheenen (case) | GSM3076899 | 0.9979 | 0.0007 | 0.0014 |
| van Rheenen (case) | GSM3080013 | 0.9631 | 0.0356 | 0.0013 |
| van Rheenen (case) | GSM3079751 | 0.9968 | 0.0020 | 0.0013 |
| van Rheenen (case) | GSM3076597 | 0.9984 | 0.0004 | 0.0013 |
| van Rheenen (case) | GSM3078174 | 0.9500 | 0.0488 | 0.0012 |
| van Rheenen (case) | GSM3077684 | 0.9818 | 0.0170 | 0.0012 |
| van Rheenen (case) | GSM3077251 | 0.9824 | 0.0164 | 0.0012 |
| van Rheenen (case) | GSM3076600 | 0.9978 | 0.0010 | 0.0012 |
| van Rheenen (case) | GSM3079914 | 0.6374 | 0.3615 | 0.0012 |
| van Rheenen (case) | GSM3077084 | 0.9989 | 0.0000 | 0.0011 |
| van Rheenen (case) | GSM3079807 | 0.9965 | 0.0024 | 0.0011 |
| van Rheenen (case) | GSM3079944 | 0.9788 | 0.0202 | 0.0011 |
| van Rheenen (case) | GSM3079867 | 0.2654 | 0.7336 | 0.0010 |
| van Rheenen (case) | GSM3077332 | 0.9737 | 0.0253 | 0.0010 |
| van Rheenen (case) | GSM3077408 | 0.9988 | 0.0002 | 0.0010 |
| van Rheenen (case) | GSM3077201 | 0.8979 | 0.1011 | 0.0010 |
| van Rheenen (case) | GSM3077386 | 0.9977 | 0.0013 | 0.0010 |
| van Rheenen (case) | GSM3077253 | 0.9681 | 0.0310 | 0.0009 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3076895 | 0.9438 | 0.0553 | 0.0009 |
| van Rheenen (case) | GSM3077281 | 0.9985 | 0.0007 | 0.0009 |
| van Rheenen (case) | GSM3077295 | 0.9944 | 0.0047 | 0.0009 |
| van Rheenen (case) | GSM3080075 | 0.5460 | 0.4532 | 0.0008 |
| van Rheenen (case) | GSM3080060 | 0.9918 | 0.0074 | 0.0008 |
| van Rheenen (case) | GSM3076891 | 0.9349 | 0.0644 | 0.0008 |
| van Rheenen (case) | GSM3077599 | 0.2301 | 0.7692 | 0.0008 |
| van Rheenen (case) | GSM3079776 | 0.9985 | 0.0007 | 0.0008 |
| van Rheenen (case) | GSM3077248 | 0.9985 | 0.0008 | 0.0007 |
| van Rheenen (case) | GSM3077790 | 0.9985 | 0.0008 | 0.0007 |
| van Rheenen (case) | GSM3077991 | 0.4690 | 0.5303 | 0.0007 |
| van Rheenen (case) | GSM3076880 | 0.9909 | 0.0084 | 0.0007 |
| van Rheenen (case) | GSM3077117 | 0.9977 | 0.0016 | 0.0007 |
| van Rheenen (case) | GSM3077278 | 0.9990 | 0.0003 | 0.0007 |
| van Rheenen (case) | GSM3077350 | 0.9403 | 0.0591 | 0.0007 |
| van Rheenen (case) | GSM3079749 | 0.9930 | 0.0064 | 0.0006 |
| van Rheenen (case) | GSM3080093 | 0.9938 | 0.0056 | 0.0006 |
| van Rheenen (case) | GSM3077368 | 0.9966 | 0.0028 | 0.0006 |
| van Rheenen (case) | GSM3077081 | 0.8706 | 0.1288 | 0.0006 |
| van Rheenen (case) | GSM3076617 | 0.9993 | 0.0002 | 0.0006 |
| van Rheenen (case) | GSM3079967 | 0.9969 | 0.0026 | 0.0005 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079827 | 0.9915 | 0.0080 | 0.0005 |
| van Rheenen (case) | GSM3079968 | 0.9929 | 0.0066 | 0.0005 |
| van Rheenen (case) | GSM3080039 | 0.9946 | 0.0049 | 0.0005 |
| van Rheenen (case) | GSM3077430 | 0.9967 | 0.0028 | 0.0005 |
| van Rheenen (case) | GSM3080139 | 0.9986 | 0.0009 | 0.0005 |
| van Rheenen (case) | GSM3080065 | 0.7843 | 0.2152 | 0.0005 |
| van Rheenen (case) | GSM3079979 | 0.9988 | 0.0007 | 0.0005 |
| van Rheenen (case) | GSM3077272 | 0.3263 | 0.6733 | 0.0005 |
| van Rheenen (case) | GSM3077027 | 0.9995 | 0.0001 | 0.0005 |
| van Rheenen (case) | GSM3079972 | 0.9951 | 0.0044 | 0.0005 |
| van Rheenen (case) | GSM3080086 | 0.9652 | 0.0344 | 0.0004 |
| van Rheenen (case) | GSM3079868 | 0.9322 | 0.0673 | 0.0004 |
| van Rheenen (case) | GSM3079954 | 0.9858 | 0.0138 | 0.0004 |
| van Rheenen (case) | GSM3076768 | 0.9993 | 0.0003 | 0.0004 |
| van Rheenen (case) | GSM3080015 | 0.8961 | 0.1035 | 0.0004 |
| van Rheenen (case) | GSM3076788 | 0.9992 | 0.0004 | 0.0004 |
| van Rheenen (case) | GSM3079907 | 0.4956 | 0.5040 | 0.0004 |
| van Rheenen (case) | GSM3076706 | 0.9996 | 0.0000 | 0.0004 |
| van Rheenen (case) | GSM3077274 | 0.9977 | 0.0019 | 0.0004 |
| van Rheenen (case) | GSM3076882 | 0.8545 | 0.1452 | 0.0004 |
| van Rheenen (case) | GSM3077643 | 0.9989 | 0.0008 | 0.0003 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3079986 | 0.9253 | 0.0744 | 0.0003 |
| van Rheenen (case) | GSM3077611 | 0.9958 | 0.0039 | 0.0003 |
| van Rheenen (case) | GSM3077563 | 0.9996 | 0.0001 | 0.0003 |
| van Rheenen (case) | GSM3080122 | 0.9967 | 0.0030 | 0.0003 |
| van Rheenen (case) | GSM3077994 | 0.9808 | 0.0189 | 0.0003 |
| van Rheenen (case) | GSM3076851 | 0.9966 | 0.0031 | 0.0003 |
| van Rheenen (case) | GSM3077542 | 0.9992 | 0.0005 | 0.0003 |
| van Rheenen (case) | GSM3077199 | 0.6307 | 0.3691 | 0.0003 |
| van Rheenen (case) | GSM3080064 | 0.9556 | 0.0442 | 0.0002 |
| van Rheenen (case) | GSM3077561 | 0.8935 | 0.1063 | 0.0002 |
| van Rheenen (case) | GSM3077707 | 0.9987 | 0.0011 | 0.0002 |
| van Rheenen (case) | GSM3077293 | 0.9996 | 0.0002 | 0.0002 |
| van Rheenen (case) | GSM3077566 | 0.7984 | 0.2015 | 0.0002 |
| van Rheenen (case) | GSM3079999 | 0.9963 | 0.0036 | 0.0002 |
| van Rheenen (case) | GSM3079971 | 0.9983 | 0.0016 | 0.0002 |
| van Rheenen (case) | GSM3077741 | 0.8315 | 0.1684 | 0.0002 |
| van Rheenen (case) | GSM3079789 | 0.4606 | 0.5393 | 0.0001 |
| van Rheenen (case) | GSM3080047 | 0.9770 | 0.0229 | 0.0001 |
| van Rheenen (case) | GSM3077647 | 0.3438 | 0.6561 | 0.0001 |
| van Rheenen (case) | GSM3080050 | 0.9928 | 0.0071 | 0.0001 |
| van Rheenen (case) | GSM3080069 | 0.9961 | 0.0038 | 0.0001 |

|                    |            |        |        |        |
|--------------------|------------|--------|--------|--------|
| van Rheenen (case) | GSM3080038 | 0.9875 | 0.0124 | 0.0001 |
| van Rheenen (case) | GSM3080043 | 0.9918 | 0.0081 | 0.0001 |
| van Rheenen (case) | GSM3076604 | 0.9998 | 0.0001 | 0.0001 |
| van Rheenen (case) | GSM3080061 | 0.8817 | 0.1182 | 0.0001 |
| van Rheenen (case) | GSM3077508 | 0.9998 | 0.0001 | 0.0001 |
| van Rheenen (case) | GSM3077971 | 0.9611 | 0.0389 | 0.0001 |
| van Rheenen (case) | GSM3079801 | 0.9990 | 0.0009 | 0.0001 |
| van Rheenen (case) | GSM3079981 | 0.9980 | 0.0020 | 0.0001 |
| van Rheenen (case) | GSM3076913 | 0.9972 | 0.0027 | 0.0001 |
| van Rheenen (case) | GSM3076897 | 0.9998 | 0.0002 | 0.0001 |
| van Rheenen (case) | GSM3079937 | 0.9810 | 0.0190 | 0.0001 |
| van Rheenen (case) | GSM3076796 | 0.9998 | 0.0001 | 0.0001 |
| van Rheenen (case) | GSM3077977 | 0.0021 | 0.9979 | 0.0000 |
| van Rheenen (case) | GSM3077476 | 0.9607 | 0.0393 | 0.0000 |
| van Rheenen (case) | GSM3076595 | 0.9856 | 0.0143 | 0.0000 |
| van Rheenen (case) | GSM3079875 | 0.9951 | 0.0049 | 0.0000 |
| van Rheenen (case) | GSM3079837 | 0.9999 | 0.0001 | 0.0000 |
| van Rheenen (case) | GSM3079936 | 0.6413 | 0.3587 | 0.0000 |
| van Rheenen (case) | GSM3076931 | 0.9852 | 0.0148 | 0.0000 |
| van Rheenen (case) | GSM3077101 | 0.9950 | 0.0050 | 0.0000 |
| van Rheenen (case) | GSM3080008 | 0.9966 | 0.0034 | 0.0000 |



|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (case)    | GSM3077627 | 0.9996 | 0.0004 | 0.0000 |
| van Rheenen (case)    | GSM3080070 | 0.9945 | 0.0054 | 0.0000 |
| van Rheenen (case)    | GSM3077916 | 0.9947 | 0.0053 | 0.0000 |
| van Rheenen (case)    | GSM3076863 | 0.9999 | 0.0001 | 0.0000 |
| van Rheenen (case)    | GSM3076582 | 0.5628 | 0.4372 | 0.0000 |
| van Rheenen (case)    | GSM3077334 | 0.9589 | 0.0411 | 0.0000 |
| van Rheenen (case)    | GSM3077032 | 0.9872 | 0.0128 | 0.0000 |
| van Rheenen (case)    | GSM3080057 | 0.9959 | 0.0041 | 0.0000 |
| van Rheenen (case)    | GSM3078342 | 0.0025 | 0.9976 | 0.0000 |
| van Rheenen (case)    | GSM3077841 | 0.9456 | 0.0544 | 0.0000 |
| van Rheenen (case)    | GSM3077665 | 0.9717 | 0.0283 | 0.0000 |
| van Rheenen (case)    | GSM3077096 | 0.9970 | 0.0030 | 0.0000 |
| van Rheenen (control) | GSM3076588 | 0.9557 | 0.0441 | 0.0002 |
| van Rheenen (control) | GSM3076590 | 0.9900 | 0.0099 | 0.0002 |
| van Rheenen (control) | GSM3076592 | 0.9106 | 0.0893 | 0.0001 |
| van Rheenen (control) | GSM3076593 | 0.9996 | 0.0003 | 0.0001 |
| van Rheenen (control) | GSM3076608 | 0.9955 | 0.0001 | 0.0045 |
| van Rheenen (control) | GSM3076611 | 0.9963 | 0.0003 | 0.0034 |
| van Rheenen (control) | GSM3076613 | 0.9967 | 0.0019 | 0.0015 |
| van Rheenen (control) | GSM3076615 | 0.9226 | 0.0076 | 0.0698 |
| van Rheenen (control) | GSM3076624 | 0.9785 | 0.0214 | 0.0001 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076627 | 0.9959 | 0.0038 | 0.0003 |
| van Rheenen (control) | GSM3076629 | 0.9923 | 0.0064 | 0.0014 |
| van Rheenen (control) | GSM3076631 | 0.9980 | 0.0011 | 0.0009 |
| van Rheenen (control) | GSM3076633 | 0.9972 | 0.0028 | 0.0001 |
| van Rheenen (control) | GSM3076635 | 0.9197 | 0.0796 | 0.0006 |
| van Rheenen (control) | GSM3076637 | 0.9990 | 0.0009 | 0.0001 |
| van Rheenen (control) | GSM3076640 | 0.9968 | 0.0027 | 0.0005 |
| van Rheenen (control) | GSM3076642 | 0.6360 | 0.3635 | 0.0005 |
| van Rheenen (control) | GSM3076644 | 0.9286 | 0.0675 | 0.0039 |
| van Rheenen (control) | GSM3076649 | 0.9891 | 0.0092 | 0.0017 |
| van Rheenen (control) | GSM3076651 | 0.9847 | 0.0146 | 0.0007 |
| van Rheenen (control) | GSM3076653 | 0.8794 | 0.1182 | 0.0025 |
| van Rheenen (control) | GSM3076655 | 0.9958 | 0.0003 | 0.0038 |
| van Rheenen (control) | GSM3076657 | 0.9705 | 0.0280 | 0.0014 |
| van Rheenen (control) | GSM3076659 | 0.9996 | 0.0003 | 0.0001 |
| van Rheenen (control) | GSM3076665 | 0.6860 | 0.0006 | 0.3134 |
| van Rheenen (control) | GSM3076667 | 0.9308 | 0.0648 | 0.0044 |
| van Rheenen (control) | GSM3076671 | 0.9999 | 0.0000 | 0.0000 |
| van Rheenen (control) | GSM3076673 | 0.9978 | 0.0002 | 0.0021 |
| van Rheenen (control) | GSM3076675 | 0.9916 | 0.0010 | 0.0074 |
| van Rheenen (control) | GSM3076677 | 0.9496 | 0.0487 | 0.0017 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076686 | 0.9960 | 0.0014 | 0.0026 |
| van Rheenen (control) | GSM3076688 | 0.9806 | 0.0003 | 0.0191 |
| van Rheenen (control) | GSM3076690 | 0.9895 | 0.0038 | 0.0067 |
| van Rheenen (control) | GSM3076692 | 0.7856 | 0.0041 | 0.2103 |
| van Rheenen (control) | GSM3076695 | 0.9639 | 0.0001 | 0.0359 |
| van Rheenen (control) | GSM3076697 | 0.7674 | 0.0001 | 0.2325 |
| van Rheenen (control) | GSM3076699 | 0.9874 | 0.0088 | 0.0038 |
| van Rheenen (control) | GSM3076701 | 0.8780 | 0.0042 | 0.1178 |
| van Rheenen (control) | GSM3076710 | 0.9986 | 0.0000 | 0.0013 |
| van Rheenen (control) | GSM3076712 | 0.9980 | 0.0007 | 0.0013 |
| van Rheenen (control) | GSM3076714 | 0.9024 | 0.0053 | 0.0923 |
| van Rheenen (control) | GSM3076716 | 0.8524 | 0.0213 | 0.1263 |
| van Rheenen (control) | GSM3076720 | 0.9552 | 0.0413 | 0.0035 |
| van Rheenen (control) | GSM3076722 | 0.2036 | 0.7864 | 0.0100 |
| van Rheenen (control) | GSM3076725 | 0.9870 | 0.0011 | 0.0119 |
| van Rheenen (control) | GSM3076727 | 0.9979 | 0.0011 | 0.0010 |
| van Rheenen (control) | GSM3076731 | 0.9957 | 0.0015 | 0.0028 |
| van Rheenen (control) | GSM3076733 | 0.9994 | 0.0002 | 0.0004 |
| van Rheenen (control) | GSM3076735 | 0.9837 | 0.0105 | 0.0058 |
| van Rheenen (control) | GSM3076737 | 0.9775 | 0.0122 | 0.0103 |
| van Rheenen (control) | GSM3076739 | 0.8713 | 0.0143 | 0.1143 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076741 | 0.9959 | 0.0010 | 0.0032 |
| van Rheenen (control) | GSM3076743 | 0.9821 | 0.0036 | 0.0144 |
| van Rheenen (control) | GSM3076746 | 0.9995 | 0.0001 | 0.0004 |
| van Rheenen (control) | GSM3076749 | 0.9921 | 0.0077 | 0.0002 |
| van Rheenen (control) | GSM3076751 | 0.9453 | 0.0271 | 0.0276 |
| van Rheenen (control) | GSM3076755 | 0.8916 | 0.0887 | 0.0198 |
| van Rheenen (control) | GSM3076757 | 0.8439 | 0.0000 | 0.1561 |
| van Rheenen (control) | GSM3076758 | 0.9709 | 0.0007 | 0.0284 |
| van Rheenen (control) | GSM3076760 | 0.9665 | 0.0019 | 0.0316 |
| van Rheenen (control) | GSM3076762 | 0.9332 | 0.0664 | 0.0004 |
| van Rheenen (control) | GSM3076763 | 0.9700 | 0.0027 | 0.0273 |
| van Rheenen (control) | GSM3076765 | 0.9901 | 0.0051 | 0.0049 |
| van Rheenen (control) | GSM3076770 | 0.9908 | 0.0002 | 0.0090 |
| van Rheenen (control) | GSM3076771 | 0.9972 | 0.0019 | 0.0010 |
| van Rheenen (control) | GSM3076772 | 0.9869 | 0.0023 | 0.0108 |
| van Rheenen (control) | GSM3076774 | 0.6542 | 0.0004 | 0.3454 |
| van Rheenen (control) | GSM3076777 | 0.9998 | 0.0001 | 0.0000 |
| van Rheenen (control) | GSM3076779 | 0.9890 | 0.0021 | 0.0089 |
| van Rheenen (control) | GSM3076780 | 0.9193 | 0.0389 | 0.0418 |
| van Rheenen (control) | GSM3076782 | 0.5238 | 0.4727 | 0.0034 |
| van Rheenen (control) | GSM3076784 | 0.8358 | 0.1506 | 0.0136 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076786 | 0.1951 | 0.0121 | 0.7927 |
| van Rheenen (control) | GSM3076789 | 0.9603 | 0.0375 | 0.0022 |
| van Rheenen (control) | GSM3076793 | 0.9013 | 0.0660 | 0.0328 |
| van Rheenen (control) | GSM3076800 | 0.9932 | 0.0040 | 0.0028 |
| van Rheenen (control) | GSM3076806 | 0.9925 | 0.0071 | 0.0003 |
| van Rheenen (control) | GSM3076808 | 0.9890 | 0.0050 | 0.0061 |
| van Rheenen (control) | GSM3076810 | 0.6699 | 0.0178 | 0.3123 |
| van Rheenen (control) | GSM3076815 | 0.9991 | 0.0001 | 0.0007 |
| van Rheenen (control) | GSM3076817 | 0.9810 | 0.0178 | 0.0012 |
| van Rheenen (control) | GSM3076818 | 0.9743 | 0.0240 | 0.0017 |
| van Rheenen (control) | GSM3076820 | 0.8194 | 0.0976 | 0.0830 |
| van Rheenen (control) | GSM3076824 | 0.9974 | 0.0013 | 0.0013 |
| van Rheenen (control) | GSM3076826 | 0.9723 | 0.0003 | 0.0274 |
| van Rheenen (control) | GSM3076828 | 0.9875 | 0.0082 | 0.0043 |
| van Rheenen (control) | GSM3076830 | 0.9596 | 0.0257 | 0.0146 |
| van Rheenen (control) | GSM3076834 | 0.9658 | 0.0007 | 0.0334 |
| van Rheenen (control) | GSM3076836 | 0.9987 | 0.0010 | 0.0003 |
| van Rheenen (control) | GSM3076837 | 0.9889 | 0.0008 | 0.0103 |
| van Rheenen (control) | GSM3076839 | 0.9958 | 0.0033 | 0.0009 |
| van Rheenen (control) | GSM3076856 | 0.9965 | 0.0033 | 0.0002 |
| van Rheenen (control) | GSM3076858 | 0.9816 | 0.0031 | 0.0153 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076860 | 0.9982 | 0.0006 | 0.0012 |
| van Rheenen (control) | GSM3076862 | 0.9516 | 0.0003 | 0.0482 |
| van Rheenen (control) | GSM3076869 | 0.9875 | 0.0002 | 0.0123 |
| van Rheenen (control) | GSM3076871 | 0.9752 | 0.0007 | 0.0241 |
| van Rheenen (control) | GSM3076873 | 0.9199 | 0.0756 | 0.0045 |
| van Rheenen (control) | GSM3076875 | 0.9725 | 0.0028 | 0.0247 |
| van Rheenen (control) | GSM3076879 | 0.7857 | 0.1520 | 0.0623 |
| van Rheenen (control) | GSM3076884 | 0.9276 | 0.0720 | 0.0004 |
| van Rheenen (control) | GSM3076886 | 0.7048 | 0.2948 | 0.0004 |
| van Rheenen (control) | GSM3076888 | 0.9479 | 0.0515 | 0.0006 |
| van Rheenen (control) | GSM3076889 | 0.6252 | 0.3693 | 0.0055 |
| van Rheenen (control) | GSM3076903 | 0.8890 | 0.1103 | 0.0007 |
| van Rheenen (control) | GSM3076905 | 0.9694 | 0.0292 | 0.0015 |
| van Rheenen (control) | GSM3076907 | 0.9968 | 0.0026 | 0.0006 |
| van Rheenen (control) | GSM3076910 | 0.9977 | 0.0023 | 0.0000 |
| van Rheenen (control) | GSM3076918 | 0.9950 | 0.0003 | 0.0048 |
| van Rheenen (control) | GSM3076920 | 0.9925 | 0.0049 | 0.0026 |
| van Rheenen (control) | GSM3076923 | 0.9777 | 0.0207 | 0.0016 |
| van Rheenen (control) | GSM3076925 | 0.8678 | 0.1321 | 0.0002 |
| van Rheenen (control) | GSM3076935 | 0.9692 | 0.0255 | 0.0053 |
| van Rheenen (control) | GSM3076937 | 0.9998 | 0.0002 | 0.0000 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076939 | 0.9996 | 0.0002 | 0.0002 |
| van Rheenen (control) | GSM3076941 | 0.9988 | 0.0006 | 0.0006 |
| van Rheenen (control) | GSM3076943 | 0.9525 | 0.0448 | 0.0027 |
| van Rheenen (control) | GSM3076945 | 0.9971 | 0.0007 | 0.0022 |
| van Rheenen (control) | GSM3076947 | 0.9646 | 0.0169 | 0.0185 |
| van Rheenen (control) | GSM3076949 | 0.9118 | 0.0658 | 0.0224 |
| van Rheenen (control) | GSM3076958 | 0.9901 | 0.0095 | 0.0004 |
| van Rheenen (control) | GSM3076959 | 0.9979 | 0.0016 | 0.0005 |
| van Rheenen (control) | GSM3076961 | 0.8322 | 0.0335 | 0.1343 |
| van Rheenen (control) | GSM3076963 | 0.9234 | 0.0760 | 0.0007 |
| van Rheenen (control) | GSM3076964 | 0.9717 | 0.0000 | 0.0283 |
| van Rheenen (control) | GSM3076966 | 0.7570 | 0.1424 | 0.1006 |
| van Rheenen (control) | GSM3076969 | 0.9890 | 0.0017 | 0.0093 |
| van Rheenen (control) | GSM3076971 | 0.8500 | 0.1497 | 0.0003 |
| van Rheenen (control) | GSM3076976 | 0.6441 | 0.0165 | 0.3394 |
| van Rheenen (control) | GSM3076978 | 0.9063 | 0.0920 | 0.0017 |
| van Rheenen (control) | GSM3076980 | 0.9999 | 0.0001 | 0.0000 |
| van Rheenen (control) | GSM3076982 | 0.8810 | 0.1178 | 0.0012 |
| van Rheenen (control) | GSM3076984 | 0.9885 | 0.0054 | 0.0061 |
| van Rheenen (control) | GSM3076985 | 0.9492 | 0.0009 | 0.0499 |
| van Rheenen (control) | GSM3076986 | 0.9650 | 0.0009 | 0.0341 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3076989 | 0.9758 | 0.0003 | 0.0239 |
| van Rheenen (control) | GSM3076999 | 0.5247 | 0.0008 | 0.4745 |
| van Rheenen (control) | GSM3077002 | 0.9991 | 0.0000 | 0.0009 |
| van Rheenen (control) | GSM3077004 | 0.9974 | 0.0014 | 0.0011 |
| van Rheenen (control) | GSM3077006 | 0.7489 | 0.0215 | 0.2296 |
| van Rheenen (control) | GSM3077015 | 0.9866 | 0.0113 | 0.0020 |
| van Rheenen (control) | GSM3077018 | 0.9901 | 0.0013 | 0.0086 |
| van Rheenen (control) | GSM3077022 | 0.9997 | 0.0001 | 0.0002 |
| van Rheenen (control) | GSM3077024 | 0.9989 | 0.0002 | 0.0009 |
| van Rheenen (control) | GSM3077035 | 0.9977 | 0.0016 | 0.0007 |
| van Rheenen (control) | GSM3077037 | 0.9150 | 0.0007 | 0.0843 |
| van Rheenen (control) | GSM3077039 | 0.9969 | 0.0006 | 0.0024 |
| van Rheenen (control) | GSM3077042 | 0.9923 | 0.0011 | 0.0066 |
| van Rheenen (control) | GSM3077044 | 0.9685 | 0.0003 | 0.0312 |
| van Rheenen (control) | GSM3077047 | 0.9552 | 0.0120 | 0.0328 |
| van Rheenen (control) | GSM3077050 | 0.8606 | 0.0001 | 0.1393 |
| van Rheenen (control) | GSM3077052 | 0.9986 | 0.0007 | 0.0007 |
| van Rheenen (control) | GSM3077055 | 0.9998 | 0.0000 | 0.0002 |
| van Rheenen (control) | GSM3077059 | 0.9349 | 0.0516 | 0.0135 |
| van Rheenen (control) | GSM3077066 | 0.9717 | 0.0074 | 0.0209 |
| van Rheenen (control) | GSM3077068 | 0.9949 | 0.0011 | 0.0040 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077071 | 0.4049 | 0.5113 | 0.0839 |
| van Rheenen (control) | GSM3077073 | 0.7810 | 0.0343 | 0.1846 |
| van Rheenen (control) | GSM3077086 | 0.9878 | 0.0121 | 0.0000 |
| van Rheenen (control) | GSM3077088 | 0.9996 | 0.0003 | 0.0001 |
| van Rheenen (control) | GSM3077090 | 0.9992 | 0.0002 | 0.0006 |
| van Rheenen (control) | GSM3077093 | 0.9208 | 0.0789 | 0.0003 |
| van Rheenen (control) | GSM3077103 | 0.9871 | 0.0001 | 0.0128 |
| van Rheenen (control) | GSM3077105 | 0.9538 | 0.0000 | 0.0462 |
| van Rheenen (control) | GSM3077107 | 0.9915 | 0.0001 | 0.0084 |
| van Rheenen (control) | GSM3077110 | 0.9804 | 0.0001 | 0.0195 |
| van Rheenen (control) | GSM3077119 | 0.7047 | 0.0006 | 0.2947 |
| van Rheenen (control) | GSM3077122 | 0.5172 | 0.0009 | 0.4819 |
| van Rheenen (control) | GSM3077124 | 0.9925 | 0.0024 | 0.0051 |
| van Rheenen (control) | GSM3077129 | 0.9991 | 0.0006 | 0.0003 |
| van Rheenen (control) | GSM3077133 | 0.9843 | 0.0155 | 0.0002 |
| van Rheenen (control) | GSM3077134 | 0.9837 | 0.0010 | 0.0153 |
| van Rheenen (control) | GSM3077136 | 0.9955 | 0.0038 | 0.0008 |
| van Rheenen (control) | GSM3077138 | 0.9720 | 0.0101 | 0.0179 |
| van Rheenen (control) | GSM3077146 | 0.9998 | 0.0001 | 0.0001 |
| van Rheenen (control) | GSM3077148 | 0.9976 | 0.0022 | 0.0002 |
| van Rheenen (control) | GSM3077150 | 0.9947 | 0.0002 | 0.0051 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077153 | 0.9764 | 0.0167 | 0.0069 |
| van Rheenen (control) | GSM3077156 | 0.9944 | 0.0014 | 0.0041 |
| van Rheenen (control) | GSM3077158 | 0.8224 | 0.0032 | 0.1743 |
| van Rheenen (control) | GSM3077160 | 0.9997 | 0.0000 | 0.0003 |
| van Rheenen (control) | GSM3077162 | 0.9946 | 0.0004 | 0.0050 |
| van Rheenen (control) | GSM3077174 | 0.9964 | 0.0013 | 0.0023 |
| van Rheenen (control) | GSM3077177 | 0.9859 | 0.0007 | 0.0135 |
| van Rheenen (control) | GSM3077179 | 0.9908 | 0.0001 | 0.0091 |
| van Rheenen (control) | GSM3077189 | 0.9980 | 0.0001 | 0.0019 |
| van Rheenen (control) | GSM3077192 | 0.9433 | 0.0529 | 0.0038 |
| van Rheenen (control) | GSM3077194 | 0.9908 | 0.0084 | 0.0008 |
| van Rheenen (control) | GSM3077196 | 0.0134 | 0.0015 | 0.9851 |
| van Rheenen (control) | GSM3077205 | 0.9987 | 0.0013 | 0.0000 |
| van Rheenen (control) | GSM3077209 | 0.5748 | 0.3857 | 0.0395 |
| van Rheenen (control) | GSM3077211 | 0.9625 | 0.0034 | 0.0341 |
| van Rheenen (control) | GSM3077213 | 0.4431 | 0.5379 | 0.0190 |
| van Rheenen (control) | GSM3077215 | 0.9888 | 0.0106 | 0.0007 |
| van Rheenen (control) | GSM3077217 | 0.9862 | 0.0114 | 0.0024 |
| van Rheenen (control) | GSM3077219 | 0.9841 | 0.0152 | 0.0007 |
| van Rheenen (control) | GSM3077221 | 0.9837 | 0.0162 | 0.0001 |
| van Rheenen (control) | GSM3077229 | 0.6156 | 0.3616 | 0.0228 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077231 | 0.9494 | 0.0452 | 0.0053 |
| van Rheenen (control) | GSM3077240 | 0.9719 | 0.0138 | 0.0143 |
| van Rheenen (control) | GSM3077244 | 0.9887 | 0.0080 | 0.0033 |
| van Rheenen (control) | GSM3077254 | 0.7748 | 0.2188 | 0.0064 |
| van Rheenen (control) | GSM3077256 | 0.4815 | 0.5184 | 0.0000 |
| van Rheenen (control) | GSM3077259 | 0.9959 | 0.0041 | 0.0000 |
| van Rheenen (control) | GSM3077261 | 0.9960 | 0.0027 | 0.0013 |
| van Rheenen (control) | GSM3077283 | 0.9984 | 0.0002 | 0.0014 |
| van Rheenen (control) | GSM3077285 | 0.9975 | 0.0018 | 0.0007 |
| van Rheenen (control) | GSM3077287 | 0.9243 | 0.0000 | 0.0757 |
| van Rheenen (control) | GSM3077290 | 0.9899 | 0.0002 | 0.0099 |
| van Rheenen (control) | GSM3077305 | 0.9817 | 0.0001 | 0.0181 |
| van Rheenen (control) | GSM3077307 | 0.9988 | 0.0009 | 0.0003 |
| van Rheenen (control) | GSM3077311 | 0.9983 | 0.0006 | 0.0011 |
| van Rheenen (control) | GSM3077313 | 0.0494 | 0.0000 | 0.9506 |
| van Rheenen (control) | GSM3077315 | 0.9776 | 0.0223 | 0.0001 |
| van Rheenen (control) | GSM3077318 | 0.9991 | 0.0005 | 0.0004 |
| van Rheenen (control) | GSM3077321 | 0.9887 | 0.0046 | 0.0067 |
| van Rheenen (control) | GSM3077323 | 0.9907 | 0.0076 | 0.0017 |
| van Rheenen (control) | GSM3077336 | 0.9891 | 0.0109 | 0.0000 |
| van Rheenen (control) | GSM3077338 | 0.5075 | 0.4917 | 0.0008 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077340 | 0.9941 | 0.0042 | 0.0018 |
| van Rheenen (control) | GSM3077342 | 0.9751 | 0.0111 | 0.0139 |
| van Rheenen (control) | GSM3077355 | 0.9917 | 0.0030 | 0.0053 |
| van Rheenen (control) | GSM3077357 | 0.1932 | 0.8043 | 0.0025 |
| van Rheenen (control) | GSM3077359 | 0.9477 | 0.0514 | 0.0009 |
| van Rheenen (control) | GSM3077361 | 0.7966 | 0.0508 | 0.1526 |
| van Rheenen (control) | GSM3077370 | 0.9998 | 0.0000 | 0.0001 |
| van Rheenen (control) | GSM3077372 | 0.6931 | 0.2892 | 0.0177 |
| van Rheenen (control) | GSM3077374 | 0.6701 | 0.0009 | 0.3290 |
| van Rheenen (control) | GSM3077377 | 0.6990 | 0.1886 | 0.1124 |
| van Rheenen (control) | GSM3077388 | 0.8165 | 0.0180 | 0.1656 |
| van Rheenen (control) | GSM3077391 | 0.7282 | 0.2716 | 0.0002 |
| van Rheenen (control) | GSM3077393 | 0.8744 | 0.1248 | 0.0008 |
| van Rheenen (control) | GSM3077396 | 0.0584 | 0.5037 | 0.4378 |
| van Rheenen (control) | GSM3077398 | 0.9963 | 0.0034 | 0.0003 |
| van Rheenen (control) | GSM3077401 | 0.9415 | 0.0037 | 0.0548 |
| van Rheenen (control) | GSM3077404 | 0.9367 | 0.0289 | 0.0345 |
| van Rheenen (control) | GSM3077406 | 0.1610 | 0.0002 | 0.8388 |
| van Rheenen (control) | GSM3077410 | 0.9813 | 0.0078 | 0.0110 |
| van Rheenen (control) | GSM3077412 | 0.9963 | 0.0019 | 0.0018 |
| van Rheenen (control) | GSM3077414 | 0.9975 | 0.0019 | 0.0006 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077416 | 0.9672 | 0.0320 | 0.0008 |
| van Rheenen (control) | GSM3077419 | 0.9981 | 0.0015 | 0.0005 |
| van Rheenen (control) | GSM3077422 | 0.9885 | 0.0114 | 0.0001 |
| van Rheenen (control) | GSM3077424 | 0.8683 | 0.0085 | 0.1232 |
| van Rheenen (control) | GSM3077425 | 0.1070 | 0.8921 | 0.0010 |
| van Rheenen (control) | GSM3077449 | 0.9633 | 0.0203 | 0.0164 |
| van Rheenen (control) | GSM3077452 | 0.0988 | 0.9009 | 0.0002 |
| van Rheenen (control) | GSM3077454 | 0.5607 | 0.4346 | 0.0047 |
| van Rheenen (control) | GSM3077456 | 0.9778 | 0.0115 | 0.0108 |
| van Rheenen (control) | GSM3077459 | 0.7200 | 0.2787 | 0.0013 |
| van Rheenen (control) | GSM3077461 | 0.7288 | 0.0605 | 0.2106 |
| van Rheenen (control) | GSM3077464 | 0.9740 | 0.0057 | 0.0203 |
| van Rheenen (control) | GSM3077467 | 0.9725 | 0.0273 | 0.0001 |
| van Rheenen (control) | GSM3077483 | 0.5580 | 0.2189 | 0.2231 |
| van Rheenen (control) | GSM3077485 | 0.2182 | 0.3735 | 0.4083 |
| van Rheenen (control) | GSM3077487 | 0.8029 | 0.1969 | 0.0002 |
| van Rheenen (control) | GSM3077489 | 0.9933 | 0.0012 | 0.0056 |
| van Rheenen (control) | GSM3077495 | 0.9622 | 0.0372 | 0.0005 |
| van Rheenen (control) | GSM3077497 | 0.9911 | 0.0011 | 0.0079 |
| van Rheenen (control) | GSM3077500 | 0.9942 | 0.0056 | 0.0002 |
| van Rheenen (control) | GSM3077505 | 0.9933 | 0.0066 | 0.0002 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077510 | 0.9998 | 0.0001 | 0.0000 |
| van Rheenen (control) | GSM3077512 | 0.9922 | 0.0024 | 0.0054 |
| van Rheenen (control) | GSM3077514 | 0.9909 | 0.0022 | 0.0068 |
| van Rheenen (control) | GSM3077517 | 0.9944 | 0.0001 | 0.0055 |
| van Rheenen (control) | GSM3077520 | 0.9955 | 0.0006 | 0.0039 |
| van Rheenen (control) | GSM3077522 | 0.9233 | 0.0311 | 0.0456 |
| van Rheenen (control) | GSM3077533 | 0.9978 | 0.0000 | 0.0021 |
| van Rheenen (control) | GSM3077536 | 0.9979 | 0.0002 | 0.0019 |
| van Rheenen (control) | GSM3077544 | 0.9385 | 0.0606 | 0.0008 |
| van Rheenen (control) | GSM3077551 | 0.7879 | 0.2119 | 0.0002 |
| van Rheenen (control) | GSM3077556 | 0.9808 | 0.0190 | 0.0002 |
| van Rheenen (control) | GSM3077559 | 0.1252 | 0.8694 | 0.0054 |
| van Rheenen (control) | GSM3077571 | 0.9956 | 0.0022 | 0.0022 |
| van Rheenen (control) | GSM3077573 | 0.4012 | 0.3994 | 0.1995 |
| van Rheenen (control) | GSM3077575 | 0.9129 | 0.0334 | 0.0537 |
| van Rheenen (control) | GSM3077577 | 0.9847 | 0.0001 | 0.0152 |
| van Rheenen (control) | GSM3077589 | 0.9889 | 0.0038 | 0.0073 |
| van Rheenen (control) | GSM3077591 | 0.1010 | 0.8789 | 0.0201 |
| van Rheenen (control) | GSM3077594 | 0.7424 | 0.1510 | 0.1066 |
| van Rheenen (control) | GSM3077597 | 0.9779 | 0.0068 | 0.0153 |
| van Rheenen (control) | GSM3077601 | 0.9973 | 0.0022 | 0.0005 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077604 | 0.9991 | 0.0005 | 0.0004 |
| van Rheenen (control) | GSM3077607 | 0.9973 | 0.0021 | 0.0007 |
| van Rheenen (control) | GSM3077609 | 0.9904 | 0.0092 | 0.0005 |
| van Rheenen (control) | GSM3077614 | 0.9553 | 0.0030 | 0.0418 |
| van Rheenen (control) | GSM3077616 | 0.9995 | 0.0005 | 0.0001 |
| van Rheenen (control) | GSM3077619 | 0.9963 | 0.0005 | 0.0031 |
| van Rheenen (control) | GSM3077621 | 0.9787 | 0.0098 | 0.0116 |
| van Rheenen (control) | GSM3077630 | 0.9964 | 0.0036 | 0.0000 |
| van Rheenen (control) | GSM3077633 | 0.9196 | 0.0735 | 0.0069 |
| van Rheenen (control) | GSM3077636 | 0.9436 | 0.0564 | 0.0000 |
| van Rheenen (control) | GSM3077638 | 0.9146 | 0.0846 | 0.0008 |
| van Rheenen (control) | GSM3077652 | 0.6224 | 0.3776 | 0.0000 |
| van Rheenen (control) | GSM3077655 | 0.1347 | 0.8032 | 0.0621 |
| van Rheenen (control) | GSM3077658 | 0.0108 | 0.5914 | 0.3978 |
| van Rheenen (control) | GSM3077660 | 0.9823 | 0.0002 | 0.0175 |
| van Rheenen (control) | GSM3077668 | 0.9989 | 0.0000 | 0.0011 |
| van Rheenen (control) | GSM3077670 | 0.9872 | 0.0126 | 0.0001 |
| van Rheenen (control) | GSM3077673 | 0.9994 | 0.0002 | 0.0004 |
| van Rheenen (control) | GSM3077675 | 0.3913 | 0.3166 | 0.2921 |
| van Rheenen (control) | GSM3077677 | 0.8111 | 0.0018 | 0.1871 |
| van Rheenen (control) | GSM3077689 | 0.0286 | 0.9713 | 0.0001 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077692 | 0.9672 | 0.0127 | 0.0201 |
| van Rheenen (control) | GSM3077694 | 0.0209 | 0.9791 | 0.0001 |
| van Rheenen (control) | GSM3077696 | 0.9877 | 0.0022 | 0.0101 |
| van Rheenen (control) | GSM3077698 | 0.7118 | 0.2554 | 0.0328 |
| van Rheenen (control) | GSM3077710 | 0.9649 | 0.0134 | 0.0218 |
| van Rheenen (control) | GSM3077712 | 0.0499 | 0.9478 | 0.0023 |
| van Rheenen (control) | GSM3077714 | 0.9390 | 0.0575 | 0.0035 |
| van Rheenen (control) | GSM3077716 | 0.9368 | 0.0300 | 0.0333 |
| van Rheenen (control) | GSM3077719 | 0.5019 | 0.3169 | 0.1812 |
| van Rheenen (control) | GSM3077727 | 0.9705 | 0.0293 | 0.0003 |
| van Rheenen (control) | GSM3077729 | 0.8701 | 0.1286 | 0.0013 |
| van Rheenen (control) | GSM3077732 | 0.9859 | 0.0096 | 0.0044 |
| van Rheenen (control) | GSM3077734 | 0.9854 | 0.0067 | 0.0079 |
| van Rheenen (control) | GSM3077736 | 0.0052 | 0.8829 | 0.1119 |
| van Rheenen (control) | GSM3077739 | 0.5538 | 0.4459 | 0.0003 |
| van Rheenen (control) | GSM3077748 | 0.9177 | 0.0639 | 0.0183 |
| van Rheenen (control) | GSM3077750 | 0.9981 | 0.0017 | 0.0002 |
| van Rheenen (control) | GSM3077753 | 0.3102 | 0.5850 | 0.1048 |
| van Rheenen (control) | GSM3077757 | 0.9616 | 0.0279 | 0.0105 |
| van Rheenen (control) | GSM3077760 | 0.1978 | 0.8007 | 0.0015 |
| van Rheenen (control) | GSM3077767 | 0.8824 | 0.0050 | 0.1126 |



|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077770 | 0.2721 | 0.7009 | 0.0270 |
| van Rheenen (control) | GSM3077773 | 0.8541 | 0.1451 | 0.0008 |
| van Rheenen (control) | GSM3077776 | 0.2402 | 0.7572 | 0.0026 |
| van Rheenen (control) | GSM3077778 | 0.0035 | 0.9964 | 0.0001 |
| van Rheenen (control) | GSM3077780 | 0.0701 | 0.9217 | 0.0082 |
| van Rheenen (control) | GSM3077794 | 0.0149 | 0.9179 | 0.0672 |
| van Rheenen (control) | GSM3077796 | 0.9960 | 0.0011 | 0.0030 |
| van Rheenen (control) | GSM3077799 | 0.7436 | 0.2554 | 0.0010 |
| van Rheenen (control) | GSM3077810 | 0.0179 | 0.9783 | 0.0038 |
| van Rheenen (control) | GSM3077813 | 0.6217 | 0.0080 | 0.3703 |
| van Rheenen (control) | GSM3077816 | 0.0377 | 0.8175 | 0.1448 |
| van Rheenen (control) | GSM3077818 | 0.0698 | 0.1941 | 0.7361 |
| van Rheenen (control) | GSM3077820 | 0.1644 | 0.7768 | 0.0588 |
| van Rheenen (control) | GSM3077830 | 0.8698 | 0.0100 | 0.1201 |
| van Rheenen (control) | GSM3077833 | 0.8890 | 0.1003 | 0.0106 |
| van Rheenen (control) | GSM3077836 | 0.0165 | 0.9825 | 0.0010 |
| van Rheenen (control) | GSM3077838 | 0.4667 | 0.5326 | 0.0007 |
| van Rheenen (control) | GSM3077846 | 0.9672 | 0.0160 | 0.0168 |
| van Rheenen (control) | GSM3077849 | 0.9346 | 0.0626 | 0.0028 |
| van Rheenen (control) | GSM3077851 | 0.0448 | 0.9349 | 0.0204 |
| van Rheenen (control) | GSM3077853 | 0.0104 | 0.9892 | 0.0004 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077856 | 0.9729 | 0.0271 | 0.0000 |
| van Rheenen (control) | GSM3077859 | 0.9998 | 0.0001 | 0.0001 |
| van Rheenen (control) | GSM3077863 | 0.0800 | 0.9168 | 0.0031 |
| van Rheenen (control) | GSM3077867 | 0.2225 | 0.5559 | 0.2216 |
| van Rheenen (control) | GSM3077871 | 0.9854 | 0.0145 | 0.0001 |
| van Rheenen (control) | GSM3077874 | 0.9959 | 0.0023 | 0.0018 |
| van Rheenen (control) | GSM3077878 | 0.9772 | 0.0217 | 0.0011 |
| van Rheenen (control) | GSM3077881 | 0.9946 | 0.0010 | 0.0044 |
| van Rheenen (control) | GSM3077884 | 0.6903 | 0.3093 | 0.0004 |
| van Rheenen (control) | GSM3077886 | 0.9929 | 0.0070 | 0.0001 |
| van Rheenen (control) | GSM3077889 | 0.9674 | 0.0325 | 0.0000 |
| van Rheenen (control) | GSM3077894 | 0.4178 | 0.5810 | 0.0012 |
| van Rheenen (control) | GSM3077896 | 0.9740 | 0.0252 | 0.0008 |
| van Rheenen (control) | GSM3077899 | 0.8441 | 0.1397 | 0.0162 |
| van Rheenen (control) | GSM3077901 | 0.4718 | 0.5261 | 0.0020 |
| van Rheenen (control) | GSM3077904 | 0.0301 | 0.9410 | 0.0289 |
| van Rheenen (control) | GSM3077906 | 0.0282 | 0.9712 | 0.0006 |
| van Rheenen (control) | GSM3077909 | 0.9798 | 0.0112 | 0.0090 |
| van Rheenen (control) | GSM3077911 | 0.9793 | 0.0206 | 0.0001 |
| van Rheenen (control) | GSM3077914 | 0.9684 | 0.0315 | 0.0001 |
| van Rheenen (control) | GSM3077921 | 0.9950 | 0.0048 | 0.0001 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077923 | 0.7664 | 0.0061 | 0.2275 |
| van Rheenen (control) | GSM3077925 | 0.9741 | 0.0224 | 0.0034 |
| van Rheenen (control) | GSM3077928 | 0.9320 | 0.0580 | 0.0100 |
| van Rheenen (control) | GSM3077936 | 0.9874 | 0.0081 | 0.0045 |
| van Rheenen (control) | GSM3077939 | 0.8776 | 0.1176 | 0.0049 |
| van Rheenen (control) | GSM3077942 | 0.9291 | 0.0339 | 0.0370 |
| van Rheenen (control) | GSM3077944 | 0.2484 | 0.6408 | 0.1108 |
| van Rheenen (control) | GSM3077947 | 0.0011 | 0.9892 | 0.0097 |
| van Rheenen (control) | GSM3077950 | 0.9903 | 0.0097 | 0.0000 |
| van Rheenen (control) | GSM3077952 | 0.9640 | 0.0004 | 0.0356 |
| van Rheenen (control) | GSM3077954 | 0.9693 | 0.0001 | 0.0306 |
| van Rheenen (control) | GSM3077957 | 0.0867 | 0.0019 | 0.9114 |
| van Rheenen (control) | GSM3077963 | 0.9974 | 0.0026 | 0.0000 |
| van Rheenen (control) | GSM3077966 | 0.6035 | 0.2959 | 0.1006 |
| van Rheenen (control) | GSM3077969 | 0.9741 | 0.0203 | 0.0057 |
| van Rheenen (control) | GSM3077979 | 0.0310 | 0.9690 | 0.0000 |
| van Rheenen (control) | GSM3077982 | 0.2474 | 0.7519 | 0.0007 |
| van Rheenen (control) | GSM3077984 | 0.9948 | 0.0052 | 0.0000 |
| van Rheenen (control) | GSM3077986 | 0.8003 | 0.1784 | 0.0213 |
| van Rheenen (control) | GSM3077989 | 0.8682 | 0.0549 | 0.0769 |
| van Rheenen (control) | GSM3077997 | 0.5631 | 0.4364 | 0.0005 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3077999 | 0.3242 | 0.0008 | 0.6750 |
| van Rheenen (control) | GSM3078002 | 0.0987 | 0.0004 | 0.9009 |
| van Rheenen (control) | GSM3078004 | 0.8039 | 0.0007 | 0.1954 |
| van Rheenen (control) | GSM3078006 | 0.9729 | 0.0109 | 0.0161 |
| van Rheenen (control) | GSM3078014 | 0.7677 | 0.0001 | 0.2322 |
| van Rheenen (control) | GSM3078017 | 0.1208 | 0.0011 | 0.8781 |
| van Rheenen (control) | GSM3078021 | 0.9489 | 0.0027 | 0.0484 |
| van Rheenen (control) | GSM3078024 | 0.3349 | 0.0145 | 0.6506 |
| van Rheenen (control) | GSM3078026 | 0.9144 | 0.0083 | 0.0773 |
| van Rheenen (control) | GSM3078029 | 0.2228 | 0.7439 | 0.0333 |
| van Rheenen (control) | GSM3078031 | 0.9584 | 0.0000 | 0.0416 |
| van Rheenen (control) | GSM3078033 | 0.1481 | 0.1483 | 0.7037 |
| van Rheenen (control) | GSM3078045 | 0.9672 | 0.0274 | 0.0053 |
| van Rheenen (control) | GSM3078047 | 0.9913 | 0.0026 | 0.0061 |
| van Rheenen (control) | GSM3078049 | 0.6684 | 0.1082 | 0.2235 |
| van Rheenen (control) | GSM3078056 | 0.6405 | 0.3280 | 0.0315 |
| van Rheenen (control) | GSM3078064 | 0.0204 | 0.0083 | 0.9712 |
| van Rheenen (control) | GSM3078066 | 0.5554 | 0.2246 | 0.2200 |
| van Rheenen (control) | GSM3078071 | 0.8510 | 0.0158 | 0.1332 |
| van Rheenen (control) | GSM3078077 | 0.8963 | 0.0401 | 0.0635 |
| van Rheenen (control) | GSM3078079 | 0.4855 | 0.0012 | 0.5133 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3078082 | 0.9438 | 0.0343 | 0.0219 |
| van Rheenen (control) | GSM3078084 | 0.3620 | 0.0666 | 0.5715 |
| van Rheenen (control) | GSM3078087 | 0.9837 | 0.0154 | 0.0009 |
| van Rheenen (control) | GSM3078090 | 0.8664 | 0.0087 | 0.1249 |
| van Rheenen (control) | GSM3078095 | 0.9882 | 0.0000 | 0.0118 |
| van Rheenen (control) | GSM3078097 | 0.5458 | 0.0894 | 0.3648 |
| van Rheenen (control) | GSM3078099 | 0.9908 | 0.0001 | 0.0091 |
| van Rheenen (control) | GSM3078101 | 0.7764 | 0.0375 | 0.1861 |
| van Rheenen (control) | GSM3078103 | 0.0759 | 0.1986 | 0.7256 |
| van Rheenen (control) | GSM3078105 | 0.5722 | 0.4177 | 0.0100 |
| van Rheenen (control) | GSM3078111 | 0.4811 | 0.5105 | 0.0084 |
| van Rheenen (control) | GSM3078113 | 0.3954 | 0.0035 | 0.6011 |
| van Rheenen (control) | GSM3078116 | 0.1977 | 0.0050 | 0.7973 |
| van Rheenen (control) | GSM3078118 | 0.8298 | 0.0057 | 0.1645 |
| van Rheenen (control) | GSM3078121 | 0.0334 | 0.0438 | 0.9228 |
| van Rheenen (control) | GSM3078123 | 0.4994 | 0.0519 | 0.4487 |
| van Rheenen (control) | GSM3078126 | 0.0573 | 0.9249 | 0.0178 |
| van Rheenen (control) | GSM3078128 | 0.1198 | 0.0071 | 0.8731 |
| van Rheenen (control) | GSM3078137 | 0.1761 | 0.0020 | 0.8219 |
| van Rheenen (control) | GSM3078141 | 0.9074 | 0.0055 | 0.0872 |
| van Rheenen (control) | GSM3078144 | 0.1083 | 0.6711 | 0.2206 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3078147 | 0.9378 | 0.0562 | 0.0060 |
| van Rheenen (control) | GSM3078149 | 0.9975 | 0.0012 | 0.0014 |
| van Rheenen (control) | GSM3078152 | 0.9449 | 0.0230 | 0.0321 |
| van Rheenen (control) | GSM3078156 | 0.0000 | 0.0000 | 1.0000 |
| van Rheenen (control) | GSM3078159 | 0.9013 | 0.0913 | 0.0075 |
| van Rheenen (control) | GSM3078161 | 0.7480 | 0.1521 | 0.0999 |
| van Rheenen (control) | GSM3078195 | 0.7386 | 0.1207 | 0.1407 |
| van Rheenen (control) | GSM3078198 | 0.4374 | 0.0051 | 0.5575 |
| van Rheenen (control) | GSM3078200 | 0.0454 | 0.0047 | 0.9499 |
| van Rheenen (control) | GSM3078201 | 0.0174 | 0.0005 | 0.9822 |
| van Rheenen (control) | GSM3078210 | 0.0795 | 0.6607 | 0.2599 |
| van Rheenen (control) | GSM3078212 | 0.0545 | 0.3518 | 0.5937 |
| van Rheenen (control) | GSM3078216 | 0.9129 | 0.0704 | 0.0167 |
| van Rheenen (control) | GSM3078218 | 0.1721 | 0.0000 | 0.8279 |
| van Rheenen (control) | GSM3078221 | 0.2076 | 0.0282 | 0.7642 |
| van Rheenen (control) | GSM3078225 | 0.2842 | 0.0011 | 0.7147 |
| van Rheenen (control) | GSM3078239 | 0.1876 | 0.5293 | 0.2831 |
| van Rheenen (control) | GSM3078261 | 0.0643 | 0.9352 | 0.0004 |
| van Rheenen (control) | GSM3078263 | 0.0391 | 0.4630 | 0.4979 |
| van Rheenen (control) | GSM3078266 | 0.3157 | 0.1720 | 0.5123 |
| van Rheenen (control) | GSM3078268 | 0.3334 | 0.6642 | 0.0024 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3078271 | 0.0003 | 0.9997 | 0.0000 |
| van Rheenen (control) | GSM3078279 | 0.0076 | 0.9915 | 0.0009 |
| van Rheenen (control) | GSM3078281 | 0.6171 | 0.2726 | 0.1103 |
| van Rheenen (control) | GSM3078285 | 0.0209 | 0.6804 | 0.2987 |
| van Rheenen (control) | GSM3078287 | 0.2769 | 0.5983 | 0.1248 |
| van Rheenen (control) | GSM3078290 | 0.1544 | 0.8017 | 0.0439 |
| van Rheenen (control) | GSM3078292 | 0.0098 | 0.9773 | 0.0129 |
| van Rheenen (control) | GSM3078294 | 0.5721 | 0.3986 | 0.0293 |
| van Rheenen (control) | GSM3078297 | 0.0136 | 0.9775 | 0.0089 |
| van Rheenen (control) | GSM3078299 | 0.2688 | 0.5744 | 0.1568 |
| van Rheenen (control) | GSM3078306 | 0.4880 | 0.1430 | 0.3690 |
| van Rheenen (control) | GSM3078314 | 0.1563 | 0.8179 | 0.0258 |
| van Rheenen (control) | GSM3078316 | 0.6786 | 0.0964 | 0.2250 |
| van Rheenen (control) | GSM3078326 | 0.0004 | 0.9966 | 0.0030 |
| van Rheenen (control) | GSM3078329 | 0.5766 | 0.2635 | 0.1599 |
| van Rheenen (control) | GSM3078331 | 0.0130 | 0.2330 | 0.7540 |
| van Rheenen (control) | GSM3078345 | 0.0304 | 0.9445 | 0.0251 |
| van Rheenen (control) | GSM3078348 | 0.0023 | 0.9662 | 0.0316 |
| van Rheenen (control) | GSM3078351 | 0.8485 | 0.0042 | 0.1473 |
| van Rheenen (control) | GSM3078353 | 0.2695 | 0.0395 | 0.6910 |
| van Rheenen (control) | GSM3078355 | 0.7697 | 0.2170 | 0.0133 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3078357 | 0.0017 | 0.6759 | 0.3224 |
| van Rheenen (control) | GSM3078362 | 0.8847 | 0.0350 | 0.0803 |
| van Rheenen (control) | GSM3078364 | 0.8740 | 0.0236 | 0.1025 |
| van Rheenen (control) | GSM3078366 | 0.8975 | 0.1019 | 0.0006 |
| van Rheenen (control) | GSM3078368 | 0.0000 | 0.9003 | 0.0996 |
| van Rheenen (control) | GSM3078370 | 0.7700 | 0.0059 | 0.2241 |
| van Rheenen (control) | GSM3078372 | 0.1228 | 0.8718 | 0.0054 |
| van Rheenen (control) | GSM3078374 | 0.9425 | 0.0565 | 0.0010 |
| van Rheenen (control) | GSM3078378 | 0.9364 | 0.0425 | 0.0211 |
| van Rheenen (control) | GSM3078380 | 0.0193 | 0.0716 | 0.9090 |
| van Rheenen (control) | GSM3078383 | 0.3724 | 0.3843 | 0.2433 |
| van Rheenen (control) | GSM3078385 | 0.0090 | 0.0108 | 0.9803 |
| van Rheenen (control) | GSM3078399 | 0.0260 | 0.0077 | 0.9662 |
| van Rheenen (control) | GSM3078407 | 0.0262 | 0.8432 | 0.1306 |
| van Rheenen (control) | GSM3078417 | 0.2404 | 0.7546 | 0.0050 |
| van Rheenen (control) | GSM3078419 | 0.9546 | 0.0063 | 0.0391 |
| van Rheenen (control) | GSM3078422 | 0.0019 | 0.9976 | 0.0005 |
| van Rheenen (control) | GSM3078429 | 0.1317 | 0.0324 | 0.8360 |
| van Rheenen (control) | GSM3078432 | 0.0175 | 0.1116 | 0.8709 |
| van Rheenen (control) | GSM3078439 | 0.9815 | 0.0161 | 0.0024 |
| van Rheenen (control) | GSM3078441 | 0.0284 | 0.1278 | 0.8438 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3078447 | 0.6279 | 0.1022 | 0.2699 |
| van Rheenen (control) | GSM3078457 | 0.0006 | 0.9547 | 0.0447 |
| van Rheenen (control) | GSM3078459 | 0.9381 | 0.0196 | 0.0423 |
| van Rheenen (control) | GSM3078461 | 0.0004 | 0.0002 | 0.9995 |
| van Rheenen (control) | GSM3078468 | 0.3954 | 0.0599 | 0.5447 |
| van Rheenen (control) | GSM3078471 | 0.7794 | 0.1080 | 0.1126 |
| van Rheenen (control) | GSM3078473 | 0.0261 | 0.7582 | 0.2157 |
| van Rheenen (control) | GSM3078476 | 0.8792 | 0.0416 | 0.0792 |
| van Rheenen (control) | GSM3078478 | 0.3391 | 0.0546 | 0.6063 |
| van Rheenen (control) | GSM3078481 | 0.3577 | 0.0897 | 0.5527 |
| van Rheenen (control) | GSM3078483 | 0.8682 | 0.1109 | 0.0209 |
| van Rheenen (control) | GSM3078485 | 0.7851 | 0.0003 | 0.2146 |
| van Rheenen (control) | GSM3078487 | 0.7449 | 0.0298 | 0.2254 |
| van Rheenen (control) | GSM3078489 | 0.1367 | 0.0009 | 0.8624 |
| van Rheenen (control) | GSM3078491 | 0.3481 | 0.6352 | 0.0168 |
| van Rheenen (control) | GSM3078494 | 0.4524 | 0.2246 | 0.3230 |
| van Rheenen (control) | GSM3079744 | 0.9893 | 0.0107 | 0.0000 |
| van Rheenen (control) | GSM3079760 | 0.9380 | 0.0324 | 0.0296 |
| van Rheenen (control) | GSM3079787 | 0.9722 | 0.0274 | 0.0004 |
| van Rheenen (control) | GSM3079796 | 0.1818 | 0.8084 | 0.0098 |
| van Rheenen (control) | GSM3079819 | 0.8061 | 0.1687 | 0.0252 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3079831 | 0.8525 | 0.1389 | 0.0087 |
| van Rheenen (control) | GSM3079840 | 0.9773 | 0.0164 | 0.0063 |
| van Rheenen (control) | GSM3079853 | 0.9996 | 0.0000 | 0.0003 |
| van Rheenen (control) | GSM3079865 | 0.9388 | 0.0223 | 0.0388 |
| van Rheenen (control) | GSM3079872 | 0.4577 | 0.1739 | 0.3684 |
| van Rheenen (control) | GSM3079873 | 0.9666 | 0.0326 | 0.0008 |
| van Rheenen (control) | GSM3079878 | 0.9315 | 0.0151 | 0.0534 |
| van Rheenen (control) | GSM3079879 | 0.9978 | 0.0008 | 0.0015 |
| van Rheenen (control) | GSM3079880 | 0.9845 | 0.0128 | 0.0027 |
| van Rheenen (control) | GSM3079882 | 0.9952 | 0.0010 | 0.0038 |
| van Rheenen (control) | GSM3079883 | 0.8325 | 0.1644 | 0.0031 |
| van Rheenen (control) | GSM3079886 | 0.7447 | 0.2532 | 0.0021 |
| van Rheenen (control) | GSM3079888 | 0.8416 | 0.0870 | 0.0714 |
| van Rheenen (control) | GSM3079892 | 0.9693 | 0.0173 | 0.0134 |
| van Rheenen (control) | GSM3079894 | 0.3823 | 0.6144 | 0.0033 |
| van Rheenen (control) | GSM3079898 | 0.4660 | 0.5308 | 0.0031 |
| van Rheenen (control) | GSM3079900 | 0.8340 | 0.1649 | 0.0010 |
| van Rheenen (control) | GSM3079903 | 0.9733 | 0.0241 | 0.0026 |
| van Rheenen (control) | GSM3079905 | 0.9612 | 0.0248 | 0.0141 |
| van Rheenen (control) | GSM3079909 | 0.9190 | 0.0743 | 0.0067 |
| van Rheenen (control) | GSM3079911 | 0.9737 | 0.0178 | 0.0085 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3079915 | 0.9918 | 0.0070 | 0.0011 |
| van Rheenen (control) | GSM3079917 | 0.9988 | 0.0006 | 0.0006 |
| van Rheenen (control) | GSM3079921 | 0.6514 | 0.3299 | 0.0187 |
| van Rheenen (control) | GSM3079923 | 0.9333 | 0.0525 | 0.0142 |
| van Rheenen (control) | GSM3079927 | 0.9950 | 0.0040 | 0.0011 |
| van Rheenen (control) | GSM3079929 | 0.7693 | 0.2275 | 0.0032 |
| van Rheenen (control) | GSM3079932 | 0.9599 | 0.0336 | 0.0066 |
| van Rheenen (control) | GSM3079934 | 0.9974 | 0.0021 | 0.0005 |
| van Rheenen (control) | GSM3079938 | 0.9137 | 0.0857 | 0.0007 |
| van Rheenen (control) | GSM3079941 | 0.9737 | 0.0231 | 0.0031 |
| van Rheenen (control) | GSM3079942 | 0.8891 | 0.1107 | 0.0001 |
| van Rheenen (control) | GSM3079946 | 0.9953 | 0.0025 | 0.0022 |
| van Rheenen (control) | GSM3079947 | 0.9995 | 0.0002 | 0.0002 |
| van Rheenen (control) | GSM3079948 | 0.9715 | 0.0284 | 0.0000 |
| van Rheenen (control) | GSM3079949 | 0.9192 | 0.0565 | 0.0243 |
| van Rheenen (control) | GSM3079951 | 0.9881 | 0.0115 | 0.0004 |
| van Rheenen (control) | GSM3079952 | 0.9868 | 0.0128 | 0.0004 |
| van Rheenen (control) | GSM3079955 | 0.9974 | 0.0015 | 0.0011 |
| van Rheenen (control) | GSM3079959 | 0.9960 | 0.0026 | 0.0014 |
| van Rheenen (control) | GSM3079962 | 0.9635 | 0.0256 | 0.0108 |
| van Rheenen (control) | GSM3079966 | 0.9601 | 0.0398 | 0.0001 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3079969 | 0.9741 | 0.0205 | 0.0054 |
| van Rheenen (control) | GSM3079973 | 0.9946 | 0.0037 | 0.0017 |
| van Rheenen (control) | GSM3079976 | 0.8612 | 0.1313 | 0.0075 |
| van Rheenen (control) | GSM3079980 | 0.4580 | 0.4956 | 0.0464 |
| van Rheenen (control) | GSM3079983 | 0.9472 | 0.0477 | 0.0051 |
| van Rheenen (control) | GSM3079987 | 0.8349 | 0.1645 | 0.0006 |
| van Rheenen (control) | GSM3079990 | 0.9586 | 0.0413 | 0.0001 |
| van Rheenen (control) | GSM3079994 | 0.9923 | 0.0042 | 0.0036 |
| van Rheenen (control) | GSM3079997 | 0.9771 | 0.0204 | 0.0024 |
| van Rheenen (control) | GSM3080001 | 0.7697 | 0.2007 | 0.0296 |
| van Rheenen (control) | GSM3080004 | 0.9985 | 0.0013 | 0.0002 |
| van Rheenen (control) | GSM3080007 | 0.7834 | 0.0911 | 0.1255 |
| van Rheenen (control) | GSM3080010 | 0.9783 | 0.0206 | 0.0011 |
| van Rheenen (control) | GSM3080014 | 0.8935 | 0.0982 | 0.0083 |
| van Rheenen (control) | GSM3080016 | 0.3579 | 0.6395 | 0.0025 |
| van Rheenen (control) | GSM3080017 | 0.9979 | 0.0015 | 0.0006 |
| van Rheenen (control) | GSM3080021 | 0.8874 | 0.0085 | 0.1042 |
| van Rheenen (control) | GSM3080024 | 0.8486 | 0.1401 | 0.0113 |
| van Rheenen (control) | GSM3080025 | 0.9534 | 0.0460 | 0.0006 |
| van Rheenen (control) | GSM3080026 | 0.9255 | 0.0705 | 0.0040 |
| van Rheenen (control) | GSM3080030 | 0.9278 | 0.0519 | 0.0204 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3080031 | 0.5984 | 0.2435 | 0.1581 |
| van Rheenen (control) | GSM3080032 | 0.7154 | 0.2838 | 0.0008 |
| van Rheenen (control) | GSM3080033 | 0.9892 | 0.0102 | 0.0006 |
| van Rheenen (control) | GSM3080035 | 0.4893 | 0.5007 | 0.0101 |
| van Rheenen (control) | GSM3080036 | 0.9890 | 0.0092 | 0.0018 |
| van Rheenen (control) | GSM3080045 | 0.9561 | 0.0432 | 0.0008 |
| van Rheenen (control) | GSM3080052 | 0.9992 | 0.0008 | 0.0000 |
| van Rheenen (control) | GSM3080058 | 0.6768 | 0.3202 | 0.0030 |
| van Rheenen (control) | GSM3080062 | 0.9959 | 0.0015 | 0.0026 |
| van Rheenen (control) | GSM3080071 | 0.9909 | 0.0088 | 0.0003 |
| van Rheenen (control) | GSM3080078 | 0.8601 | 0.1399 | 0.0001 |
| van Rheenen (control) | GSM3080081 | 0.9590 | 0.0403 | 0.0007 |
| van Rheenen (control) | GSM3080082 | 0.9785 | 0.0090 | 0.0125 |
| van Rheenen (control) | GSM3080085 | 0.9917 | 0.0083 | 0.0000 |
| van Rheenen (control) | GSM3080088 | 0.9402 | 0.0596 | 0.0002 |
| van Rheenen (control) | GSM3080089 | 0.9996 | 0.0003 | 0.0002 |
| van Rheenen (control) | GSM3080090 | 0.9999 | 0.0001 | 0.0000 |
| van Rheenen (control) | GSM3080091 | 0.8950 | 0.1033 | 0.0017 |
| van Rheenen (control) | GSM3080092 | 0.9093 | 0.0784 | 0.0123 |
| van Rheenen (control) | GSM3080094 | 0.9099 | 0.0879 | 0.0022 |
| van Rheenen (control) | GSM3080095 | 0.9732 | 0.0176 | 0.0093 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3080096 | 0.7561 | 0.0142 | 0.2298 |
| van Rheenen (control) | GSM3080097 | 0.9995 | 0.0003 | 0.0001 |
| van Rheenen (control) | GSM3080100 | 0.9117 | 0.0030 | 0.0852 |
| van Rheenen (control) | GSM3080104 | 0.9994 | 0.0001 | 0.0005 |
| van Rheenen (control) | GSM3080106 | 0.9084 | 0.0371 | 0.0544 |
| van Rheenen (control) | GSM3080110 | 0.9918 | 0.0021 | 0.0061 |
| van Rheenen (control) | GSM3080112 | 0.9627 | 0.0152 | 0.0222 |
| van Rheenen (control) | GSM3080116 | 0.9926 | 0.0029 | 0.0045 |
| van Rheenen (control) | GSM3080117 | 0.9920 | 0.0041 | 0.0039 |
| van Rheenen (control) | GSM3080121 | 0.8306 | 0.0212 | 0.1482 |
| van Rheenen (control) | GSM3080123 | 0.3190 | 0.6803 | 0.0007 |
| van Rheenen (control) | GSM3080126 | 0.3185 | 0.3222 | 0.3593 |
| van Rheenen (control) | GSM3080128 | 0.9862 | 0.0106 | 0.0032 |
| van Rheenen (control) | GSM3080131 | 0.9999 | 0.0000 | 0.0001 |
| van Rheenen (control) | GSM3080132 | 0.9776 | 0.0001 | 0.0222 |
| van Rheenen (control) | GSM3080136 | 0.9706 | 0.0093 | 0.0201 |
| van Rheenen (control) | GSM3080137 | 0.9971 | 0.0002 | 0.0027 |
| van Rheenen (control) | GSM3080140 | 0.9012 | 0.0139 | 0.0849 |
| van Rheenen (control) | GSM3080142 | 0.9781 | 0.0051 | 0.0168 |
| van Rheenen (control) | GSM3080145 | 0.9279 | 0.0408 | 0.0313 |
| van Rheenen (control) | GSM3080146 | 0.9963 | 0.0002 | 0.0035 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3080150 | 0.9998 | 0.0000 | 0.0001 |
| van Rheenen (control) | GSM3080151 | 0.9915 | 0.0012 | 0.0073 |
| van Rheenen (control) | GSM3080152 | 0.9928 | 0.0026 | 0.0045 |
| van Rheenen (control) | GSM3080154 | 0.7544 | 0.0429 | 0.2027 |
| van Rheenen (control) | GSM3080155 | 0.9892 | 0.0049 | 0.0059 |
| van Rheenen (control) | GSM3080156 | 0.9066 | 0.0161 | 0.0773 |
| van Rheenen (control) | GSM3080157 | 0.9895 | 0.0036 | 0.0069 |
| van Rheenen (control) | GSM3080158 | 0.9989 | 0.0004 | 0.0007 |
| van Rheenen (control) | GSM3080159 | 0.9931 | 0.0005 | 0.0064 |
| van Rheenen (control) | GSM3080161 | 0.9114 | 0.0472 | 0.0414 |
| van Rheenen (control) | GSM3080162 | 0.9980 | 0.0011 | 0.0009 |
| van Rheenen (control) | GSM3080163 | 0.9926 | 0.0066 | 0.0008 |
| van Rheenen (control) | GSM3080164 | 0.9911 | 0.0069 | 0.0021 |
| van Rheenen (control) | GSM3080165 | 0.9965 | 0.0024 | 0.0011 |
| van Rheenen (control) | GSM3080166 | 0.9948 | 0.0029 | 0.0023 |
| van Rheenen (control) | GSM3080167 | 0.9762 | 0.0230 | 0.0008 |
| van Rheenen (control) | GSM3080169 | 0.9931 | 0.0060 | 0.0010 |
| van Rheenen (control) | GSM3080170 | 0.9276 | 0.0084 | 0.0640 |
| van Rheenen (control) | GSM3080171 | 0.9667 | 0.0056 | 0.0277 |
| van Rheenen (control) | GSM3080172 | 0.7020 | 0.2801 | 0.0179 |
| van Rheenen (control) | GSM3080173 | 0.9962 | 0.0032 | 0.0006 |

|                       |            |        |        |        |
|-----------------------|------------|--------|--------|--------|
| van Rheenen (control) | GSM3080174 | 0.9994 | 0.0002 | 0.0004 |
| van Rheenen (control) | GSM3080175 | 0.9943 | 0.0031 | 0.0026 |
| van Rheenen (control) | GSM3080176 | 0.9727 | 0.0101 | 0.0173 |
| van Rheenen (control) | GSM3080177 | 0.9887 | 0.0104 | 0.0010 |
| van Rheenen (control) | GSM3080178 | 0.9953 | 0.0017 | 0.0030 |
| van Rheenen (control) | GSM3080179 | 0.6958 | 0.0204 | 0.2838 |
| Zucca                 | SLA3014    | 0.4762 | 0.0042 | 0.5196 |
| Zucca                 | SLA0110    | 0.7524 | 0.0053 | 0.2423 |
| Zucca                 | SLA0514    | 0.7832 | 0.0438 | 0.1731 |
| Zucca                 | SLA1213    | 0.8645 | 0.0042 | 0.1313 |
| Zucca                 | SLA615     | 0.6436 | 0.3336 | 0.0229 |
| Zucca                 | SLA2411    | 0.9495 | 0.0389 | 0.0116 |
| Zucca                 | SLA715     | 0.0051 | 0.9873 | 0.0076 |
| Zucca                 | SLA0210    | 0.9936 | 0.0001 | 0.0063 |
| Zucca                 | SLA1812    | 0.6049 | 0.3906 | 0.0045 |
| Zucca                 | SLA0109    | 0.9959 | 0.0001 | 0.0040 |
| Zucca                 | SLA2311    | 0.9981 | 0.0000 | 0.0019 |
| Zucca                 | SLA3315    | 0.9434 | 0.0563 | 0.0003 |
| Zucca                 | SLA2014    | 0.9536 | 0.0463 | 0.0001 |
| Zucca                 | SLA3311    | 0.9982 | 0.0017 | 0.0001 |
| Zucca                 | SLA2710    | 0.9988 | 0.0012 | 0.0000 |

Table A35. Posterior probabilities of being assigned to the KCL BrainBank-defined clusters for the TargetALS and van Rheenen case and control datasets and the Zucca case-only dataset.



| Gene            | log2FoldChange (lfc) | lfc SE | Statistic | Degrees of Freedom | p-value  | Adjusted p-value |
|-----------------|----------------------|--------|-----------|--------------------|----------|------------------|
| ENSG00000146469 | 0.5826               | 0.1822 | 7.9985    | 110.28             | 1.40E-12 | 1.80E-10         |
| ENSG00000233123 | 0.4996               | 0.2028 | 7.7631    | 99.88              | 7.40E-12 | 4.80E-10         |
| ENSG00000006128 | 0.4815               | 0.1777 | 7.0345    | 93.67              | 3.20E-10 | 1.40E-08         |
| ENSG00000157005 | 0.8417               | 0.2725 | 6.9332    | 97.40              | 4.50E-10 | 1.50E-08         |
| ENSG00000223930 | 0.2921               | 0.2232 | 6.6654    | 107.58             | 1.20E-09 | 3.10E-08         |
| ENSG00000246363 | 0.1792               | 0.1803 | 6.6720    | 98.31              | 1.50E-09 | 3.30E-08         |
| ENSG00000144227 | 0.4924               | 0.1627 | 6.6168    | 96.80              | 2.00E-09 | 3.80E-08         |
| ENSG00000141433 | 0.4349               | 0.1888 | 6.4265    | 91.06              | 5.90E-09 | 9.60E-08         |
| ENSG00000185149 | 0.2026               | 0.3090 | 5.9753    | 97.17              | 3.80E-08 | 5.50E-07         |
| ENSG00000179520 | 0.3825               | 0.2334 | 5.7730    | 105.26             | 8.00E-08 | 1.00E-06         |
| ENSG00000239672 | 0.1115               | 0.1238 | 5.7050    | 89.95              | 1.50E-07 | 1.30E-06         |
| ENSG00000159248 | 0.1933               | 0.1515 | 5.7757    | 86.79              | 1.20E-07 | 1.30E-06         |
| ENSG00000164600 | 0.3274               | 0.2167 | 5.7873    | 86.19              | 1.10E-07 | 1.30E-06         |
| ENSG00000145708 | 0.4307               | 0.1846 | 5.6454    | 107.32             | 1.40E-07 | 1.30E-06         |
| ENSG00000152595 | 0.4981               | 0.1935 | 5.7258    | 87.90              | 1.40E-07 | 1.30E-06         |
| ENSG00000285634 | 0.1003               | 0.1638 | 5.6423    | 89.85              | 1.90E-07 | 1.50E-06         |
| ENSG00000186081 | 0.3526               | 0.3386 | 5.5727    | 108.11             | 1.90E-07 | 1.50E-06         |
| ENSG00000205279 | 0.2187               | 0.2709 | 5.6046    | 91.71              | 2.20E-07 | 1.60E-06         |
| ENSG00000236714 | 0.4243               | 0.2311 | 5.6003    | 83.80              | 2.70E-07 | 1.80E-06         |
| ENSG00000169035 | 0.1416               | 0.2054 | 5.5062    | 94.98              | 3.10E-07 | 1.90E-06         |
| ENSG00000231824 | 0.6064               | 0.2400 | 5.5160    | 96.62              | 2.90E-07 | 1.90E-06         |
| ENSG00000287611 | 0.2132               | 0.1720 | 5.4080    | 99.44              | 4.40E-07 | 2.60E-06         |
| ENSG00000254101 | 0.1455               | 0.2118 | 5.3584    | 101.32             | 5.30E-07 | 3.00E-06         |
| ENSG00000147571 | 0.6703               | 0.3016 | 5.3224    | 105.90             | 5.80E-07 | 3.10E-06         |
| ENSG00000224404 | 0.1092               | 0.1903 | 5.3469    | 85.69              | 7.30E-07 | 3.80E-06         |
| ENSG00000188729 | 0.4901               | 0.2948 | 5.2314    | 108.18             | 8.30E-07 | 4.20E-06         |
| ENSG00000183090 | -0.0761              | 0.2179 | 5.2296    | 98.52              | 9.60E-07 | 4.60E-06         |
| ENSG00000176697 | 0.1810               | 0.1423 | 5.2128    | 95.55              | 1.10E-06 | 5.00E-06         |
| ENSG00000228999 | 0.5340               | 0.4209 | 5.1440    | 104.41             | 1.30E-06 | 5.50E-06         |
| ENSG00000250634 | 0.5519               | 0.2149 | 5.1427    | 107.88             | 1.20E-06 | 5.50E-06         |
| ENSG00000202048 | 0.1086               | 0.2250 | 4.6348    | 105.08             | 1.00E-05 | 4.40E-05         |
| ENSG00000165899 | 0.0392               | 0.1702 | 4.5758    | 99.95              | 1.40E-05 | 5.60E-05         |
| ENSG00000261757 | 0.6922               | 0.3229 | 4.5259    | 92.56              | 1.80E-05 | 7.10E-05         |
| ENSG00000164326 | 0.5162               | 0.3652 | 4.4130    | 106.96             | 2.40E-05 | 9.40E-05         |
| ENSG00000287844 | -0.0424              | 0.2224 | 4.4095    | 98.41              | 2.70E-05 | 9.70E-05         |
| ENSG00000174899 | 0.3241               | 0.3399 | 4.4019    | 100.95             | 2.70E-05 | 9.70E-05         |
| ENSG00000256193 | -0.0790              | 0.1865 | 4.4520    | 77.26              | 2.80E-05 | 9.80E-05         |
| ENSG00000229618 | -0.0465              | 0.1608 | 4.4306    | 83.26              | 2.80E-05 | 9.80E-05         |
| ENSG00000170231 | 0.1262               | 0.2016 | 4.3718    | 95.84              | 3.10E-05 | 1.10E-04         |
| ENSG00000261325 | 0.1944               | 0.3365 | 4.3363    | 110.45             | 3.20E-05 | 1.10E-04         |
| ENSG00000184385 | 0.2499               | 0.1928 | 4.3667    | 89.47              | 3.40E-05 | 1.10E-04         |
| ENSG00000150175 | 0.1795               | 0.2367 | 4.3001    | 109.86             | 3.70E-05 | 1.20E-04         |
| ENSG00000285735 | 0.4971               | 0.3623 | 4.2899    | 104.89             | 4.00E-05 | 1.20E-04         |
| ENSG00000182632 | 0.1653               | 0.2239 | 4.1510    | 92.55              | 7.40E-05 | 2.10E-04         |

|                 |         |        |        |        |          |          |
|-----------------|---------|--------|--------|--------|----------|----------|
| ENSG00000170290 | 0.7859  | 0.5126 | 4.1357 | 110.66 | 6.90E-05 | 2.10E-04 |
| ENSG00000286016 | 1.4401  | 0.5520 | 4.0463 | 110.88 | 9.70E-05 | 2.80E-04 |
| ENSG00000279952 | 0.0247  | 0.2134 | 4.0202 | 83.73  | 1.30E-04 | 3.50E-04 |
| ENSG00000280776 | -0.1193 | 0.1695 | 3.9769 | 95.67  | 1.40E-04 | 3.70E-04 |
| ENSG00000151790 | 0.1886  | 0.2028 | 3.9349 | 102.33 | 1.50E-04 | 4.10E-04 |
| ENSG00000100362 | 0.4285  | 0.2576 | 3.9480 | 90.51  | 1.60E-04 | 4.10E-04 |
| ENSG00000169676 | -0.0942 | 0.2181 | 3.6289 | 98.54  | 4.50E-04 | 1.20E-03 |
| ENSG00000111863 | 0.0218  | 0.2133 | 3.6337 | 90.24  | 4.60E-04 | 1.20E-03 |
| ENSG00000126545 | 0.5930  | 0.8212 | 3.5656 | 107.03 | 5.40E-04 | 1.30E-03 |
| ENSG00000267623 | 0.1263  | 0.2689 | 3.5508 | 101.28 | 5.80E-04 | 1.40E-03 |
| ENSG00000261502 | 0.3522  | 0.2578 | 3.5138 | 106.26 | 6.50E-04 | 1.50E-03 |
| ENSG00000131885 | 0.4960  | 0.2605 | 3.5129 | 71.93  | 7.70E-04 | 1.80E-03 |
| ENSG00000117594 | 0.5609  | 0.2504 | 3.4351 | 109.06 | 8.40E-04 | 1.90E-03 |
| ENSG00000255087 | 0.1233  | 0.2625 | 3.4343 | 88.40  | 9.10E-04 | 2.00E-03 |
| ENSG00000223812 | 0.0953  | 0.1904 | 3.4123 | 82.97  | 1.00E-03 | 2.20E-03 |
| ENSG00000128564 | 0.1898  | 0.2351 | 3.4000 | 91.14  | 1.00E-03 | 2.20E-03 |
| ENSG00000138678 | 0.1171  | 0.1920 | 3.3294 | 92.63  | 1.30E-03 | 2.70E-03 |
| ENSG00000132744 | 0.5304  | 0.4546 | 3.3102 | 109.93 | 1.30E-03 | 2.70E-03 |
| ENSG00000260658 | 0.0460  | 0.2875 | 3.3007 | 100.62 | 1.30E-03 | 2.80E-03 |
| ENSG00000107165 | 0.2340  | 0.2287 | 3.2995 | 87.58  | 1.40E-03 | 2.90E-03 |
| ENSG00000265179 | 0.2833  | 0.2576 | 3.2782 | 91.89  | 1.50E-03 | 3.00E-03 |
| ENSG00000276462 | -0.0214 | 0.2670 | 3.2630 | 85.77  | 1.60E-03 | 3.10E-03 |
| ENSG00000106236 | 0.0239  | 0.2223 | 3.0808 | 99.51  | 2.70E-03 | 5.20E-03 |
| ENSG00000075673 | -0.5552 | 0.3807 | 3.0720 | 100.40 | 2.70E-03 | 5.30E-03 |
| ENSG00000266573 | -0.2465 | 0.2537 | 2.9543 | 91.92  | 4.00E-03 | 7.60E-03 |
| ENSG00000117322 | 0.7721  | 0.4437 | 2.8580 | 108.69 | 5.10E-03 | 9.60E-03 |
| ENSG00000286063 | 0.4493  | 0.3273 | 2.7852 | 105.59 | 6.30E-03 | 1.20E-02 |
| ENSG00000225280 | 0.8616  | 0.6064 | 2.7201 | 110.87 | 7.60E-03 | 1.40E-02 |
| ENSG00000279875 | -0.1172 | 0.2996 | 2.6537 | 107.89 | 9.20E-03 | 1.60E-02 |
| ENSG00000225449 | 0.5431  | 0.2423 | 2.6718 | 94.90  | 8.90E-03 | 1.60E-02 |
| ENSG00000228735 | -0.3704 | 0.2249 | 2.6427 | 76.21  | 1.00E-02 | 1.70E-02 |
| ENSG00000287907 | 0.0617  | 0.2912 | 2.5788 | 99.67  | 1.10E-02 | 2.00E-02 |
| ENSG00000268297 | 0.0661  | 0.2207 | 2.5171 | 95.54  | 1.40E-02 | 2.20E-02 |
| ENSG00000242159 | 0.1469  | 0.2523 | 2.5271 | 93.97  | 1.30E-02 | 2.20E-02 |
| ENSG00000227582 | 0.4623  | 0.3679 | 2.5140 | 107.52 | 1.30E-02 | 2.20E-02 |
| ENSG00000122025 | -0.1181 | 0.2100 | 2.4134 | 91.72  | 1.80E-02 | 2.90E-02 |
| ENSG00000228772 | -0.2214 | 0.2469 | 2.3699 | 91.70  | 2.00E-02 | 3.20E-02 |
| ENSG00000254510 | 0.0482  | 0.3211 | 2.2773 | 102.91 | 2.50E-02 | 4.00E-02 |
| ENSG00000286736 | 0.0391  | 0.2594 | 2.2500 | 100.80 | 2.70E-02 | 4.10E-02 |
| ENSG00000119888 | 0.3776  | 0.3102 | 2.2609 | 110.98 | 2.60E-02 | 4.10E-02 |
| ENSG00000200959 | -0.0129 | 0.3323 | 2.2040 | 109.26 | 3.00E-02 | 4.60E-02 |
| ENSG00000132677 | 1.2614  | 0.4052 | 2.1997 | 110.85 | 3.00E-02 | 4.60E-02 |
| ENSG00000234665 | 0.7950  | 0.4356 | 2.1870 | 105.92 | 3.10E-02 | 4.70E-02 |
| ENSG00000258859 | -0.1401 | 0.2806 | 2.0334 | 91.50  | 4.50E-02 | 6.70E-02 |
| ENSG00000274330 | -0.4950 | 0.2849 | 1.9645 | 93.30  | 5.30E-02 | 7.70E-02 |
| ENSG00000229722 | 1.1299  | 0.5798 | 1.9214 | 104.17 | 5.70E-02 | 8.40E-02 |

|                 |         |        |         |        |          |          |
|-----------------|---------|--------|---------|--------|----------|----------|
| ENSG00000256971 | -0.1039 | 0.2652 | 1.8975  | 81.77  | 6.10E-02 | 8.80E-02 |
| ENSG00000120875 | 0.1897  | 0.2462 | 1.8693  | 105.01 | 6.40E-02 | 9.20E-02 |
| ENSG00000248837 | -0.6334 | 0.2125 | 1.8386  | 87.80  | 6.90E-02 | 9.80E-02 |
| ENSG00000286810 | 0.6573  | 0.2933 | 1.7586  | 101.23 | 8.20E-02 | 1.10E-01 |
| ENSG00000226405 | 0.9211  | 0.4922 | 1.7836  | 104.05 | 7.70E-02 | 1.10E-01 |
| ENSG00000287593 | -0.2611 | 0.2325 | 1.6326  | 81.24  | 1.10E-01 | 1.40E-01 |
| ENSG00000216753 | 0.3224  | 0.3742 | 1.6290  | 97.69  | 1.10E-01 | 1.40E-01 |
| ENSG00000285578 | 0.0606  | 0.4793 | 1.5717  | 109.58 | 1.20E-01 | 1.60E-01 |
| ENSG00000130701 | -0.1332 | 0.5085 | 1.5452  | 98.58  | 1.30E-01 | 1.70E-01 |
| ENSG00000225493 | 0.4354  | 0.2641 | 1.5214  | 89.51  | 1.30E-01 | 1.70E-01 |
| ENSG00000285561 | -0.3713 | 0.2248 | 1.4150  | 96.51  | 1.60E-01 | 2.10E-01 |
| ENSG00000286666 | -0.1954 | 0.2788 | 1.3761  | 102.42 | 1.70E-01 | 2.20E-01 |
| ENSG00000174576 | -0.2569 | 0.5316 | 1.3091  | 94.96  | 1.90E-01 | 2.50E-01 |
| ENSG00000271538 | 0.0750  | 0.2435 | 1.3033  | 97.58  | 2.00E-01 | 2.50E-01 |
| ENSG00000179477 | -0.3787 | 0.2521 | 1.2159  | 98.79  | 2.30E-01 | 2.80E-01 |
| ENSG00000261738 | -0.2143 | 0.2554 | 1.2061  | 90.70  | 2.30E-01 | 2.90E-01 |
| ENSG00000254681 | 0.0922  | 0.5426 | 1.0700  | 109.17 | 2.90E-01 | 3.50E-01 |
| ENSG00000237390 | 0.7004  | 0.2926 | 1.0810  | 110.92 | 2.80E-01 | 3.50E-01 |
| ENSG00000229635 | 0.3925  | 0.3115 | 1.0206  | 104.37 | 3.10E-01 | 3.70E-01 |
| ENSG00000243323 | 0.0630  | 0.2761 | -0.9369 | 90.09  | 3.50E-01 | 4.10E-01 |
| ENSG00000259520 | 0.2809  | 0.3394 | 0.9513  | 108.52 | 3.40E-01 | 4.10E-01 |
| ENSG00000286292 | 0.3259  | 0.3065 | 0.8013  | 103.08 | 4.30E-01 | 5.00E-01 |
| ENSG00000241945 | -0.8688 | 0.6353 | 0.7611  | 107.48 | 4.50E-01 | 5.10E-01 |
| ENSG00000254363 | 0.0074  | 0.3298 | 0.7739  | 107.73 | 4.40E-01 | 5.10E-01 |
| ENSG00000174403 | 0.0308  | 0.2412 | 0.6103  | 105.19 | 5.40E-01 | 6.20E-01 |
| ENSG00000122012 | -0.5557 | 0.2640 | 0.5481  | 94.68  | 5.90E-01 | 6.60E-01 |
| ENSG00000227723 | 0.7703  | 0.4205 | 0.5483  | 107.04 | 5.90E-01 | 6.60E-01 |
| ENSG00000281383 | -2.4226 | 0.8698 | 0.5042  | 104.89 | 6.20E-01 | 6.80E-01 |
| ENSG00000218772 | 0.3719  | 0.5009 | 0.4929  | 101.58 | 6.20E-01 | 6.90E-01 |
| ENSG00000156076 | -0.3244 | 0.2400 | -0.4618 | 98.76  | 6.50E-01 | 7.00E-01 |
| ENSG00000160221 | -0.6366 | 0.6024 | 0.4285  | 109.55 | 6.70E-01 | 7.20E-01 |
| ENSG00000277918 | -0.2268 | 0.5116 | 0.4067  | 106.86 | 6.90E-01 | 7.40E-01 |
| ENSG00000178401 | 0.2587  | 0.2269 | 0.3703  | 106.51 | 7.10E-01 | 7.60E-01 |
| ENSG00000286109 | 0.3874  | 0.3940 | 0.3355  | 101.58 | 7.40E-01 | 7.80E-01 |
| ENSG00000223553 | -0.1307 | 0.2817 | 0.3057  | 109.90 | 7.60E-01 | 8.00E-01 |
| ENSG00000104938 | -0.2947 | 0.4624 | 0.2051  | 107.45 | 8.40E-01 | 8.70E-01 |
| ENSG00000273214 | 0.5610  | 0.3931 | -0.1563 | 88.01  | 8.80E-01 | 9.00E-01 |
| ENSG00000254561 | -0.2467 | 0.1987 | 0.1129  | 108.58 | 9.10E-01 | 9.30E-01 |
| ENSG00000137860 | 0.2537  | 0.3138 | -0.0929 | 110.33 | 9.30E-01 | 9.40E-01 |
| ENSG00000143858 | -0.3986 | 0.2703 | 0.0217  | 105.86 | 9.80E-01 | 9.80E-01 |
| ENSG00000205634 | -0.2825 | 0.2264 | -0.0349 | 103.13 | 9.70E-01 | 9.80E-01 |

*Table A36. Results of the differential expression of KCL BrainBank Cluster 1 with DESeq2, comparing people with ALS to controls. A positive log<sub>2</sub>FoldChange refers to upregulation in gene expression in cases and vice versa. The independent hypothesis weighting method was used for p-value correction.*

| Scenario                           | Dataset                                      | Cluster                  | Number of Samples | Number of Genes | Best Hyperparameter                      | ROC AUC (mean $\pm$ SD) | Precision (mean $\pm$ SD) | Recall (mean $\pm$ SD) | F1-Score (mean $\pm$ SD) |
|------------------------------------|--|--------------------------|-------------------|-----------------|--|-------------------------|---------------------------|------------------------|--------------------------|
| 1<br>(All Genes)                   | KCL BrainBank<br>(case-control)              | 1<br>(informative genes) | 119               | 131             | C=0.01, penalty='l1', solver='liblinear' | 0.832 $\pm$ 0.139       | 0.864 $\pm$ 0.125         | 0.739 $\pm$ 0.173      | 0.789 $\pm$ 0.137        |
|                                    |  | 1 (random genes)         | 119               | 131             | NA                                       | 0.569 $\pm$ 0.106       | 0.413 $\pm$ 0.0954        | 0.405 $\pm$ 0.149      | 0.399 $\pm$ 0.110        |
|                                    | TargetALS<br>(case-control)                  | 1                        | 121               | 71              | C=1.0, penalty='l2', solver='lbfgs'      | 0.965 $\pm$ 0.0498      | 0.952 $\pm$ 0.0487        | 0.949 $\pm$ 0.0680     | 0.948 $\pm$ 0.0418       |
|                                    |  | 2                        | 32                | 148             | C=1.0, penalty='l2', solver='lbfgs'      | 0.964 $\pm$ 0.0619      | 0.933 $\pm$ 0.0673        | 0.964 $\pm$ 0.0619     | 0.948 $\pm$ 0.0589       |
|                                    |  | 3                        | 49                | 247             | C=1.0, penalty='l1', solver='liblinear'  | 0.976 $\pm$ 0.0532      | 0.958 $\pm$ 0.0589        | 1.00 $\pm$ 0.000       | 0.978 $\pm$ 0.0314       |
|                                    | Van Rheezen<br>(case-control)                | 1                        | 858               | 57              | C=1.0, penalty='l1', solver='liblinear'  | 1.00 $\pm$ 0.000        | 1.00 $\pm$ 0.000          | 1.00 $\pm$ 0.000       | 1.00 $\pm$ 0.000         |
|                                    |  | 1 (after removing NME1)  | 858               | 56              | C=0.1, penalty='l1', solver='liblinear'  | 0.685 $\pm$ 0.0505      | 0.532 $\pm$ 0.0467        | 0.657 $\pm$ 0.0818     | 0.584 $\pm$ 0.0440       |
|                                    |  | 2                        | 110               | 230             | C=0.1, penalty='l2', solver='liblinear'  | 0.857 $\pm$ 0.103       | 0.690 $\pm$ 0.241         | 0.675 $\pm$ 0.199      | 0.665 $\pm$ 0.187        |
|                                    |  | 3                        | 74                | 247             | C=1.0, penalty=none, solver='newton-cg'  | 0.907 $\pm$ 0.130       | 0.833 $\pm$ 0.179         | 0.867 $\pm$ 0.221      | 0.838 $\pm$ 0.182        |
|                                    | TargetALS<br>(motor cortex-occipital cortex) | 1                        | 131               | 53              | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
|                                    |  | 2                        | 34                | 106             | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
|                                    |  | 3                        | 48                | 195             | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
|                                    | TargetALS<br>(motor cortex-cerebellum)       | 1                        | 187               | 40              | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
|                                    |  | 2                        | 43                | 110             | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
|                                    |  | 3                        | 66                | 197             | C=1.0, penalty='l1', solver='liblinear'  | 1.000 $\pm$ 0.000       | 1.000 $\pm$ 0.000         | 1.000 $\pm$ 0.000      | 1.000 $\pm$ 0.000        |
| 2<br>(Removal of Correlated Genes) | KCL BrainBank<br>(case-control)              | 1                        | 119               | 31              | C=0.1, penalty='l1', solver='liblinear'  | 0.812 $\pm$ 0.110       | 0.877 $\pm$ 0.093         | 0.756 $\pm$ 0.154      | 0.805 $\pm$ 0.113        |
|                                    | TargetALS<br>(case-control)                  | 1                        | 121               | 21              | C=1.0, penalty='l2', solver='liblinear'  | 0.937 $\pm$ 0.0837      | 0.938 $\pm$ 0.0657        | 0.917 $\pm$ 0.0907     | 0.925 $\pm$ 0.00928      |
|                                    |  | 2                        | 32                | 9               | C=1.0, penalty='l1', solver='liblinear'  | 0.964 $\pm$ 0.0619      | 0.964 $\pm$ 0.0619        | 0.964 $\pm$ 0.0619     | 0.964 $\pm$ 0.0619       |
|                                    |  | 3                        | 49                | 15              | C=0.1, penalty='l1', solver='liblinear'  | 0.955 $\pm$ 0.0633      | 1.00 $\pm$ 0.000          | 0.554 $\pm$ 0.180      | 0.695 $\pm$ 0.156        |
|                                    | Van Rheezen<br>(case-control)                | 1                        | 858               | 48              | C=1.0, penalty='l1', solver='liblinear'  | 1.00 $\pm$ 0.000        | 1.00 $\pm$ 0.000          | 1.00 $\pm$ 0.000       | 1.00 $\pm$ 0.000         |
|                                    |  | 2                        | 110               | 131             | C=0.01, penalty='l2', solver='liblinear' | 0.786 $\pm$ 0.0984      | 0.563 $\pm$ 0.181         | 0.708 $\pm$ 0.164      | 0.603 $\pm$ 0.110        |
|                                    |  | 3                        | 74                | 79              | C=0.1, penalty='l2', solver='lbfgs'      | 0.845 $\pm$ 0.126       | 0.782 $\pm$ 0.236         | 0.733 $\pm$ 0.249      | 0.730 $\pm$ 0.220        |

|  |  |                                 |     |     |   |   |                   |                   |                   |                |
|--|--|---------------------------------|-----|-----|---|---|-------------------|-------------------|-------------------|----------------|
|  | TargetALS<br>(motor cortex-<br>occipital cortex) | 1                               | 131 | 8   | C=1.0, penalty='l1', solver='liblinear' | 0.997 ±<br>0.00990                      | 0.974 ±<br>0.0542 | 0.979 ±<br>0.0423 | 0.975 ± 0.0324    |                |
|  |  | 2                               | 34  | 10  | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 0.933 ±<br>0.0943 | 0.963 ± 0.0524    |                |
|  |  | 3                               | 48  | 14  | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  | TargetALS<br>(motor cortex-<br>cerebellum)       | 1                               | 187 | 9   | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  |  | 2                               | 43  | 110 | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  |  | 3                               | 66  | 13  | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  | 3<br>(Genes<br>Common to All<br>Folds)           | KCL BrainBank<br>(case-control) | 1   | 119 | 7                                       | C=0.1, penalty='l1', solver='liblinear' | 0.833 ± 0.114     | 0.893 ±<br>0.0930 | 0.767 ± 0.137     | 0.817 ± 0.100  |
|  |  | TargetALS<br>(case-control)     | 1   | 121 | 2                                       | C=0.1, penalty='l2', solver='lbfgs'     | 0.832 ± 0.120     | 0.907 ±<br>0.0741 | 0.827 ± 0.135     | 0.856 ± 0.0781 |
|  |  | Van Rheenen<br>(case-control)   | 1   | 858 | 38                                      | C=0.1, penalty='l1', solver='liblinear' | 0.691 ±<br>0.0559 | 0.530 ±<br>0.0560 | 0.675 ±<br>0.0861 | 0.591 ± 0.0613 |
| 2  |  |                                 | 110 | 54  | C=0.01, penalty='l2', solver='lbfgs'    | 0.790 ± 0.145                           | 0.625 ± 0.203     | 0.625 ± 0.212     | 0.600 ± 0.162     |                |
| 3  |  |                                 | 74  | 19  | C=0.01, penalty='l2', solver='lbfgs'    | 0.752 ± 0.162                           | 0.655 ± 0.260     | 0.583 ± 0.201     | 0.573 ± 0.178     |                |
| TargetALS<br>(motor cortex-<br>occipital cortex) |  | 1                               | 131 | 3   | C=0.0001, penalty='l2', solver='lbfgs'  | 0.790 ± 0.150                           | 0.906 ± 0.111     | 0.638 ± 0.139     | 0.735 ± 0.111     |                |
| TargetALS(motor<br>cortex-<br>cerebellum)        |  | 1                               | 187 | 6   | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  |  | 2                               | 43  | 1   | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |
|  |  | 3                               | 66  | 2   | C=1.0, penalty='l1', solver='liblinear' | 1.000 ± 0.000                           | 1.000 ± 0.000     | 1.000 ± 0.000     | 1.000 ± 0.000     |                |

*Table A37. Performance metrics of the cluster-specific logistic regression classifier models with ten-fold cross validation for the three case-control datasets, and two motor cortex-other brain region datasets in TargetALS under each scenario. The number of genes in scenario 1 refers to the genes shared by cases and controls in each dataset of the KCL BrainBank case-defined informative genes which constitute that cluster. The number of genes in scenario 2 refers to the average number of genes over all folds after removal of correlated genes. For scenario 3, the genes common to all folds refers to genes present in all ten folds after the effects of multicollinearity was removed. The 'best hyperparameter' column details the parameters which were supplied to train each logistic regression model, selected after performing hyperparameter tuning using GridSearchCV. ROC AUC: Area under the Receiver Operating Characteristic Curve.*

| Scenario | Cluster | Ensembl ID      | Gene Symbol        | SHAP Importance |
|----------|---------|-----------------|--------------------|-----------------|
| 1        | 1       | ENSG00000146469 | VIP                | 0.0479          |
| 1        | 1       | ENSG00000156076 | WIF1               | 0.0391          |
| 1        | 1       | ENSG00000157005 | SST                | 0.0355          |
| 1        | 1       | ENSG00000233123 | LINC01007          | 0.0347          |
| 1        | 1       | ENSG00000185149 | NPY2R              | 0.0346          |
| 1        | 1       | ENSG00000117594 | HSD11B1            | 0.0342          |
| 1        | 1       | ENSG00000248837 | LOC105374524       | 0.0334          |
| 1        | 1       | ENSG00000122012 | SV2C               | 0.0326          |
| 1        | 1       | ENSG00000287593 | Antisense to ADTRP | 0.0324          |
| 1        | 1       | ENSG00000254101 | LINC02055          | 0.0323          |
| 1        | 1       | ENSG00000287611 | Lnc-HRH4-2         | 0.0314          |
| 1        | 1       | ENSG00000254561 | None               | 0.0313          |
| 1        | 1       | ENSG00000231824 | AKAIN1             | 0.0312          |
| 1        | 1       | ENSG00000179520 | SLC17A8            | 0.0296          |
| 1        | 1       | ENSG00000117322 | CR2                | 0.0274          |
| 1        | 1       | ENSG00000285561 | None               | 0.0273          |
| 1        | 1       | ENSG00000205634 | LINC00898          | 0.0268          |
| 1        | 1       | ENSG00000261738 | MIR3976HG          | 0.0246          |
| 1        | 1       | ENSG00000174403 | CRMA               | 0.0245          |
| 1        | 1       | ENSG00000144227 | NXPH2              | 0.0236          |
| 1        | 1       | ENSG00000141433 | ADCYAP1            | 0.0235          |
| 1        | 1       | ENSG00000205279 | CTXN3              | 0.0231          |
| 1        | 1       | ENSG00000120875 | DUSP4              | 0.0214          |
| 1        | 1       | ENSG00000006128 | TAC1               | 0.0213          |
| 1        | 1       | ENSG00000286109 | Lnc-KCNK1-1        | 0.0212          |
| 1        | 1       | ENSG00000223930 | Lnc-ZMAT3-3        | 0.0209          |
| 1        | 1       | ENSG00000286292 | None               | 0.0207          |
| 1        | 1       | ENSG00000271538 | LINC02427          | 0.0206          |

|   |   |                 |                   |        |
|---|---|-----------------|-------------------|--------|
| 1 | 1 | ENSG00000286810 | None              | 0.0205 |
| 1 | 1 | ENSG00000143858 | SYT2              | 0.0200 |
| 1 | 1 | ENSG00000126545 | CSN1S1            | 0.0196 |
| 1 | 1 | ENSG00000132677 | RHBG              | 0.0196 |
| 1 | 1 | ENSG00000228999 | LINC01830         | 0.0195 |
| 1 | 1 | ENSG00000152595 | MEPE              | 0.0191 |
| 1 | 1 | ENSG00000128564 | VGF               | 0.0180 |
| 1 | 1 | ENSG00000274330 | ADAM20 Pseudogene | 0.0179 |
| 1 | 1 | ENSG00000159248 | GJD2              | 0.0177 |
| 1 | 1 | ENSG00000280776 | LINC01202         | 0.0174 |
| 1 | 1 | ENSG00000250634 | LINC01182         | 0.0169 |
| 1 | 1 | ENSG00000255087 | LOC101929473      | 0.0157 |
| 1 | 1 | ENSG00000234665 | LERFS             | 0.0156 |
| 1 | 1 | ENSG00000182632 | CCNYL2            | 0.0154 |
| 1 | 1 | ENSG00000229722 | Lnc-SGK1-3        | 0.0153 |
| 1 | 1 | ENSG00000145708 | CRHBP             | 0.0153 |
| 1 | 1 | ENSG00000285634 | LOC105376121      | 0.0153 |
| 1 | 1 | ENSG00000147571 | CRH               | 0.0144 |
| 1 | 1 | ENSG00000100362 | PVALB             | 0.0142 |
| 1 | 1 | ENSG00000164326 | CARTPT            | 0.0141 |
| 1 | 1 | ENSG00000227723 | Lnc-MYB-5         | 0.0136 |
| 1 | 1 | ENSG00000243323 | PTPRVP            | 0.0134 |
| 1 | 1 | ENSG00000160221 | GATD3             | 0.0127 |
| 1 | 1 | ENSG00000179477 | ALOX12B           | 0.0126 |
| 1 | 1 | ENSG00000138678 | GPAT3             | 0.0126 |
| 1 | 1 | ENSG00000286063 | None              | 0.0123 |
| 1 | 1 | ENSG00000277918 | RNVU1-28          | 0.0119 |
| 1 | 1 | ENSG00000256193 | LINC00507         | 0.0117 |
| 1 | 1 | ENSG00000227582 | ADGRF5P1          | 0.0107 |

|   |   |                 |  |        |
|---|---|-----------------|--|--------|
| 1 | 1 | ENSG00000239672 | NME1                                       | 0.0106 |
| 1 | 1 | ENSG00000254681 | PKD1P5                                     | 0.0106 |
| 1 | 1 | ENSG00000225280 | LOC105372558                               | 0.0105 |
| 1 | 1 | ENSG00000200959 | SNORA74A                                   | 0.0104 |
| 1 | 1 | ENSG00000229635 | Pseudogene<br>Similar to Part of<br>FBXW1B | 0.0104 |
| 1 | 1 | ENSG00000225493 | LINC01107                                  | 0.0104 |
| 1 | 1 | ENSG00000246363 | LINC02458                                  | 0.0101 |
| 1 | 1 | ENSG00000218772 | FAM8A6P                                    | 0.0100 |
| 1 | 1 | ENSG00000224404 | Lnc-LARGE1-1                               | 0.0099 |
| 1 | 1 | ENSG00000107165 | TYRP1                                      | 0.0096 |
| 1 | 1 | ENSG00000254363 | LOC101929719                               | 0.0096 |
| 1 | 1 | ENSG00000286016 | None                                       | 0.0095 |
| 1 | 1 | ENSG00000228772 | Lnc-PRL-3                                  | 0.0095 |
| 1 | 1 | ENSG00000216753 | HMGA1P7                                    | 0.0093 |
| 1 | 1 | ENSG00000186081 | KRT5                                       | 0.0092 |
| 1 | 1 | ENSG00000174899 | SLC66A1L                                   | 0.0090 |
| 1 | 1 | ENSG00000254510 | Lnc-NPAS4-1                                | 0.0089 |
| 1 | 1 | ENSG00000268297 | CLEC4GP1                                   | 0.0088 |
| 1 | 1 | ENSG00000104938 | CLEC4M                                     | 0.0088 |
| 1 | 1 | ENSG00000184385 | UMODL1-AS1                                 | 0.0087 |
| 1 | 1 | ENSG00000236714 | LINC01844                                  | 0.0086 |
| 1 | 1 | ENSG00000169676 | DRD5                                       | 0.0086 |
| 1 | 1 | ENSG00000225449 | RAB6C-AS1                                  | 0.0085 |
| 1 | 1 | ENSG00000229618 | Lnc-ARL4A-54                               | 0.0080 |
| 1 | 1 | ENSG00000075673 | ATP12A                                     | 0.0080 |
| 1 | 1 | ENSG00000241945 | PWP2                                       | 0.0078 |
| 1 | 1 | ENSG00000151790 | TDO2                                       | 0.0077 |
| 1 | 1 | ENSG00000137860 | SLC28A2                                    | 0.0075 |

|   |   |                 |                             |        |
|---|---|-----------------|-----------------------------|--------|
| 1 | 1 | ENSG00000286666 | None                        | 0.0075 |
| 1 | 1 | ENSG00000266573 | Lnc-HRH4-7                  | 0.0071 |
| 1 | 1 | ENSG00000130701 | RBBP8NL                     | 0.0071 |
| 1 | 1 | ENSG00000261502 | Lnc-CDH8-10                 | 0.0067 |
| 1 | 1 | ENSG00000267623 | Cyclin Y-Like<br>Pseudogene | 0.0066 |
| 1 | 1 | ENSG00000228735 | LOC124901635                | 0.0065 |
| 1 | 1 | ENSG00000106236 | NPTX2                       | 0.0063 |
| 1 | 1 | ENSG00000281383 | Lnc-KCNE1B-<br>157          | 0.0063 |
| 1 | 1 | ENSG00000188729 | OSTN                        | 0.0062 |
| 1 | 1 | ENSG00000287907 | None                        | 0.0061 |
| 1 | 1 | ENSG00000256971 | LINC00508                   | 0.0060 |
| 1 | 1 | ENSG00000286736 | None                        | 0.0058 |
| 1 | 1 | ENSG00000131885 | KRT17P1                     | 0.0058 |
| 1 | 1 | ENSG00000122025 | FLT3                        | 0.0056 |
| 1 | 1 | ENSG00000165899 | OTOGL                       | 0.0055 |
| 1 | 1 | ENSG00000202048 | SNORD114-20                 | 0.0054 |
| 1 | 1 | ENSG00000150175 | FRMPD2B                     | 0.0054 |
| 1 | 1 | ENSG00000169035 | KLK7                        | 0.0053 |
| 1 | 1 | ENSG00000287844 | None                        | 0.0053 |
| 1 | 1 | ENSG00000226405 | HSD17B12<br>Pseudogene      | 0.0051 |
| 1 | 1 | ENSG00000285578 | Lnc-DUSP22-2                | 0.0051 |
| 1 | 1 | ENSG00000285735 | LINC02717                   | 0.0050 |
| 1 | 1 | ENSG00000279875 | None                        | 0.0050 |
| 1 | 1 | ENSG00000170290 | SLN                         | 0.0048 |
| 1 | 1 | ENSG00000237390 | Lnc-RHBG-1                  | 0.0048 |
| 1 | 1 | ENSG00000111863 | ADTRP                       | 0.0048 |
| 1 | 1 | ENSG00000261325 | LINC02192                   | 0.0047 |
| 1 | 1 | ENSG00000223812 | PYDC2-AS1                   | 0.0044 |

|   |   |                 |                    |        |
|---|---|-----------------|--------------------|--------|
| 1 | 1 | ENSG00000261757 | miR-1255           | 0.0043 |
| 1 | 1 | ENSG00000132744 | ACY3               | 0.0041 |
| 1 | 1 | ENSG00000164600 | NEUROD6            | 0.0041 |
| 1 | 1 | ENSG00000259520 | SLC28A2-AS1        | 0.0040 |
| 1 | 1 | ENSG00000119888 | EPCAM              | 0.0040 |
| 1 | 1 | ENSG00000276462 | LINC03025          | 0.0040 |
| 1 | 1 | ENSG00000170231 | FABP6              | 0.0039 |
| 1 | 1 | ENSG00000178401 | DNAJC22            | 0.0039 |
| 1 | 1 | ENSG00000265179 | Lnc-YES1-8         | 0.0038 |
| 1 | 1 | ENSG00000258859 | LINC02296          | 0.0038 |
| 1 | 1 | ENSG00000242159 | ABCF2P1            | 0.0037 |
| 1 | 1 | ENSG00000260658 | Lnc-CDH8-10        | 0.0036 |
| 1 | 1 | ENSG00000174576 | NPAS4              | 0.0035 |
| 1 | 1 | ENSG00000279952 | None               | 0.0034 |
| 1 | 1 | ENSG00000223553 | SMPD4P1            | 0.0032 |
| 1 | 1 | ENSG00000273214 | Lnc-POLR2F-1       | 0.0028 |
| 1 | 1 | ENSG00000183090 | FREM3              | 0.0024 |
| 1 | 1 | ENSG00000176697 | BDNF               | 0.0023 |
| 2 | 1 | ENSG00000146469 | VIP                | 0.3590 |
| 2 | 1 | ENSG00000156076 | WIF1               | 0.1171 |
| 2 | 1 | ENSG00000117594 | HSD11B1            | 0.0436 |
| 2 | 1 | ENSG00000254561 | None               | 0.0377 |
| 2 | 1 | ENSG00000117322 | CR2                | 0.0303 |
| 2 | 1 | ENSG00000205634 | LINC00898          | 0.0265 |
| 2 | 1 | ENSG00000228999 | LINC01830          | 0.0214 |
| 2 | 1 | ENSG00000287593 | Antisense to ADTRP | 0.0131 |
| 2 | 1 | ENSG00000126545 | CSN1S1             | 0.0067 |
| 2 | 1 | ENSG00000286016 | None               | 0.0066 |
| 2 | 1 | ENSG00000227582 | ADGRF5P1           | 0.0064 |

|   |   |                 |             |        |
|---|---|-----------------|-------------|--------|
| 2 | 1 | ENSG00000286810 | None        | 0.0062 |
| 2 | 1 | ENSG00000285561 | None        | 0.0049 |
| 2 | 1 | ENSG00000107165 | TYRP1       | 0.0036 |
| 2 | 1 | ENSG00000122012 | SV2C        | 0.0022 |
| 2 | 1 | ENSG00000286109 | Lnc-KCNK1-1 | 0.0019 |
| 2 | 1 | ENSG00000250634 | LINC01182   | 0.0017 |
| 2 | 1 | ENSG00000120875 | DUSP4       | 0.0015 |
| 2 | 1 | ENSG00000271538 | LINC02427   | 0.0006 |
| 2 | 1 | ENSG00000243323 | PTPRVP      | 0.0004 |
| 2 | 1 | ENSG00000234665 | LERFS       | 0.0002 |

Table A38. KCL BrainBank Case-Control SHAP values under each scenario, for each cluster. Scenario 1 refers to all shared genes in the KCL BrainBank case-derived signatures. Scenario 2 removes multicollinearity from the gene signatures.



| Scenario | Cluster | Ensembl ID      | Gene Symbol            | SHAP Importance |
|----------|---------|-----------------|------------------------|-----------------|
| 1        | 1       | ENSG00000170290 | SLN                    | 0.0600          |
| 1        | 1       | ENSG00000261325 | LINC02192              | 0.0336          |
| 1        | 1       | ENSG00000261757 | miR-1255               | 0.0321          |
| 1        | 1       | ENSG00000225493 | LINC01107              | 0.0311          |
| 1        | 1       | ENSG00000226405 | HSD17B12<br>Pseudogene | 0.0290          |
| 1        | 1       | ENSG00000285578 | Lnc-DUSP22-2           | 0.0285          |
| 1        | 1       | ENSG00000200959 | SNORA74A               | 0.0251          |
| 1        | 1       | ENSG00000131885 | KRT17P1                | 0.0243          |
| 1        | 1       | ENSG00000160221 | GATD3                  | 0.0230          |
| 1        | 1       | ENSG00000218772 | FAM8A6P                | 0.0224          |
| 1        | 1       | ENSG00000277918 | RNVU1-28               | 0.0213          |
| 1        | 1       | ENSG00000227723 | Lnc-MYB-5              | 0.0206          |
| 1        | 1       | ENSG00000100362 | PVALB                  | 0.0191          |
| 1        | 1       | ENSG00000254363 | LOC101929719           | 0.0191          |
| 1        | 1       | ENSG00000152595 | MEPE                   | 0.0190          |
| 1        | 1       | ENSG00000225280 | LOC105372558           | 0.0186          |
| 1        | 1       | ENSG00000285735 | LINC02717              | 0.0183          |
| 1        | 1       | ENSG00000128564 | VGF                    | 0.0178          |
| 1        | 1       | ENSG00000185149 | NPY2R                  | 0.0158          |
| 1        | 1       | ENSG00000132744 | ACY3                   | 0.0155          |
| 1        | 1       | ENSG00000231824 | AKAIN1                 | 0.0151          |
| 1        | 1       | ENSG00000120875 | DUSP4                  | 0.0146          |
| 1        | 1       | ENSG00000117322 | CR2                    | 0.0146          |
| 1        | 1       | ENSG00000188729 | OSTN                   | 0.0141          |
| 1        | 1       | ENSG00000286292 | None                   | 0.0137          |
| 1        | 1       | ENSG00000260658 | Lnc-CDH8-10            | 0.0117          |

|   |   |                 |                       |        |
|---|---|-----------------|-----------------------|--------|
| 1 | 1 | ENSG00000202048 | SNORD114-20           | 0.0117 |
| 1 | 1 | ENSG00000147571 | CRH                   | 0.0116 |
| 1 | 1 | ENSG00000237390 | Lnc-RHBG-1            | 0.0115 |
| 1 | 1 | ENSG00000205279 | CTXN3                 | 0.0112 |
| 1 | 1 | ENSG00000265179 | Lnc-YES1-8            | 0.0106 |
| 1 | 1 | ENSG00000174576 | NPAS4                 | 0.0100 |
| 1 | 1 | ENSG00000174899 | SLC66A1L              | 0.0097 |
| 1 | 1 | ENSG00000157005 | SST                   | 0.0097 |
| 1 | 1 | ENSG00000132677 | RHBG                  | 0.0097 |
| 1 | 1 | ENSG00000183090 | FREM3                 | 0.0093 |
| 1 | 1 | ENSG00000179477 | ALOX12B               | 0.0091 |
| 1 | 1 | ENSG00000256971 | LINC00508             | 0.0088 |
| 1 | 1 | ENSG00000223930 | Lnc-ZMAT3-3           | 0.0083 |
| 1 | 1 | ENSG00000268297 | CLEC4GP1              | 0.0083 |
| 1 | 1 | ENSG00000126545 | CSN1S1                | 0.0081 |
| 1 | 1 | ENSG00000146469 | VIP                   | 0.0079 |
| 1 | 1 | ENSG00000075673 | ATP12A                | 0.0079 |
| 1 | 1 | ENSG00000216753 | HMGA1P7               | 0.0076 |
| 1 | 1 | ENSG00000273214 | Lnc-POLR2F-1          | 0.0068 |
| 1 | 1 | ENSG00000254510 | Lnc-NPAS4-1           | 0.0065 |
| 1 | 1 | ENSG00000287593 | Antisense to<br>ADTRP | 0.0065 |
| 1 | 1 | ENSG00000130701 | RBBP8NL               | 0.0063 |
| 1 | 1 | ENSG00000286063 | None                  | 0.0057 |
| 1 | 1 | ENSG00000229722 | Lnc-SGK1-3            | 0.0056 |
| 1 | 1 | ENSG00000287907 | None                  | 0.0053 |
| 1 | 1 | ENSG00000254681 | PKD1P5                | 0.0051 |
| 1 | 1 | ENSG00000236714 | LINC01844             | 0.0048 |
| 1 | 1 | ENSG00000234665 | LERFS                 | 0.0045 |
| 1 | 1 | ENSG00000255087 | LOC101929473          | 0.0042 |

|   |   |                 |                      |        |
|---|---|-----------------|----------------------|--------|
| 1 | 1 | ENSG00000276462 | LINC03025            | 0.0042 |
| 1 | 1 | ENSG00000279875 | None                 | 0.0041 |
| 1 | 1 | ENSG00000287844 | None                 | 0.0040 |
| 1 | 1 | ENSG00000241945 | PWP2                 | 0.0039 |
| 1 | 1 | ENSG00000243323 | PTPRVP               | 0.0038 |
| 1 | 1 | ENSG00000274330 | ADAM20<br>Pseudogene | 0.0037 |
| 1 | 1 | ENSG00000104938 | CLEC4M               | 0.0035 |
| 1 | 1 | ENSG00000164326 | CARTPT               | 0.0033 |
| 1 | 1 | ENSG00000186081 | KRT5                 | 0.0033 |
| 1 | 1 | ENSG00000233123 | LINC01007            | 0.0032 |
| 1 | 1 | ENSG00000228772 | Lnc-PRL-3            | 0.0031 |
| 1 | 1 | ENSG00000006128 | TAC1                 | 0.0031 |
| 1 | 1 | ENSG00000227582 | ADGRF5P1             | 0.0026 |
| 1 | 1 | ENSG00000141433 | ADCYAP1              | 0.0020 |
| 1 | 1 | ENSG00000150175 | FRMPD2B              | 0.0017 |
| 1 | 1 | ENSG00000228999 | LINC01830            | 0.0011 |
| 2 | 1 | ENSG00000170290 | SLN                  | 0.1289 |
| 2 | 1 | ENSG00000225493 | LINC01107            | 0.0494 |
| 2 | 1 | ENSG00000131885 | KRT17P1              | 0.0466 |
| 2 | 1 | ENSG00000227723 | Lnc-MYB-5            | 0.0449 |
| 2 | 1 | ENSG00000261757 | miR-1255             | 0.0445 |
| 2 | 1 | ENSG00000261325 | LINC02192            | 0.0424 |
| 2 | 1 | ENSG00000160221 | GATD3                | 0.0346 |
| 2 | 1 | ENSG00000285578 | Lnc-DUSP22-2         | 0.0304 |
| 2 | 1 | ENSG00000128564 | VGF                  | 0.0293 |
| 2 | 1 | ENSG00000075673 | ATP12A               | 0.0289 |
| 2 | 1 | ENSG00000200959 | SNORA74A             | 0.0263 |
| 2 | 1 | ENSG00000277918 | RNVU1-28             | 0.0242 |
| 2 | 1 | ENSG00000231824 | AKAIN1               | 0.0213 |

|   |   |                 |                       |        |
|---|---|-----------------|-----------------------|--------|
| 2 | 1 | ENSG00000185149 | NPY2R                 | 0.0209 |
| 2 | 1 | ENSG00000164326 | CARTPT                | 0.0190 |
| 2 | 1 | ENSG00000276462 | LINC03025             | 0.0179 |
| 2 | 1 | ENSG00000256971 | LINC00508             | 0.0152 |
| 2 | 1 | ENSG00000179477 | ALOX12B               | 0.0147 |
| 2 | 1 | ENSG00000132744 | ACY3                  | 0.0142 |
| 2 | 1 | ENSG00000287593 | Antisense to<br>ADTRP | 0.0138 |
| 2 | 1 | ENSG00000268297 | CLEC4GP1              | 0.0133 |
| 2 | 1 | ENSG00000216753 | HMGA1P7               | 0.0128 |
| 2 | 1 | ENSG00000228999 | LINC01830             | 0.0119 |
| 2 | 1 | ENSG00000228772 | Lnc-PRL-3             | 0.0107 |
| 2 | 1 | ENSG00000254681 | PKD1P5                | 0.0104 |
| 2 | 1 | ENSG00000234665 | LERFS                 | 0.0101 |
| 2 | 1 | ENSG00000254363 | LOC101929719          | 0.0096 |
| 2 | 1 | ENSG00000104938 | CLEC4M                | 0.0091 |
| 2 | 1 | ENSG00000120875 | DUSP4                 | 0.0077 |
| 2 | 1 | ENSG00000286292 | None                  | 0.0076 |
| 2 | 1 | ENSG00000130701 | RBBP8NL               | 0.0074 |
| 2 | 1 | ENSG00000225280 | LOC105372558          | 0.0073 |
| 2 | 1 | ENSG00000202048 | SNORD114-20           | 0.0068 |
| 2 | 1 | ENSG00000279875 | None                  | 0.0064 |
| 2 | 1 | ENSG00000287907 | None                  | 0.0061 |
| 2 | 1 | ENSG00000183090 | FREM3                 | 0.0050 |
| 2 | 1 | ENSG00000174576 | NPAS4                 | 0.0049 |
| 2 | 1 | ENSG00000273214 | Lnc-POLR2F-1          | 0.0047 |
| 2 | 1 | ENSG00000241945 | PWP2                  | 0.0045 |
| 2 | 1 | ENSG00000286063 | None                  | 0.0038 |
| 2 | 1 | ENSG00000152595 | MEPE                  | 0.0035 |
| 2 | 1 | ENSG00000227582 | ADGRF5P1              | 0.0034 |

|   |   |                 |               |        |
|---|---|-----------------|---------------|--------|
| 2 | 1 | ENSG00000265179 | Lnc-YES1-8    | 0.0029 |
| 2 | 1 | ENSG00000260658 | Lnc-CDH8-10   | 0.0017 |
| 2 | 1 | ENSG00000285735 | LINC02717     | 0.0016 |
| 2 | 1 | ENSG00000132677 | RHBG          | 0.0014 |
| 2 | 1 | ENSG00000223930 | Lnc-ZMAT3-3   | 0.0010 |
| 1 | 2 | ENSG00000135245 | HILPDA        | 0.0106 |
| 1 | 2 | ENSG00000159167 | STC1          | 0.0104 |
| 1 | 2 | ENSG00000167772 | ANGPTL4       | 0.0076 |
| 1 | 2 | ENSG00000141574 | SECTM1        | 0.0073 |
| 1 | 2 | ENSG00000148926 | ADM           | 0.0072 |
| 1 | 2 | ENSG00000166592 | RRAD          | 0.0065 |
| 1 | 2 | ENSG00000163638 | ADAMTS9       | 0.0063 |
| 1 | 2 | ENSG00000186431 | FCAR          | 0.0054 |
| 1 | 2 | ENSG00000187634 | SAMD11        | 0.0052 |
| 1 | 2 | ENSG00000163395 | IGFN1         | 0.0044 |
| 1 | 2 | ENSG00000285938 | BCL6-AS1      | 0.0044 |
| 1 | 2 | ENSG00000253686 | LINC01484     | 0.0039 |
| 1 | 2 | ENSG00000103710 | RASL12        | 0.0039 |
| 1 | 2 | ENSG00000112299 | VNN1          | 0.0039 |
| 1 | 2 | ENSG00000077238 | IL4R          | 0.0037 |
| 1 | 2 | ENSG00000250863 | Lnc-KCTD8-1   | 0.0036 |
| 1 | 2 | ENSG00000258647 | LINC00930     | 0.0036 |
| 1 | 2 | ENSG00000144837 | PLA1A         | 0.0034 |
| 1 | 2 | ENSG00000100060 | MFNG          | 0.0034 |
| 1 | 2 | ENSG00000169894 | MUC3A         | 0.0034 |
| 1 | 2 | ENSG00000235750 | KIAA0040      | 0.0034 |
| 1 | 2 | ENSG00000260337 | Lnc-FAM174B-1 | 0.0034 |
| 1 | 2 | ENSG00000120708 | TGFBI         | 0.0034 |
| 1 | 2 | ENSG00000160111 | CPAMD8        | 0.0034 |
| 1 | 2 | ENSG00000124762 | CDKN1A        | 0.0034 |

|   |   |                 |               |        |
|---|---|-----------------|---------------|--------|
| 1 | 2 | ENSG00000125810 | CD93          | 0.0033 |
| 1 | 2 | ENSG00000020633 | RUNX3         | 0.0033 |
| 1 | 2 | ENSG00000115607 | IL18RAP       | 0.0033 |
| 1 | 2 | ENSG00000143546 | S100A8        | 0.0031 |
| 1 | 2 | ENSG00000118729 | CASQ2         | 0.0031 |
| 1 | 2 | ENSG00000258676 | Lnc-ST8SIA2-1 | 0.0031 |
| 1 | 2 | ENSG00000185201 | IFITM2        | 0.0031 |
| 1 | 2 | ENSG00000196154 | S100A4        | 0.0031 |
| 1 | 2 | ENSG00000175591 | P2RY2         | 0.0031 |
| 1 | 2 | ENSG00000125731 | SH2D3A        | 0.0029 |
| 1 | 2 | ENSG00000115604 | IL18R1        | 0.0029 |
| 1 | 2 | ENSG00000229926 | IL9RP1        | 0.0029 |
| 1 | 2 | ENSG00000232803 | SLCO4A1-AS1   | 0.0028 |
| 1 | 2 | ENSG00000138722 | MMRN1         | 0.0026 |
| 1 | 2 | ENSG00000060138 | YBX3          | 0.0026 |
| 1 | 2 | ENSG00000115590 | IL1R2         | 0.0024 |
| 1 | 2 | ENSG00000177464 | GPR4          | 0.0024 |
| 1 | 2 | ENSG00000281327 | LINC01338     | 0.0024 |
| 1 | 2 | ENSG00000241158 | ADAMTS9-AS1   | 0.0024 |
| 1 | 2 | ENSG00000196616 | ADH1B         | 0.0024 |
| 1 | 2 | ENSG00000205592 | MUC19         | 0.0024 |
| 1 | 2 | ENSG00000163736 | PPBP          | 0.0023 |
| 1 | 2 | ENSG00000163220 | S100A9        | 0.0023 |
| 1 | 2 | ENSG00000262003 | LOC101927727  | 0.0023 |
| 1 | 2 | ENSG00000124253 | PCK1          | 0.0023 |
| 1 | 2 | ENSG00000173597 | SULT1B1       | 0.0023 |
| 1 | 2 | ENSG00000236908 | LINC02827     | 0.0021 |
| 1 | 2 | ENSG00000105641 | SLC5A5        | 0.0021 |
| 1 | 2 | ENSG00000267065 | LINC02080     | 0.0021 |
| 1 | 2 | ENSG00000112303 | VNN2          | 0.0021 |

|   |   |                 |              |        |
|---|---|-----------------|--------------|--------|
| 1 | 2 | ENSG00000090339 | ICAM1        | 0.0021 |
| 1 | 2 | ENSG00000100985 | MMP9         | 0.0020 |
| 1 | 2 | ENSG00000152049 | KCNE4        | 0.0020 |
| 1 | 2 | ENSG00000182885 | ADGRG3       | 0.0020 |
| 1 | 2 | ENSG00000251493 | FOXD1        | 0.0020 |
| 1 | 2 | ENSG00000148604 | RGR          | 0.0020 |
| 1 | 2 | ENSG00000174226 | SNX31        | 0.0020 |
| 1 | 2 | ENSG00000070729 | CNGB1        | 0.0018 |
| 1 | 2 | ENSG00000112175 | BMP5         | 0.0018 |
| 1 | 2 | ENSG00000128016 | ZFP36        | 0.0018 |
| 1 | 2 | ENSG00000100336 | APOL4        | 0.0018 |
| 1 | 2 | ENSG00000205358 | MT1H         | 0.0018 |
| 1 | 2 | ENSG00000099994 | SUSD2        | 0.0018 |
| 1 | 2 | ENSG00000272512 | Lnc-HES4-2   | 0.0018 |
| 1 | 2 | ENSG0000013588  | GPRC5A       | 0.0016 |
| 1 | 2 | ENSG00000159212 | CLIC6        | 0.0016 |
| 1 | 2 | ENSG00000149596 | JPH2         | 0.0016 |
| 1 | 2 | ENSG00000166523 | CLEC4E       | 0.0016 |
| 1 | 2 | ENSG00000184557 | SOCS3        | 0.0016 |
| 1 | 2 | ENSG00000179023 | KLHDC7A      | 0.0016 |
| 1 | 2 | ENSG00000162383 | SLC1A7       | 0.0016 |
| 1 | 2 | ENSG00000270640 | Lnc-BABAM2-2 | 0.0016 |
| 1 | 2 | ENSG00000106366 | SERPINE1     | 0.0016 |
| 1 | 2 | ENSG00000169429 | CXCL8        | 0.0015 |
| 1 | 2 | ENSG00000230122 | ECEL1P3      | 0.0015 |
| 1 | 2 | ENSG00000184058 | TBX1         | 0.0015 |
| 1 | 2 | ENSG00000112936 | C7           | 0.0015 |
| 1 | 2 | ENSG00000249307 | LINC01088    | 0.0015 |
| 1 | 2 | ENSG00000128274 | A4GALT       | 0.0015 |
| 1 | 2 | ENSG00000162747 | FCGR3B       | 0.0015 |

|   |   |                 |                                    |        |
|---|---|-----------------|------------------------------------|--------|
| 1 | 2 | ENSG00000108823 | SGCA                               | 0.0013 |
| 1 | 2 | ENSG00000129654 | FOXJ1                              | 0.0013 |
| 1 | 2 | ENSG00000171049 | FPR2                               | 0.0013 |
| 1 | 2 | ENSG00000278130 | FAM166A<br>Pseudogene              | 0.0013 |
| 1 | 2 | ENSG00000167244 | IGF2                               | 0.0013 |
| 1 | 2 | ENSG00000173110 | HSPA6                              | 0.0013 |
| 1 | 2 | ENSG00000160183 | TMPRSS3                            | 0.0013 |
| 1 | 2 | ENSG00000004939 | SLC4A1                             | 0.0013 |
| 1 | 2 | ENSG00000256955 | Lnc-MMP17-1                        | 0.0013 |
| 1 | 2 | ENSG00000015520 | NPC1L1                             | 0.0013 |
| 1 | 2 | ENSG00000142973 | CYP4B1                             | 0.0013 |
| 1 | 2 | ENSG00000229380 | PRKAR1B-AS2                        | 0.0013 |
| 1 | 2 | ENSG00000125430 | HS3ST3B1                           | 0.0011 |
| 1 | 2 | ENSG00000124107 | SLPI                               | 0.0011 |
| 1 | 2 | ENSG00000287652 | Antisense to<br>DGCR8 and<br>CDC45 | 0.0011 |
| 1 | 2 | ENSG00000110852 | CLEC2B                             | 0.0011 |
| 1 | 2 | ENSG00000261170 | LOC107984827                       | 0.0011 |
| 1 | 2 | ENSG00000118271 | TTR                                | 0.0010 |
| 1 | 2 | ENSG00000111057 | KRT18                              | 0.0010 |
| 1 | 2 | ENSG00000115648 | MLPH                               | 0.0010 |
| 1 | 2 | ENSG00000170345 | FOS                                | 0.0010 |
| 1 | 2 | ENSG00000163464 | CXCR1                              | 0.0010 |
| 1 | 2 | ENSG00000196954 | CASP4                              | 0.0010 |
| 1 | 2 | ENSG00000188536 | HBA2                               | 0.0010 |
| 1 | 2 | ENSG00000198848 | CES1                               | 0.0010 |
| 1 | 2 | ENSG00000287338 | Lnc-TLR5-1                         | 0.0008 |
| 1 | 2 | ENSG00000281732 | LOC284933                          | 0.0008 |
| 1 | 2 | ENSG00000115602 | IL1RL1                             | 0.0008 |

|   |   |                 |                 |        |
|---|---|-----------------|-----------------|--------|
| 1 | 2 | ENSG00000074219 | TEAD2           | 0.0008 |
| 1 | 2 | ENSG00000163623 | NKX6-1          | 0.0008 |
| 1 | 2 | ENSG00000108821 | COL1A1          | 0.0008 |
| 1 | 2 | ENSG00000109758 | HGFAC           | 0.0008 |
| 1 | 2 | ENSG00000267304 | Lnc-TJP3-2      | 0.0008 |
| 1 | 2 | ENSG00000047457 | CP              | 0.0008 |
| 1 | 2 | ENSG00000149573 | MPZL2           | 0.0008 |
| 1 | 2 | ENSG00000163739 | CXCL1           | 0.0007 |
| 1 | 2 | ENSG00000162692 | VCAM1           | 0.0007 |
| 1 | 2 | ENSG00000050327 | ARHGEF5         | 0.0007 |
| 1 | 2 | ENSG00000228133 | LOC105371485    | 0.0007 |
| 1 | 2 | ENSG00000175084 | DES             | 0.0007 |
| 1 | 2 | ENSG00000088882 | CPXM1           | 0.0007 |
| 1 | 2 | ENSG00000226390 | KCNQ2-AS1       | 0.0005 |
| 1 | 2 | ENSG00000176692 | FOXC2           | 0.0005 |
| 1 | 2 | ENSG00000279821 | None            | 0.0005 |
| 1 | 2 | ENSG00000237424 | FOXD2-AS1       | 0.0005 |
| 1 | 2 | ENSG00000254362 | Lnc-PPP2R2A-2   | 0.0005 |
| 1 | 2 | ENSG00000143867 | OSR1            | 0.0005 |
| 1 | 2 | ENSG00000140839 | CLEC18B         | 0.0005 |
| 1 | 2 | ENSG00000177575 | CD163           | 0.0005 |
| 1 | 2 | ENSG00000249669 | CARMN           | 0.0003 |
| 1 | 2 | ENSG00000276317 | Lnc-GATA5-10    | 0.0003 |
| 1 | 2 | ENSG00000186564 | FOXD2           | 0.0003 |
| 1 | 2 | ENSG00000276412 | Lnc-CNTNAP3B-13 | 0.0003 |
| 1 | 2 | ENSG00000149452 | SLC22A8         | 0.0003 |
| 1 | 2 | ENSG00000287689 | None            | 0.0003 |
| 1 | 2 | ENSG00000171345 | KRT19           | 0.0003 |
| 1 | 2 | ENSG00000262152 | GREP1           | 0.0002 |

|   |   |                 |              |        |
|---|---|-----------------|--------------|--------|
| 1 | 2 | ENSG00000168079 | SCARA5       | 0.0002 |
| 1 | 2 | ENSG00000115594 | IL1R1        | 0.0002 |
| 1 | 2 | ENSG00000173530 | TNFRSF10D    | 0.0002 |
| 1 | 2 | ENSG00000173421 | IHO1         | 0.0002 |
| 2 | 2 | ENSG00000167772 | ANGPTL4      | 0.1156 |
| 2 | 2 | ENSG00000148926 | ADM          | 0.0540 |
| 2 | 2 | ENSG00000159167 | STC1         | 0.0462 |
| 2 | 2 | ENSG00000267065 | LINC02080    | 0.0093 |
| 2 | 2 | ENSG00000174226 | SNX31        | 0.0091 |
| 2 | 2 | ENSG00000250863 | Lnc-KCTD8-1  | 0.0047 |
| 2 | 2 | ENSG00000109758 | HGFAC        | 0.0026 |
| 2 | 2 | ENSG00000205592 | MUC19        | 0.0007 |
| 2 | 2 | ENSG00000149452 | SLC22A8      | 0.0007 |
| 2 | 2 | ENSG00000186564 | FOXD2        | 0.0005 |
| 2 | 2 | ENSG00000099994 | SUSD2        | 0.0002 |
| 1 | 3 | ENSG00000273259 | Thioesterase | 0.1406 |
| 1 | 3 | ENSG00000005844 | ITGAL        | 0.0435 |
| 1 | 3 | ENSG00000131401 | NAPSB        | 0.0312 |
| 1 | 3 | ENSG00000265531 | FCGR1CP      | 0.0301 |
| 1 | 3 | ENSG00000244731 | C4A          | 0.0285 |
| 1 | 3 | ENSG00000073737 | DHRS9        | 0.0111 |
| 1 | 3 | ENSG00000172243 | CLEC7A       | 0.0108 |
| 1 | 3 | ENSG00000128262 | POM121L9P    | 0.0090 |
| 1 | 3 | ENSG00000231131 | LNCAROD      | 0.0050 |
| 1 | 3 | ENSG00000254081 | LINC01299    | 0.0037 |
| 1 | 3 | ENSG00000115523 | GNLY         | 0.0034 |
| 1 | 3 | ENSG00000070190 | DAPP1        | 0.0030 |
| 1 | 3 | ENSG00000125735 | TNFSF14      | 0.0027 |
| 1 | 3 | ENSG00000261795 | Lnc-PDGFA-4  | 0.0025 |
| 1 | 3 | ENSG00000198774 | RASSF9       | 0.0023 |

|   |   |                 |                          |        |
|---|---|-----------------|--------------------------|--------|
| 1 | 3 | ENSG00000179420 | OR6W1P                   | 0.0023 |
| 1 | 3 | ENSG00000287939 | None                     | 0.0020 |
| 1 | 3 | ENSG00000254415 | SIGLEC14                 | 0.0020 |
| 1 | 3 | ENSG00000270547 | LINC01235                | 0.0019 |
| 1 | 3 | ENSG00000283787 | PRR33                    | 0.0017 |
| 1 | 3 | ENSG00000122585 | NPY                      | 0.0017 |
| 1 | 3 | ENSG00000229391 | HLA-DRB6                 | 0.0017 |
| 1 | 3 | ENSG00000236700 | LINC01010                | 0.0011 |
| 1 | 3 | ENSG00000128652 | HOXD3                    | 0.0010 |
| 1 | 3 | ENSG00000272808 | GCAWKR                   | 0.0010 |
| 1 | 3 | ENSG00000250215 | CIR1P2                   | 0.0007 |
| 1 | 3 | ENSG00000260922 | Antisense to<br>ADAMTS18 | 0.0006 |
| 1 | 3 | ENSG00000187908 | DMBT1                    | 0.0005 |
| 1 | 3 | ENSG00000267287 | Lnc-NFATC1-1             | 0.0004 |
| 1 | 3 | ENSG00000124915 | MYRF-AS1                 | 0.0003 |
| 1 | 3 | ENSG00000261997 | None                     | 0.0001 |
| 2 | 3 | ENSG00000244731 | C4A                      | 0.3211 |
| 2 | 3 | ENSG00000273259 | Thioesterase             | 0.1712 |
| 2 | 3 | ENSG00000198774 | RASSF9                   | 0.0018 |

*Table A39. TargetALS Case-Control SHAP values under each scenario, for each cluster. Scenario 1 refers to all shared genes in the KCL BrainBank case-derived signatures. Scenario 2 removes multicollinearity from the gene signatures.*

| Scenario | Cluster | Ensembl ID      | Gene Symbol | SHAP Importance |
|----------|---------|-----------------|-------------|-----------------|
| 1        | 1       | ENSG00000239672 | NME1        | 0.484219        |
| 1        | 1       | ENSG00000138678 | GPAT3       | 0.000331        |
| 1        | 1       | ENSG00000236714 | LINC01844   | 0.000112        |
| 1        | 1       | ENSG00000111863 | ADTRP       | 0.000082        |
| 1        | 1       | ENSG00000178401 | DNAJC22     | 0.000034        |
| 1        | 1       | ENSG00000147571 | CRH         | 0.000019        |
| 1        | 1       | ENSG00000169676 | DRD5        | 0.000012        |
| 1        | 1       | ENSG00000160221 | GATD3       | 0.000010        |
| 1        | 1       | ENSG00000205279 | CTXN3       | 0.000006        |
| 1        | 1       | ENSG00000188729 | OSTN        | 0.000004        |
| 1        | 1       | ENSG00000117594 | HSD11B1     | 0.000003        |
| 1        | 1       | ENSG00000176697 | BDNF        | 0.000003        |
| 1        | 1       | ENSG00000132677 | RHBG        | 0.000001        |
| 1        | 1       | ENSG00000174576 | NPAS4       | 0.000001        |
| 2        | 1       | ENSG00000239672 | NME1        | 0.484133        |
| 2        | 1       | ENSG00000138678 | GPAT3       | 0.000488        |
| 2        | 1       | ENSG00000236714 | LINC01844   | 0.000082        |
| 2        | 1       | ENSG00000111863 | ADTRP       | 0.000044        |
| 2        | 1       | ENSG00000178401 | DNAJC22     | 0.000023        |
| 2        | 1       | ENSG00000160221 | GATD3       | 0.000016        |
| 2        | 1       | ENSG00000147571 | CRH         | 0.000015        |
| 2        | 1       | ENSG00000205279 | CTXN3       | 0.000009        |
| 2        | 1       | ENSG00000169676 | DRD5        | 0.000009        |
| 2        | 1       | ENSG00000188729 | OSTN        | 0.000006        |
| 2        | 1       | ENSG00000132677 | RHBG        | 0.000003        |
| 2        | 1       | ENSG00000117594 | HSD11B1     | 0.000001        |
| 1        | 2       | ENSG00000188511 | MIR3667HG   | 0.037730        |

|   |   |                 |         |          |
|---|---|-----------------|---------|----------|
| 1 | 2 | ENSG00000204389 | HSPA1A  | 0.033230 |
| 1 | 2 | ENSG00000166523 | CLEC4E  | 0.027560 |
| 1 | 2 | ENSG00000182885 | ADGRG3  | 0.026113 |
| 1 | 2 | ENSG00000173641 | HSPB7   | 0.024598 |
| 1 | 2 | ENSG00000112303 | VNN2    | 0.023829 |
| 1 | 2 | ENSG00000137801 | THBS1   | 0.023749 |
| 1 | 2 | ENSG00000164692 | COL1A2  | 0.023026 |
| 1 | 2 | ENSG00000162692 | VCAM1   | 0.022004 |
| 1 | 2 | ENSG00000184557 | SOCS3   | 0.021545 |
| 1 | 2 | ENSG00000133392 | MYH11   | 0.020179 |
| 1 | 2 | ENSG00000173597 | SULT1B1 | 0.020133 |
| 1 | 2 | ENSG00000280109 | PLAC4   | 0.019823 |
| 1 | 2 | ENSG00000205364 | MT1M    | 0.019318 |
| 1 | 2 | ENSG00000100985 | MMP9    | 0.019249 |
| 1 | 2 | ENSG00000124253 | PCK1    | 0.017700 |
| 1 | 2 | ENSG00000112299 | VNN1    | 0.017642 |
| 1 | 2 | ENSG00000143867 | OSR1    | 0.017573 |
| 1 | 2 | ENSG00000144837 | PLA1A   | 0.017206 |
| 1 | 2 | ENSG00000196616 | ADH1B   | 0.017160 |
| 1 | 2 | ENSG00000142173 | COL6A2  | 0.017068 |
| 1 | 2 | ENSG00000163395 | IGFN1   | 0.016816 |
| 1 | 2 | ENSG00000135245 | HILPDA  | 0.016793 |
| 1 | 2 | ENSG00000183508 | TENT5C  | 0.016368 |
| 1 | 2 | ENSG00000110719 | TCIRG1  | 0.016288 |
| 1 | 2 | ENSG00000108823 | SGCA    | 0.016058 |
| 1 | 2 | ENSG00000112499 | SLC22A2 | 0.015955 |
| 1 | 2 | ENSG00000241644 | INMT    | 0.015783 |
| 1 | 2 | ENSG00000125144 | MT1G    | 0.015576 |
| 1 | 2 | ENSG00000162458 | FBLIM1  | 0.015496 |
| 1 | 2 | ENSG00000102802 | MEDAG   | 0.015393 |

|   |   |                 |         |          |
|---|---|-----------------|---------|----------|
| 1 | 2 | ENSG0000015520  | NPC1L1  | 0.014681 |
| 1 | 2 | ENSG00000205038 | PKHD1L1 | 0.014566 |
| 1 | 2 | ENSG00000213719 | CLIC1   | 0.014279 |
| 1 | 2 | ENSG00000183888 | SRARP   | 0.014130 |
| 1 | 2 | ENSG00000175591 | P2RY2   | 0.013912 |
| 1 | 2 | ENSG00000112936 | C7      | 0.013797 |
| 1 | 2 | ENSG00000105641 | SLC5A5  | 0.013751 |
| 1 | 2 | ENSG00000130635 | COL5A1  | 0.013717 |
| 1 | 2 | ENSG00000144810 | COL8A1  | 0.013717 |
| 1 | 2 | ENSG00000107438 | PDLIM1  | 0.013108 |
| 1 | 2 | ENSG00000103710 | RASL12  | 0.013017 |
| 1 | 2 | ENSG00000000971 | CFH     | 0.012798 |
| 1 | 2 | ENSG00000182718 | ANXA2   | 0.012730 |
| 1 | 2 | ENSG00000112214 | FHL5    | 0.012684 |
| 1 | 2 | ENSG00000141052 | MYOCD   | 0.012580 |
| 1 | 2 | ENSG00000187513 | GJA4    | 0.012569 |
| 1 | 2 | ENSG00000174226 | SNX31   | 0.012523 |
| 1 | 2 | ENSG00000177464 | GPR4    | 0.012466 |
| 1 | 2 | ENSG00000166482 | MFAP4   | 0.012454 |
| 1 | 2 | ENSG00000186431 | FCAR    | 0.012339 |
| 1 | 2 | ENSG00000105974 | CAV1    | 0.012305 |
| 1 | 2 | ENSG00000163736 | PPBP    | 0.012236 |
| 1 | 2 | ENSG00000128016 | ZFP36   | 0.012029 |
| 1 | 2 | ENSG00000265107 | GJA5    | 0.011961 |
| 1 | 2 | ENSG00000185585 | OLFML2A | 0.011892 |
| 1 | 2 | ENSG00000100060 | MFNG    | 0.011880 |
| 1 | 2 | ENSG00000003436 | TFPI    | 0.011846 |
| 1 | 2 | ENSG00000160593 | JAML    | 0.011628 |
| 1 | 2 | ENSG00000118729 | CASQ2   | 0.011455 |
| 1 | 2 | ENSG00000134531 | EMP1    | 0.011203 |

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| 1 | 2 | ENSG00000167772 | ANGPTL4  | 0.011180 |
| 1 | 2 | ENSG00000125810 | CD93     | 0.011008 |
| 1 | 2 | ENSG00000115607 | IL18RAP  | 0.010847 |
| 1 | 2 | ENSG00000163017 | ACTG2    | 0.010824 |
| 1 | 2 | ENSG00000000938 | FGR      | 0.010778 |
| 1 | 2 | ENSG00000115594 | IL1R1    | 0.010698 |
| 1 | 2 | ENSG00000004939 | SLC4A1   | 0.010686 |
| 1 | 2 | ENSG00000117595 | IRF6     | 0.010618 |
| 1 | 2 | ENSG00000060138 | YBX3     | 0.010572 |
| 1 | 2 | ENSG00000120708 | TGFBI    | 0.010537 |
| 1 | 2 | ENSG00000173068 | BNC2     | 0.010491 |
| 1 | 2 | ENSG00000130176 | CNN1     | 0.010399 |
| 1 | 2 | ENSG00000148604 | RGR      | 0.010308 |
| 1 | 2 | ENSG00000122862 | SRGN     | 0.010273 |
| 1 | 2 | ENSG00000149257 | SERPINH1 | 0.010262 |
| 1 | 2 | ENSG00000145623 | OSMR     | 0.010227 |
| 1 | 2 | ENSG00000187498 | COL4A1   | 0.010135 |
| 1 | 2 | ENSG00000140682 | TGFB111  | 0.009940 |
| 1 | 2 | ENSG00000162998 | FRZB     | 0.009929 |
| 1 | 2 | ENSG00000169894 | MUC3A    | 0.009871 |
| 1 | 2 | ENSG00000163638 | ADAMTS9  | 0.009688 |
| 1 | 2 | ENSG00000090339 | ICAM1    | 0.009688 |
| 1 | 2 | ENSG00000145779 | TNFAIP8  | 0.009596 |
| 1 | 2 | ENSG00000135842 | NIBAN1   | 0.009504 |
| 1 | 2 | ENSG0000020633  | RUNX3    | 0.009493 |
| 1 | 2 | ENSG00000162383 | SLC1A7   | 0.009298 |
| 1 | 2 | ENSG00000125733 | TRIP10   | 0.009240 |
| 1 | 2 | ENSG00000088882 | CPXM1    | 0.008999 |
| 1 | 2 | ENSG00000176692 | FOXC2    | 0.008953 |
| 1 | 2 | ENSG00000156463 | SH3RF2   | 0.008930 |



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| 1 | 2 | ENSG00000168079 | SCARA5    | 0.008747 |
| 1 | 2 | ENSG00000101335 | MYL9      | 0.008747 |
| 1 | 2 | ENSG00000126778 | SIX1      | 0.008735 |
| 1 | 2 | ENSG00000196154 | S100A4    | 0.008678 |
| 1 | 2 | ENSG00000174348 | PODN      | 0.008414 |
| 1 | 2 | ENSG00000251493 | FOXD1     | 0.008391 |
| 1 | 2 | ENSG00000169908 | TM4SF1    | 0.008333 |
| 1 | 2 | ENSG00000124212 | PTGIS     | 0.008299 |
| 1 | 2 | ENSG00000163464 | CXCR1     | 0.008287 |
| 1 | 2 | ENSG00000099994 | SUSD2     | 0.008242 |
| 1 | 2 | ENSG00000125731 | SH2D3A    | 0.008184 |
| 1 | 2 | ENSG00000106624 | AEBP1     | 0.008173 |
| 1 | 2 | ENSG00000154188 | ANGPT1    | 0.008058 |
| 1 | 2 | ENSG00000149596 | JPH2      | 0.007955 |
| 1 | 2 | ENSG00000159167 | STC1      | 0.007943 |
| 1 | 2 | ENSG00000173530 | TNFRSF10D | 0.007909 |
| 1 | 2 | ENSG00000137834 | SMAD6     | 0.007886 |
| 1 | 2 | ENSG00000106034 | CPED1     | 0.007805 |
| 1 | 2 | ENSG00000176046 | NUPR1     | 0.007782 |
| 1 | 2 | ENSG00000128917 | DLL4      | 0.007656 |
| 1 | 2 | ENSG00000185885 | IFITM1    | 0.007656 |
| 1 | 2 | ENSG00000163739 | CXCL1     | 0.007587 |
| 1 | 2 | ENSG00000198959 | TGM2      | 0.007576 |
| 1 | 2 | ENSG00000173918 | C1QTNF1   | 0.007541 |
| 1 | 2 | ENSG00000165474 | GJB2      | 0.007438 |
| 1 | 2 | ENSG00000142973 | CYP4B1    | 0.007369 |
| 1 | 2 | ENSG00000185499 | MUC1      | 0.007346 |
| 1 | 2 | ENSG00000074047 | GLI2      | 0.007105 |
| 1 | 2 | ENSG00000187922 | LCN10     | 0.007048 |

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| 1 | 2 | ENSG00000197901 | SLC22A6  | 0.007025 |
| 1 | 2 | ENSG00000112837 | TBX18    | 0.006910 |
| 1 | 2 | ENSG00000124762 | CDKN1A   | 0.006864 |
| 1 | 2 | ENSG00000142089 | IFITM3   | 0.006864 |
| 1 | 2 | ENSG00000221869 | CEBPD    | 0.006853 |
| 1 | 2 | ENSG00000184811 | TRARG1   | 0.006830 |
| 1 | 2 | ENSG00000130600 | H19      | 0.006784 |
| 1 | 2 | ENSG00000132357 | CARD6    | 0.006589 |
| 1 | 2 | ENSG00000244734 | HBB      | 0.006520 |
| 1 | 2 | ENSG00000096696 | DSP      | 0.006508 |
| 1 | 2 | ENSG00000169429 | CXCL8    | 0.006474 |
| 1 | 2 | ENSG00000184058 | TBX1     | 0.006428 |
| 1 | 2 | ENSG00000143546 | S100A8   | 0.006428 |
| 1 | 2 | ENSG00000170577 | SIX2     | 0.006359 |
| 1 | 2 | ENSG00000149573 | MPZL2    | 0.006313 |
| 1 | 2 | ENSG00000168542 | COL3A1   | 0.006302 |
| 1 | 2 | ENSG00000111057 | KRT18    | 0.006256 |
| 1 | 2 | ENSG00000198542 | ITGBL1   | 0.006221 |
| 1 | 2 | ENSG00000142102 | PGGHG    | 0.006015 |
| 1 | 2 | ENSG00000094963 | FMO2     | 0.005911 |
| 1 | 2 | ENSG00000187634 | SAMD11   | 0.005900 |
| 1 | 2 | ENSG00000115604 | IL18R1   | 0.005762 |
| 1 | 2 | ENSG00000153404 | PLEKHG4B | 0.005693 |
| 1 | 2 | ENSG00000159403 | C1R      | 0.005693 |
| 1 | 2 | ENSG00000115648 | MLPH     | 0.005682 |
| 1 | 2 | ENSG00000124549 | BTN2A3P  | 0.005406 |
| 1 | 2 | ENSG00000128274 | A4GALT   | 0.005406 |
| 1 | 2 | ENSG00000110852 | CLEC2B   | 0.005395 |
| 1 | 2 | ENSG00000152049 | KCNE4    | 0.005372 |
| 1 | 2 | ENSG00000142798 | HSPG2    | 0.005372 |

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| 1 | 2 | ENSG00000196954 | CASP4    | 0.005337 |
| 1 | 2 | ENSG00000129654 | FOXJ1    | 0.005315 |
| 1 | 2 | ENSG00000011422 | PLAUR    | 0.005269 |
| 1 | 2 | ENSG00000107796 | ACTA2    | 0.005211 |
| 1 | 2 | ENSG00000141574 | SECTM1   | 0.005154 |
| 1 | 2 | ENSG00000124107 | SLPI     | 0.005096 |
| 1 | 2 | ENSG00000050327 | ARHGEF5  | 0.005051 |
| 1 | 2 | ENSG00000186150 | UBL4B    | 0.005039 |
| 1 | 2 | ENSG00000150048 | CLEC1A   | 0.004901 |
| 1 | 2 | ENSG00000047457 | CP       | 0.004832 |
| 1 | 2 | ENSG00000136732 | GYPC     | 0.004809 |
| 1 | 2 | ENSG00000074219 | TEAD2    | 0.004775 |
| 1 | 2 | ENSG00000125430 | HS3ST3B1 | 0.004752 |
| 1 | 2 | ENSG00000047617 | ANO2     | 0.004660 |
| 1 | 2 | ENSG00000118503 | TNFAIP3  | 0.004637 |
| 1 | 2 | ENSG00000108821 | COL1A1   | 0.004637 |
| 1 | 2 | ENSG00000117318 | ID3      | 0.004626 |
| 1 | 2 | ENSG00000115590 | IL1R2    | 0.004511 |
| 1 | 2 | ENSG00000166592 | RRAD     | 0.004442 |
| 1 | 2 | ENSG00000161638 | ITGA5    | 0.004350 |
| 1 | 2 | ENSG00000109758 | HGFAC    | 0.004281 |
| 1 | 2 | ENSG00000013588 | GPRC5A   | 0.004258 |
| 1 | 2 | ENSG00000187955 | COL14A1  | 0.004224 |
| 1 | 2 | ENSG00000197405 | C5AR1    | 0.004144 |
| 1 | 2 | ENSG00000186564 | FOXD2    | 0.004098 |
| 1 | 2 | ENSG00000206538 | VGLL3    | 0.004098 |
| 1 | 2 | ENSG00000179023 | KLHDC7A  | 0.004029 |
| 1 | 2 | ENSG00000175084 | DES      | 0.003994 |
| 1 | 2 | ENSG00000122176 | FMOD     | 0.003994 |
| 1 | 2 | ENSG00000115602 | IL1RL1   | 0.003983 |

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| 1 | 2 | ENSG00000177575 | CD163    | 0.003983 |
| 1 | 2 | ENSG00000172935 | MRGPRF   | 0.003972 |
| 1 | 2 | ENSG00000111341 | MGP      | 0.003949 |
| 1 | 2 | ENSG00000185201 | IFITM2   | 0.003822 |
| 1 | 2 | ENSG00000027644 | INSRR    | 0.003776 |
| 1 | 2 | ENSG00000269113 | TRABD2B  | 0.003765 |
| 1 | 2 | ENSG00000149452 | SLC22A8  | 0.003753 |
| 1 | 2 | ENSG00000115165 | CYTIP    | 0.003730 |
| 1 | 2 | ENSG00000198467 | TPM2     | 0.003719 |
| 1 | 2 | ENSG00000137507 | LRRC32   | 0.003696 |
| 1 | 2 | ENSG00000171345 | KRT19    | 0.003639 |
| 1 | 2 | ENSG00000152779 | SLC16A12 | 0.003627 |
| 1 | 2 | ENSG00000163817 | SLC6A20  | 0.003604 |
| 1 | 2 | ENSG00000187479 | C11orf96 | 0.003581 |
| 1 | 2 | ENSG00000205592 | MUC19    | 0.003478 |
| 1 | 2 | ENSG00000164867 | NOS3     | 0.003375 |
| 1 | 2 | ENSG00000205358 | MT1H     | 0.003352 |
| 1 | 2 | ENSG00000160183 | TMPRSS3  | 0.003202 |
| 1 | 2 | ENSG00000100336 | APOL4    | 0.003134 |
| 1 | 2 | ENSG00000159212 | CLIC6    | 0.003122 |
| 1 | 2 | ENSG00000149591 | TAGLN    | 0.003088 |
| 1 | 2 | ENSG00000164707 | SLC13A4  | 0.003042 |
| 1 | 2 | ENSG00000077238 | IL4R     | 0.003007 |
| 1 | 2 | ENSG00000173421 | IHO1     | 0.002938 |
| 1 | 2 | ENSG00000138722 | MMRN1    | 0.002904 |
| 1 | 2 | ENSG00000118271 | TTR      | 0.002893 |
| 1 | 2 | ENSG00000163220 | S100A9   | 0.002870 |
| 1 | 2 | ENSG00000165507 | DEPP1    | 0.002812 |
| 1 | 2 | ENSG00000235750 | KIAA0040 | 0.002789 |
| 1 | 2 | ENSG00000138061 | CYP1B1   | 0.002755 |

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| 1 | 2 | ENSG00000151929 | BAG3      | 0.002606 |
| 1 | 2 | ENSG00000106366 | SERPINE1  | 0.002537 |
| 1 | 2 | ENSG00000152977 | ZIC1      | 0.002502 |
| 1 | 2 | ENSG00000160111 | CPAMD8    | 0.002479 |
| 1 | 2 | ENSG00000170345 | FOS       | 0.002479 |
| 1 | 2 | ENSG00000123374 | CDK2      | 0.002376 |
| 1 | 2 | ENSG00000054598 | FOXC1     | 0.002365 |
| 1 | 2 | ENSG00000163431 | LMOD1     | 0.002353 |
| 1 | 2 | ENSG00000164294 | GPX8      | 0.002238 |
| 1 | 2 | ENSG00000171049 | FPR2      | 0.002112 |
| 1 | 2 | ENSG00000112175 | BMP5      | 0.001986 |
| 1 | 2 | ENSG00000183615 | FAM167B   | 0.001917 |
| 1 | 2 | ENSG00000100504 | PYGL      | 0.001825 |
| 1 | 2 | ENSG00000028137 | TNFRSF1B  | 0.001814 |
| 1 | 2 | ENSG00000168427 | KLHL30    | 0.001756 |
| 1 | 2 | ENSG00000131471 | AOC3      | 0.001630 |
| 1 | 2 | ENSG00000164761 | TNFRSF11B | 0.001607 |
| 1 | 2 | ENSG00000148926 | ADM       | 0.001423 |
| 1 | 2 | ENSG00000168404 | MLKL      | 0.001102 |
| 2 | 2 | ENSG00000188511 | MIR3667HG | 0.043320 |
| 2 | 2 | ENSG00000164692 | COL1A2    | 0.041047 |
| 2 | 2 | ENSG00000173597 | SULT1B1   | 0.039486 |
| 2 | 2 | ENSG00000166523 | CLEC4E    | 0.034929 |
| 2 | 2 | ENSG00000173641 | HSPB7     | 0.034504 |
| 2 | 2 | ENSG00000183508 | TENT5C    | 0.034412 |
| 2 | 2 | ENSG00000204389 | HSPA1A    | 0.032472 |
| 2 | 2 | ENSG00000162692 | VCAM1     | 0.030406 |
| 2 | 2 | ENSG00000196616 | ADH1B     | 0.028696 |
| 2 | 2 | ENSG00000112303 | VNN2      | 0.028099 |
| 2 | 2 | ENSG00000162458 | FBLIM1    | 0.027835 |

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| 2 | 2 | ENSG00000133392 | MYH11   | 0.026515 |
| 2 | 2 | ENSG00000124253 | PCK1    | 0.026171 |
| 2 | 2 | ENSG00000213719 | CLIC1   | 0.024392 |
| 2 | 2 | ENSG00000103710 | RASL12  | 0.022819 |
| 2 | 2 | ENSG00000183888 | SRARP   | 0.022371 |
| 2 | 2 | ENSG00000144837 | PLA1A   | 0.022348 |
| 2 | 2 | ENSG00000125144 | MT1G    | 0.021901 |
| 2 | 2 | ENSG00000144810 | COL8A1  | 0.021591 |
| 2 | 2 | ENSG00000015520 | NPC1L1  | 0.021247 |
| 2 | 2 | ENSG00000163395 | IGFN1   | 0.021097 |
| 2 | 2 | ENSG00000105974 | CAV1    | 0.020478 |
| 2 | 2 | ENSG00000241644 | INMT    | 0.020328 |
| 2 | 2 | ENSG00000169429 | CXCL8   | 0.019984 |
| 2 | 2 | ENSG00000134531 | EMP1    | 0.019410 |
| 2 | 2 | ENSG00000020633 | RUNX3   | 0.018411 |
| 2 | 2 | ENSG00000130635 | COL5A1  | 0.018297 |
| 2 | 2 | ENSG00000126778 | SIX1    | 0.018090 |
| 2 | 2 | ENSG00000105641 | SLC5A5  | 0.017872 |
| 2 | 2 | ENSG00000205038 | PKHD1L1 | 0.017711 |
| 2 | 2 | ENSG00000000971 | CFH     | 0.017562 |
| 2 | 2 | ENSG00000142173 | COL6A2  | 0.017114 |
| 2 | 2 | ENSG00000140682 | TGFB111 | 0.017103 |
| 2 | 2 | ENSG00000130176 | CNN1    | 0.016977 |
| 2 | 2 | ENSG00000141052 | MYOCD   | 0.016942 |
| 2 | 2 | ENSG00000145623 | OSMR    | 0.016736 |
| 2 | 2 | ENSG00000175591 | P2RY2   | 0.016690 |
| 2 | 2 | ENSG00000074047 | GLI2    | 0.016632 |
| 2 | 2 | ENSG00000163638 | ADAMTS9 | 0.016403 |
| 2 | 2 | ENSG00000177464 | GPR4    | 0.015840 |
| 2 | 2 | ENSG00000280109 | PLAC4   | 0.015278 |

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| 2 | 2 | ENSG00000150048 | CLEC1A   | 0.015197 |
| 2 | 2 | ENSG00000149596 | JPH2     | 0.014842 |
| 2 | 2 | ENSG00000112936 | C7       | 0.014738 |
| 2 | 2 | ENSG00000117595 | IRF6     | 0.014348 |
| 2 | 2 | ENSG00000265107 | GJA5     | 0.014291 |
| 2 | 2 | ENSG00000197405 | C5AR1    | 0.013900 |
| 2 | 2 | ENSG00000162383 | SLC1A7   | 0.013682 |
| 2 | 2 | ENSG00000251493 | FOXD1    | 0.013671 |
| 2 | 2 | ENSG00000162998 | FRZB     | 0.013476 |
| 2 | 2 | ENSG00000159403 | C1R      | 0.013441 |
| 2 | 2 | ENSG00000148604 | RGR      | 0.013349 |
| 2 | 2 | ENSG00000205364 | MT1M     | 0.013326 |
| 2 | 2 | ENSG00000130600 | H19      | 0.013166 |
| 2 | 2 | ENSG00000159167 | STC1     | 0.012959 |
| 2 | 2 | ENSG00000187513 | GJA4     | 0.012821 |
| 2 | 2 | ENSG00000163017 | ACTG2    | 0.012661 |
| 2 | 2 | ENSG00000149257 | SERPINH1 | 0.012580 |
| 2 | 2 | ENSG00000099994 | SUSD2    | 0.012420 |
| 2 | 2 | ENSG00000186150 | UBL4B    | 0.012305 |
| 2 | 2 | ENSG00000094963 | FMO2     | 0.011800 |
| 2 | 2 | ENSG00000108821 | COL1A1   | 0.010939 |
| 2 | 2 | ENSG00000164867 | NOS3     | 0.010916 |
| 2 | 2 | ENSG00000125430 | HS3ST3B1 | 0.010778 |
| 2 | 2 | ENSG00000142798 | HSPG2    | 0.010434 |
| 2 | 2 | ENSG00000166592 | RRAD     | 0.010399 |
| 2 | 2 | ENSG00000182718 | ANXA2    | 0.010227 |
| 2 | 2 | ENSG00000003436 | TFPI     | 0.010067 |
| 2 | 2 | ENSG00000125733 | TRIP10   | 0.010044 |
| 2 | 2 | ENSG00000153404 | PLEKHG4B | 0.009906 |
| 2 | 2 | ENSG00000137834 | SMAD6    | 0.009722 |

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| 2 | 2 | ENSG00000184058 | TBX1     | 0.009665 |
| 2 | 2 | ENSG00000013588 | GPRC5A   | 0.009630 |
| 2 | 2 | ENSG00000135245 | HILPDA   | 0.009562 |
| 2 | 2 | ENSG00000185585 | OLFML2A  | 0.009148 |
| 2 | 2 | ENSG00000169894 | MUC3A    | 0.008953 |
| 2 | 2 | ENSG00000118729 | CASQ2    | 0.008907 |
| 2 | 2 | ENSG00000109758 | HGFAC    | 0.008827 |
| 2 | 2 | ENSG00000167772 | ANGPTL4  | 0.008758 |
| 2 | 2 | ENSG00000197901 | SLC22A6  | 0.008678 |
| 2 | 2 | ENSG00000143546 | S100A8   | 0.008597 |
| 2 | 2 | ENSG00000174226 | SNX31    | 0.008597 |
| 2 | 2 | ENSG00000106034 | CPED1    | 0.008551 |
| 2 | 2 | ENSG00000173068 | BNC2     | 0.008460 |
| 2 | 2 | ENSG00000156463 | SH3RF2   | 0.008333 |
| 2 | 2 | ENSG00000235750 | KIAA0040 | 0.008219 |
| 2 | 2 | ENSG00000176692 | FOXC2    | 0.008046 |
| 2 | 2 | ENSG00000142973 | CYP4B1   | 0.007966 |
| 2 | 2 | ENSG00000111057 | KRT18    | 0.007955 |
| 2 | 2 | ENSG00000124549 | BTN2A3P  | 0.007736 |
| 2 | 2 | ENSG00000112214 | FHL5     | 0.007622 |
| 2 | 2 | ENSG00000088882 | CPXM1    | 0.007461 |
| 2 | 2 | ENSG00000115594 | IL1R1    | 0.007438 |
| 2 | 2 | ENSG00000138722 | MMRN1    | 0.007381 |
| 2 | 2 | ENSG00000117318 | ID3      | 0.007335 |
| 2 | 2 | ENSG00000050327 | ARHGEF5  | 0.007300 |
| 2 | 2 | ENSG00000111341 | MGP      | 0.007208 |
| 2 | 2 | ENSG00000132357 | CARD6    | 0.007151 |
| 2 | 2 | ENSG00000124212 | PTGIS    | 0.007094 |
| 2 | 2 | ENSG00000112499 | SLC22A2  | 0.007013 |
| 2 | 2 | ENSG00000106624 | AEBP1    | 0.006921 |

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| 2 | 2 | ENSG00000120708 | TGFBI    | 0.006876 |
| 2 | 2 | ENSG00000100985 | MMP9     | 0.006726 |
| 2 | 2 | ENSG00000112299 | VNN1     | 0.006692 |
| 2 | 2 | ENSG00000125731 | SH2D3A   | 0.006336 |
| 2 | 2 | ENSG00000000938 | FGR      | 0.006210 |
| 2 | 2 | ENSG00000163817 | SLC6A20  | 0.006175 |
| 2 | 2 | ENSG00000152779 | SLC16A12 | 0.006072 |
| 2 | 2 | ENSG00000151929 | BAG3     | 0.005797 |
| 2 | 2 | ENSG00000142102 | PGGHG    | 0.005785 |
| 2 | 2 | ENSG00000168079 | SCARA5   | 0.005659 |
| 2 | 2 | ENSG00000137507 | LRRC32   | 0.005636 |
| 2 | 2 | ENSG00000187498 | COL4A1   | 0.005579 |
| 2 | 2 | ENSG00000206538 | VGLL3    | 0.005567 |
| 2 | 2 | ENSG00000166482 | MFAP4    | 0.005544 |
| 2 | 2 | ENSG00000047457 | CP       | 0.005464 |
| 2 | 2 | ENSG00000112175 | BMP5     | 0.005441 |
| 2 | 2 | ENSG00000106366 | SERPINE1 | 0.005349 |
| 2 | 2 | ENSG00000149591 | TAGLN    | 0.005280 |
| 2 | 2 | ENSG00000077238 | IL4R     | 0.005246 |
| 2 | 2 | ENSG00000187479 | C11orf96 | 0.005211 |
| 2 | 2 | ENSG00000128917 | DLL4     | 0.005188 |
| 2 | 2 | ENSG00000142089 | IFITM3   | 0.005177 |
| 2 | 2 | ENSG00000174348 | PODN     | 0.005096 |
| 2 | 2 | ENSG00000187922 | LCN10    | 0.004959 |
| 2 | 2 | ENSG00000205358 | MT1H     | 0.004832 |
| 2 | 2 | ENSG00000141574 | SECTM1   | 0.004729 |
| 2 | 2 | ENSG00000027644 | INSRR    | 0.004729 |
| 2 | 2 | ENSG00000168427 | KLHL30   | 0.004683 |
| 2 | 2 | ENSG00000152049 | KCNE4    | 0.004660 |
| 2 | 2 | ENSG00000124762 | CDKN1A   | 0.004431 |

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| 2 | 2 | ENSG00000159212 | CLIC6   | 0.004419 |
| 2 | 2 | ENSG00000115607 | IL18RAP | 0.004362 |
| 2 | 2 | ENSG00000054598 | FOXC1   | 0.004362 |
| 2 | 2 | ENSG00000176046 | NUPR1   | 0.004293 |
| 2 | 2 | ENSG00000122176 | FMOD    | 0.004213 |
| 2 | 2 | ENSG00000184811 | TRARG1  | 0.004155 |
| 2 | 2 | ENSG00000152977 | ZIC1    | 0.004086 |
| 2 | 2 | ENSG00000164707 | SLC13A4 | 0.004075 |
| 2 | 2 | ENSG00000112837 | TBX18   | 0.004063 |
| 2 | 2 | ENSG00000172935 | MRGPRF  | 0.004040 |
| 2 | 2 | ENSG00000128274 | A4GALT  | 0.004029 |
| 2 | 2 | ENSG00000149452 | SLC22A8 | 0.003857 |
| 2 | 2 | ENSG00000175084 | DES     | 0.003811 |
| 2 | 2 | ENSG00000173918 | C1QTNF1 | 0.003799 |
| 2 | 2 | ENSG00000168542 | COL3A1  | 0.003788 |
| 2 | 2 | ENSG00000123374 | CDK2    | 0.003742 |
| 2 | 2 | ENSG00000186564 | FOXD2   | 0.003558 |
| 2 | 2 | ENSG00000160183 | TMPRSS3 | 0.003524 |
| 2 | 2 | ENSG00000102802 | MEDAG   | 0.003489 |
| 2 | 2 | ENSG00000143867 | OSR1    | 0.003444 |
| 2 | 2 | ENSG00000165474 | GJB2    | 0.003398 |
| 2 | 2 | ENSG00000115590 | IL1R2   | 0.003122 |
| 2 | 2 | ENSG00000169908 | TM4SF1  | 0.003111 |
| 2 | 2 | ENSG00000205592 | MUC19   | 0.003042 |
| 2 | 2 | ENSG00000124107 | SLPI    | 0.003019 |
| 2 | 2 | ENSG00000163431 | LMOD1   | 0.002743 |
| 2 | 2 | ENSG00000115648 | MLPH    | 0.002525 |
| 2 | 2 | ENSG00000173421 | IHO1    | 0.002445 |
| 2 | 2 | ENSG00000110852 | CLEC2B  | 0.002261 |
| 2 | 2 | ENSG00000011422 | PLAUR   | 0.002238 |

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| 2 | 2 | ENSG00000187634 | SAMD11    | 0.002215 |
| 2 | 2 | ENSG00000170577 | SIX2      | 0.002215 |
| 2 | 2 | ENSG00000183615 | FAM167B   | 0.002158 |
| 2 | 2 | ENSG00000173530 | TNFRSF10D | 0.002135 |
| 2 | 2 | ENSG00000118271 | TTR       | 0.002135 |
| 2 | 2 | ENSG00000100060 | MFNG      | 0.002032 |
| 2 | 2 | ENSG00000149573 | MPZL2     | 0.001963 |
| 2 | 2 | ENSG00000136732 | GYPC      | 0.001963 |
| 2 | 2 | ENSG00000163739 | CXCL1     | 0.001940 |
| 2 | 2 | ENSG00000047617 | ANO2      | 0.001630 |
| 2 | 2 | ENSG00000185201 | IFITM2    | 0.001286 |
| 2 | 2 | ENSG00000090339 | ICAM1     | 0.000964 |
| 2 | 2 | ENSG00000128016 | ZFP36     | 0.000930 |
| 2 | 2 | ENSG00000165507 | DEPP1     | 0.000872 |
| 2 | 2 | ENSG00000198467 | TPM2      | 0.000585 |
| 2 | 2 | ENSG00000101335 | MYL9      | 0.000574 |
| 2 | 2 | ENSG00000179023 | KLHDC7A   | 0.000517 |
| 2 | 2 | ENSG00000160111 | CPAMD8    | 0.000494 |
| 2 | 2 | ENSG00000198542 | ITGBL1    | 0.000321 |
| 1 | 3 | ENSG00000155926 | SLA       | 0.032331 |
| 1 | 3 | ENSG00000183160 | TMEM119   | 0.030964 |
| 1 | 3 | ENSG00000146192 | FGD2      | 0.027797 |
| 1 | 3 | ENSG00000105695 | MAG       | 0.026590 |
| 1 | 3 | ENSG00000166473 | PKD1L2    | 0.022562 |
| 1 | 3 | ENSG00000136235 | GPNMB     | 0.022184 |
| 1 | 3 | ENSG00000126266 | FFAR1     | 0.021561 |
| 1 | 3 | ENSG00000180929 | GPR62     | 0.021522 |
| 1 | 3 | ENSG00000136867 | SLC31A2   | 0.019974 |
| 1 | 3 | ENSG00000236398 | TAS2R39   | 0.017552 |
| 1 | 3 | ENSG00000165131 | LLCFC1    | 0.017531 |

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| 1 | 3 | ENSG00000143226 | FCGR2A   | 0.017464 |
| 1 | 3 | ENSG00000240583 | AQP1     | 0.017397 |
| 1 | 3 | ENSG00000125735 | TNFSF14  | 0.017224 |
| 1 | 3 | ENSG00000038945 | MSR1     | 0.016908 |
| 1 | 3 | ENSG00000188488 | SERPINA5 | 0.016778 |
| 1 | 3 | ENSG00000025708 | TYMP     | 0.016637 |
| 1 | 3 | ENSG00000136167 | LCP1     | 0.016128 |
| 1 | 3 | ENSG00000105366 | SIGLEC8  | 0.016113 |
| 1 | 3 | ENSG00000142583 | SLC2A5   | 0.016110 |
| 1 | 3 | ENSG00000118785 | SPP1     | 0.015850 |
| 1 | 3 | ENSG00000204655 | MOG      | 0.015451 |
| 1 | 3 | ENSG00000128645 | HOXD1    | 0.015317 |
| 1 | 3 | ENSG00000108798 | ABI3     | 0.015273 |
| 1 | 3 | ENSG00000137462 | TLR2     | 0.015217 |
| 1 | 3 | ENSG00000229140 | CCDC26   | 0.014757 |
| 1 | 3 | ENSG00000095970 | TREM2    | 0.014501 |
| 1 | 3 | ENSG00000172005 | MAL      | 0.014171 |
| 1 | 3 | ENSG00000197249 | SERPINA1 | 0.014061 |
| 1 | 3 | ENSG00000175785 | PRIMA1   | 0.013886 |
| 1 | 3 | ENSG00000013297 | CLDN11   | 0.013733 |
| 1 | 3 | ENSG00000196136 | SERPINA3 | 0.013723 |
| 1 | 3 | ENSG00000162949 | CAPN13   | 0.013558 |
| 1 | 3 | ENSG00000183196 | CHST6    | 0.013557 |
| 1 | 3 | ENSG00000179420 | OR6W1P   | 0.013476 |
| 1 | 3 | ENSG00000198774 | RASSF9   | 0.013263 |
| 1 | 3 | ENSG00000154864 | PIEZO2   | 0.013257 |
| 1 | 3 | ENSG00000171631 | P2RY6    | 0.013187 |
| 1 | 3 | ENSG00000183760 | ACP7     | 0.012953 |
| 1 | 3 | ENSG00000180353 | HCLS1    | 0.012739 |

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| 1 | 3 | ENSG00000140030 | GPR65  | 0.012567 |
| 1 | 3 | ENSG00000105383 | CD33   | 0.012469 |
| 1 | 3 | ENSG00000155307 | SAMSN1 | 0.012427 |
| 1 | 3 | ENSG00000131747 | TOP2A  | 0.012424 |
| 1 | 3 | ENSG00000180739 | S1PR5  | 0.012345 |
| 1 | 3 | ENSG00000127507 | ADGRE2 | 0.012343 |
| 1 | 3 | ENSG00000012124 | CD22   | 0.012224 |
| 1 | 3 | ENSG00000105967 | TFEC   | 0.012071 |
| 1 | 3 | ENSG00000166923 | GREM1  | 0.012002 |
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| 1 | 3 | ENSG00000244731 | C4A    | 0.011836 |
| 1 | 3 | ENSG00000112799 | LY86   | 0.011752 |
| 1 | 3 | ENSG00000140968 | IRF8   | 0.011695 |
| 1 | 3 | ENSG00000197993 | KEL    | 0.011641 |
| 1 | 3 | ENSG00000081479 | LRP2   | 0.011435 |
| 1 | 3 | ENSG00000175489 | LRRC25 | 0.011316 |
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| 1 | 3 | ENSG00000129667 | RHBDF2 | 0.011206 |
| 1 | 3 | ENSG00000119535 | CSF3R  | 0.011168 |
| 1 | 3 | ENSG00000070190 | DAPP1  | 0.010861 |
| 1 | 3 | ENSG00000165025 | SYK    | 0.010798 |
| 1 | 3 | ENSG00000275713 | H2BC9  | 0.010559 |
| 1 | 3 | ENSG00000130592 | LSP1   | 0.010312 |
| 1 | 3 | ENSG00000167208 | SNX20  | 0.010183 |
| 1 | 3 | ENSG00000139629 | GALNT6 | 0.010045 |
| 1 | 3 | ENSG00000166091 | CMTM5  | 0.010033 |
| 1 | 3 | ENSG00000159399 | HK2    | 0.010021 |
| 1 | 3 | ENSG00000225781 | OR6V1  | 0.009803 |
| 1 | 3 | ENSG00000169413 | RNASE6 | 0.009790 |

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| 1 | 3 | ENSG00000152804 | HHEX     | 0.009685 |
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| 1 | 3 | ENSG00000277775 | H3C7     | 0.009639 |
| 1 | 3 | ENSG00000010327 | STAB1    | 0.009555 |
| 1 | 3 | ENSG00000129757 | CDKN1C   | 0.009542 |
| 1 | 3 | ENSG00000153551 | CMTM7    | 0.009388 |
| 1 | 3 | ENSG00000163191 | S100A11  | 0.009330 |
| 1 | 3 | ENSG00000115956 | PLEK     | 0.009307 |
| 1 | 3 | ENSG00000026508 | CD44     | 0.009266 |
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| 1 | 3 | ENSG00000131401 | NAPSB    | 0.009190 |
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| 1 | 3 | ENSG00000108691 | CCL2     | 0.008858 |
| 1 | 3 | ENSG00000158869 | FCER1G   | 0.008850 |
| 1 | 3 | ENSG00000136286 | MYO1G    | 0.008809 |
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| 1 | 3 | ENSG00000073737 | DHRS9    | 0.008467 |
| 1 | 3 | ENSG00000174607 | UGT8     | 0.008277 |
| 1 | 3 | ENSG00000169403 | PTAFR    | 0.008175 |
| 1 | 3 | ENSG00000142512 | SIGLEC10 | 0.008154 |
| 1 | 3 | ENSG00000107099 | DOCK8    | 0.008048 |
| 1 | 3 | ENSG00000116774 | OLFML3   | 0.007968 |
| 1 | 3 | ENSG00000175567 | UCP2     | 0.007873 |
| 1 | 3 | ENSG00000160791 | CCR5     | 0.007859 |
| 1 | 3 | ENSG00000121933 | TMIGD3   | 0.007828 |
| 1 | 3 | ENSG00000251429 | AIDAP2   | 0.007749 |

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| 1 | 3 | ENSG00000203710 | CR1      | 0.007691 |
| 1 | 3 | ENSG00000179178 | TMEM125  | 0.007677 |
| 1 | 3 | ENSG00000174123 | TLR10    | 0.007667 |
| 1 | 3 | ENSG00000148773 | MKI67    | 0.007589 |
| 1 | 3 | ENSG00000184730 | APOBR    | 0.007552 |
| 1 | 3 | ENSG00000077420 | APBB1IP  | 0.007531 |
| 1 | 3 | ENSG00000090104 | RGS1     | 0.007517 |
| 1 | 3 | ENSG00000080031 | PTPRH    | 0.007506 |
| 1 | 3 | ENSG00000170458 | CD14     | 0.007470 |
| 1 | 3 | ENSG00000126860 | EVI2A    | 0.007465 |
| 1 | 3 | ENSG00000148908 | RGS10    | 0.007402 |
| 1 | 3 | ENSG00000204472 | AIF1     | 0.007390 |
| 1 | 3 | ENSG00000128340 | RAC2     | 0.007371 |
| 1 | 3 | ENSG00000221887 | HMSD     | 0.007339 |
| 1 | 3 | ENSG00000164342 | TLR3     | 0.007332 |
| 1 | 3 | ENSG00000174837 | ADGRE1   | 0.007310 |
| 1 | 3 | ENSG00000005844 | ITGAL    | 0.007291 |
| 1 | 3 | ENSG00000110079 | MS4A4A   | 0.007220 |
| 1 | 3 | ENSG00000122367 | LDB3     | 0.007210 |
| 1 | 3 | ENSG00000145287 | PLAC8    | 0.007206 |
| 1 | 3 | ENSG00000041982 | TNC      | 0.007118 |
| 1 | 3 | ENSG00000173253 | DMRT2    | 0.007037 |
| 1 | 3 | ENSG00000154642 | C21orf91 | 0.006999 |
| 1 | 3 | ENSG00000268758 | ADGRE4P  | 0.006969 |
| 1 | 3 | ENSG00000173391 | OLR1     | 0.006946 |
| 1 | 3 | ENSG00000167851 | CD300A   | 0.006936 |
| 1 | 3 | ENSG00000125730 | C3       | 0.006896 |
| 1 | 3 | ENSG00000228789 | HCG22    | 0.006796 |
| 1 | 3 | ENSG00000139292 | LGR5     | 0.006768 |
| 1 | 3 | ENSG00000204161 | TMEM273  | 0.006749 |

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| 1 | 3 | ENSG00000176381 | PRR18     | 0.006718 |
| 1 | 3 | ENSG00000101670 | LIPG      | 0.006700 |
| 1 | 3 | ENSG00000158865 | SLC5A11   | 0.006587 |
| 1 | 3 | ENSG00000162444 | RBP7      | 0.006506 |
| 1 | 3 | ENSG00000173369 | C1QB      | 0.006444 |
| 1 | 3 | ENSG00000082074 | FYB1      | 0.006411 |
| 1 | 3 | ENSG00000233828 | MIR4280HG | 0.006395 |
| 1 | 3 | ENSG00000185905 | C16orf54  | 0.006388 |
| 1 | 3 | ENSG00000140873 | ADAMTS18  | 0.006382 |
| 1 | 3 | ENSG00000129450 | SIGLEC9   | 0.006325 |
| 1 | 3 | ENSG00000187912 | CLEC17A   | 0.006314 |
| 1 | 3 | ENSG00000018280 | SLC11A1   | 0.006295 |
| 1 | 3 | ENSG00000137869 | CYP19A1   | 0.006247 |
| 1 | 3 | ENSG00000160223 | ICOSLG    | 0.006211 |
| 1 | 3 | ENSG00000169385 | RNASE2    | 0.006206 |
| 1 | 3 | ENSG00000129810 | SGO1      | 0.006147 |
| 1 | 3 | ENSG00000101049 | SGK2      | 0.006112 |
| 1 | 3 | ENSG00000115523 | GNLY      | 0.006105 |
| 1 | 3 | ENSG00000282608 | ADORA3    | 0.006053 |
| 1 | 3 | ENSG00000172243 | CLEC7A    | 0.005935 |
| 1 | 3 | ENSG00000133048 | CHI3L1    | 0.005907 |
| 1 | 3 | ENSG00000006042 | TMEM98    | 0.005842 |
| 1 | 3 | ENSG00000100292 | HMOX1     | 0.005664 |
| 1 | 3 | ENSG00000158714 | SLAMF8    | 0.005630 |
| 1 | 3 | ENSG00000105122 | RASAL3    | 0.005613 |
| 1 | 3 | ENSG00000134817 | APLNR     | 0.005608 |
| 1 | 3 | ENSG00000167588 | GPD1      | 0.005550 |
| 1 | 3 | ENSG00000110934 | BIN2      | 0.005519 |
| 1 | 3 | ENSG00000221937 | TAS2R40   | 0.005470 |
| 1 | 3 | ENSG00000129465 | RIPK3     | 0.005465 |



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| 1 | 3 | ENSG00000170775 | GPR37     | 0.005451 |
| 1 | 3 | ENSG00000011600 | TYROBP    | 0.005409 |
| 1 | 3 | ENSG00000118640 | VAMP8     | 0.005400 |
| 1 | 3 | ENSG00000232560 | LINC01549 | 0.005231 |
| 1 | 3 | ENSG00000197430 | OPALIN    | 0.005218 |
| 1 | 3 | ENSG00000169896 | ITGAM     | 0.005133 |
| 1 | 3 | ENSG00000006747 | SCIN      | 0.005105 |
| 1 | 3 | ENSG00000167755 | KLK6      | 0.005019 |
| 1 | 3 | ENSG00000160255 | ITGB2     | 0.005015 |
| 1 | 3 | ENSG00000011426 | ANLN      | 0.005013 |
| 1 | 3 | ENSG00000133321 | PLAAT4    | 0.005004 |
| 1 | 3 | ENSG00000155629 | PIK3AP1   | 0.004973 |
| 1 | 3 | ENSG00000014257 | ACP3      | 0.004916 |
| 1 | 3 | ENSG00000051523 | CYBA      | 0.004890 |
| 1 | 3 | ENSG00000103089 | FA2H      | 0.004639 |
| 1 | 3 | ENSG00000166927 | MS4A7     | 0.004593 |
| 1 | 3 | ENSG00000239961 | LILRA4    | 0.004546 |
| 1 | 3 | ENSG00000130300 | PLVAP     | 0.004513 |
| 1 | 3 | ENSG00000157227 | MMP14     | 0.004492 |
| 1 | 3 | ENSG00000081237 | PTPRC     | 0.004440 |
| 1 | 3 | ENSG00000171051 | FPR1      | 0.004416 |
| 1 | 3 | ENSG00000064886 | CHI3L2    | 0.004389 |
| 1 | 3 | ENSG00000205116 | TMEM88B   | 0.004372 |
| 1 | 3 | ENSG00000174125 | TLR1      | 0.004285 |
| 1 | 3 | ENSG00000286522 | H3C2      | 0.004250 |
| 1 | 3 | ENSG00000167641 | PPP1R14A  | 0.004235 |
| 1 | 3 | ENSG00000066336 | SPI1      | 0.004036 |
| 1 | 3 | ENSG00000104972 | LILRB1    | 0.004006 |
| 1 | 3 | ENSG00000138316 | ADAMTS14  | 0.003994 |
| 1 | 3 | ENSG00000104974 | LILRA1    | 0.003954 |

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| 1 | 3 | ENSG00000132965 | ALOX5AP   | 0.003940 |
| 1 | 3 | ENSG00000137752 | CASP1     | 0.003932 |
| 1 | 3 | ENSG00000226496 | LINC00323 | 0.003929 |
| 1 | 3 | ENSG00000163823 | CCR1      | 0.003887 |
| 1 | 3 | ENSG00000019582 | CD74      | 0.003861 |
| 1 | 3 | ENSG00000213186 | TRIM59    | 0.003788 |
| 1 | 3 | ENSG00000161896 | IP6K3     | 0.003683 |
| 1 | 3 | ENSG00000012779 | ALOX5     | 0.003681 |
| 1 | 3 | ENSG00000158715 | SLC45A3   | 0.003648 |
| 1 | 3 | ENSG00000132702 | HAPLN2    | 0.003521 |
| 1 | 3 | ENSG00000134516 | DOCK2     | 0.003451 |
| 1 | 3 | ENSG00000185811 | IKZF1     | 0.003415 |
| 1 | 3 | ENSG00000105697 | HAMP      | 0.003380 |
| 1 | 3 | ENSG00000187908 | DMBT1     | 0.003368 |
| 1 | 3 | ENSG00000275395 | FCGBP     | 0.003365 |
| 1 | 3 | ENSG00000186417 | GLDN      | 0.003362 |
| 1 | 3 | ENSG00000113396 | SLC27A6   | 0.003266 |
| 1 | 3 | ENSG00000152689 | RASGRP3   | 0.003220 |
| 1 | 3 | ENSG00000205403 | CFI       | 0.003197 |
| 1 | 3 | ENSG00000150656 | CNDP1     | 0.003172 |
| 1 | 3 | ENSG00000225217 | HSPA7     | 0.003141 |
| 1 | 3 | ENSG00000162511 | LAPTM5    | 0.003116 |
| 1 | 3 | ENSG00000101336 | HCK       | 0.003066 |
| 1 | 3 | ENSG00000173372 | C1QA      | 0.003050 |
| 1 | 3 | ENSG00000171860 | C3AR1     | 0.003035 |
| 1 | 3 | ENSG00000179468 | OR9A2     | 0.003003 |
| 1 | 3 | ENSG00000270547 | LINC01235 | 0.002988 |
| 1 | 3 | ENSG00000064300 | NGFR      | 0.002956 |
| 1 | 3 | ENSG00000100368 | CSF2RB    | 0.002944 |
| 1 | 3 | ENSG00000271605 | MILR1     | 0.002848 |

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| 1 | 3 | ENSG00000152766 | ANKRD22 | 0.002706 |
| 1 | 3 | ENSG00000168329 | CX3CR1  | 0.002616 |
| 1 | 3 | ENSG00000114013 | CD86    | 0.002565 |
| 1 | 3 | ENSG00000138964 | PARVG   | 0.002512 |
| 1 | 3 | ENSG00000117228 | GBP1    | 0.002491 |
| 1 | 3 | ENSG00000110077 | MS4A6A  | 0.002466 |
| 1 | 3 | ENSG00000258227 | CLEC5A  | 0.002459 |
| 1 | 3 | ENSG00000187554 | TLR5    | 0.002413 |
| 1 | 3 | ENSG00000132854 | KANK4   | 0.002406 |
| 1 | 3 | ENSG00000163563 | MNDA    | 0.002368 |
| 1 | 3 | ENSG00000166928 | MS4A14  | 0.002360 |
| 1 | 3 | ENSG00000171840 | NINJ2   | 0.002289 |
| 1 | 3 | ENSG00000141526 | SLC16A3 | 0.002176 |
| 1 | 3 | ENSG00000198835 | GJC2    | 0.001980 |
| 1 | 3 | ENSG00000159216 | RUNX1   | 0.001955 |
| 1 | 3 | ENSG00000100365 | NCF4    | 0.001923 |
| 1 | 3 | ENSG00000184574 | LPAR5   | 0.001908 |
| 1 | 3 | ENSG00000163565 | IFI16   | 0.001908 |
| 1 | 3 | ENSG00000167613 | LAIR1   | 0.001822 |
| 1 | 3 | ENSG00000012223 | LTF     | 0.001770 |
| 1 | 3 | ENSG00000235568 | NFAM1   | 0.001748 |
| 1 | 3 | ENSG00000203747 | FCGR3A  | 0.001700 |
| 1 | 3 | ENSG00000066294 | CD84    | 0.001622 |
| 1 | 3 | ENSG00000172548 | NIPAL4  | 0.001317 |
| 1 | 3 | ENSG00000136960 | ENPP2   | 0.001112 |
| 1 | 3 | ENSG00000128652 | HOXD3   | 0.000866 |
| 2 | 3 | ENSG00000146192 | FGD2    | 0.049253 |
| 2 | 3 | ENSG00000155926 | SLA     | 0.047209 |
| 2 | 3 | ENSG00000183160 | TMEM119 | 0.040072 |
| 2 | 3 | ENSG00000166473 | PKD1L2  | 0.032514 |

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| 2 | 3 | ENSG00000137462 | TLR2     | 0.031074 |
| 2 | 3 | ENSG00000180929 | GPR62    | 0.028495 |
| 2 | 3 | ENSG00000188488 | SERPINA5 | 0.027904 |
| 2 | 3 | ENSG00000198774 | RASSF9   | 0.027734 |
| 2 | 3 | ENSG00000240583 | AQP1     | 0.027165 |
| 2 | 3 | ENSG00000136286 | MYO1G    | 0.025475 |
| 2 | 3 | ENSG00000136235 | GPNMB    | 0.025122 |
| 2 | 3 | ENSG00000105366 | SIGLEC8  | 0.024713 |
| 2 | 3 | ENSG00000204482 | LST1     | 0.019663 |
| 2 | 3 | ENSG00000165131 | LLCFC1   | 0.019407 |
| 2 | 3 | ENSG00000140030 | GPR65    | 0.018647 |
| 2 | 3 | ENSG00000105695 | MAG      | 0.018559 |
| 2 | 3 | ENSG00000160791 | CCR5     | 0.018419 |
| 2 | 3 | ENSG00000071991 | CDH19    | 0.018402 |
| 2 | 3 | ENSG00000236398 | TAS2R39  | 0.018060 |
| 2 | 3 | ENSG00000142583 | SLC2A5   | 0.016963 |
| 2 | 3 | ENSG00000139629 | GALNT6   | 0.016861 |
| 2 | 3 | ENSG00000183196 | CHST6    | 0.016081 |
| 2 | 3 | ENSG00000129450 | SIGLEC9  | 0.015321 |
| 2 | 3 | ENSG00000073737 | DHRS9    | 0.015017 |
| 2 | 3 | ENSG00000172005 | MAL      | 0.014901 |
| 2 | 3 | ENSG00000173369 | C1QB     | 0.014786 |
| 2 | 3 | ENSG00000166091 | CMTM5    | 0.014603 |
| 2 | 3 | ENSG00000196136 | SERPINA3 | 0.014592 |
| 2 | 3 | ENSG00000129757 | CDKN1C   | 0.014577 |
| 2 | 3 | ENSG00000110079 | MS4A4A   | 0.014229 |
| 2 | 3 | ENSG00000183760 | ACP7     | 0.013745 |
| 2 | 3 | ENSG00000134817 | APLNR    | 0.013617 |
| 2 | 3 | ENSG00000126266 | FFAR1    | 0.013343 |
| 2 | 3 | ENSG00000127412 | TRPV5    | 0.013316 |

|   |   |                 |          |          |
|---|---|-----------------|----------|----------|
| 2 | 3 | ENSG00000064886 | CHI3L2   | 0.013099 |
| 2 | 3 | ENSG00000172243 | CLEC7A   | 0.013094 |
| 2 | 3 | ENSG00000185905 | C16orf54 | 0.012916 |
| 2 | 3 | ENSG00000179420 | OR6W1P   | 0.012738 |
| 2 | 3 | ENSG00000171631 | P2RY6    | 0.012193 |
| 2 | 3 | ENSG00000131747 | TOP2A    | 0.011871 |
| 2 | 3 | ENSG00000132854 | KANK4    | 0.011831 |
| 2 | 3 | ENSG00000204655 | MOG      | 0.011796 |
| 2 | 3 | ENSG00000140968 | IRF8     | 0.011456 |
| 2 | 3 | ENSG00000176381 | PRR18    | 0.011431 |
| 2 | 3 | ENSG00000108691 | CCL2     | 0.011160 |
| 2 | 3 | ENSG00000221887 | HMSD     | 0.010678 |
| 2 | 3 | ENSG00000090382 | LYZ      | 0.010667 |
| 2 | 3 | ENSG00000158865 | SLC5A11  | 0.010517 |
| 2 | 3 | ENSG00000128645 | HOXD1    | 0.010463 |
| 2 | 3 | ENSG00000025708 | TYMP     | 0.010398 |
| 2 | 3 | ENSG00000185811 | IKZF1    | 0.010100 |
| 2 | 3 | ENSG00000130300 | PLVAP    | 0.009862 |
| 2 | 3 | ENSG00000105967 | TFEC     | 0.009819 |
| 2 | 3 | ENSG00000010327 | STAB1    | 0.009764 |
| 2 | 3 | ENSG00000251429 | AIDAP2   | 0.008936 |
| 2 | 3 | ENSG00000125735 | TNFSF14  | 0.008839 |
| 2 | 3 | ENSG00000197430 | OPALIN   | 0.008822 |
| 2 | 3 | ENSG00000166927 | MS4A7    | 0.008767 |
| 2 | 3 | ENSG00000225781 | OR6V1    | 0.008634 |
| 2 | 3 | ENSG00000140873 | ADAMTS18 | 0.008371 |
| 2 | 3 | ENSG00000179468 | OR9A2    | 0.008351 |
| 2 | 3 | ENSG00000180739 | S1PR5    | 0.007086 |
| 2 | 3 | ENSG00000150656 | CNDP1    | 0.007024 |
| 2 | 3 | ENSG00000173372 | C1QA     | 0.006814 |

|   |   |                 |           |          |
|---|---|-----------------|-----------|----------|
| 2 | 3 | ENSG00000101049 | SGK2      | 0.006754 |
| 2 | 3 | ENSG00000038945 | MSR1      | 0.006727 |
| 2 | 3 | ENSG00000174837 | ADGRE1    | 0.006726 |
| 2 | 3 | ENSG00000197249 | SERPINA1  | 0.006623 |
| 2 | 3 | ENSG00000187908 | DMBT1     | 0.006608 |
| 2 | 3 | ENSG00000006747 | SCIN      | 0.006294 |
| 2 | 3 | ENSG00000157227 | MMP14     | 0.006226 |
| 2 | 3 | ENSG00000105122 | RASAL3    | 0.006202 |
| 2 | 3 | ENSG00000148773 | MKI67     | 0.006193 |
| 2 | 3 | ENSG00000026508 | CD44      | 0.006003 |
| 2 | 3 | ENSG00000090104 | RGS1      | 0.005966 |
| 2 | 3 | ENSG00000101670 | LIPG      | 0.005717 |
| 2 | 3 | ENSG00000137752 | CASP1     | 0.005704 |
| 2 | 3 | ENSG00000160223 | ICOSLG    | 0.005695 |
| 2 | 3 | ENSG00000175785 | PRIMA1    | 0.005673 |
| 2 | 3 | ENSG00000108798 | ABI3      | 0.005503 |
| 2 | 3 | ENSG00000103089 | FA2H      | 0.005374 |
| 2 | 3 | ENSG00000213186 | TRIM59    | 0.005181 |
| 2 | 3 | ENSG00000162511 | LAPTM5    | 0.005143 |
| 2 | 3 | ENSG00000126860 | EVI2A     | 0.005017 |
| 2 | 3 | ENSG00000018280 | SLC11A1   | 0.004972 |
| 2 | 3 | ENSG00000041982 | TNC       | 0.004963 |
| 2 | 3 | ENSG00000275713 | H2BC9     | 0.004927 |
| 2 | 3 | ENSG00000268758 | ADGRE4P   | 0.004900 |
| 2 | 3 | ENSG00000171860 | C3AR1     | 0.004898 |
| 2 | 3 | ENSG00000233828 | MIR4280HG | 0.004877 |
| 2 | 3 | ENSG00000133321 | PLAAT4    | 0.004837 |
| 2 | 3 | ENSG00000169413 | RNASE6    | 0.004812 |
| 2 | 3 | ENSG00000158715 | SLC45A3   | 0.004710 |
| 2 | 3 | ENSG00000104972 | LILRB1    | 0.004657 |

|   |   |                 |          |          |
|---|---|-----------------|----------|----------|
| 2 | 3 | ENSG00000154864 | PIEZO2   | 0.004563 |
| 2 | 3 | ENSG00000197471 | SPN      | 0.004538 |
| 2 | 3 | ENSG00000221937 | TAS2R40  | 0.004536 |
| 2 | 3 | ENSG00000186417 | GLDN     | 0.004518 |
| 2 | 3 | ENSG00000081479 | LRP2     | 0.004229 |
| 2 | 3 | ENSG00000139292 | LGR5     | 0.003801 |
| 2 | 3 | ENSG00000164342 | TLR3     | 0.003656 |
| 2 | 3 | ENSG00000170775 | GPR37    | 0.003562 |
| 2 | 3 | ENSG00000286522 | H3C2     | 0.003537 |
| 2 | 3 | ENSG00000134061 | CD180    | 0.003520 |
| 2 | 3 | ENSG00000175489 | LRRC25   | 0.003509 |
| 2 | 3 | ENSG00000128283 | CDC42EP1 | 0.003484 |
| 2 | 3 | ENSG00000105697 | HAMP     | 0.003393 |
| 2 | 3 | ENSG00000104974 | LILRA1   | 0.003388 |
| 2 | 3 | ENSG00000159216 | RUNX1    | 0.003207 |
| 2 | 3 | ENSG00000282608 | ADORA3   | 0.003077 |
| 2 | 3 | ENSG00000204472 | AIF1     | 0.003051 |
| 2 | 3 | ENSG00000167208 | SNX20    | 0.002941 |
| 2 | 3 | ENSG00000275395 | FCGBP    | 0.002849 |
| 2 | 3 | ENSG00000095970 | TREM2    | 0.002546 |
| 2 | 3 | ENSG00000166928 | MS4A14   | 0.002540 |
| 2 | 3 | ENSG00000114013 | CD86     | 0.002510 |
| 2 | 3 | ENSG00000167588 | GPD1     | 0.002439 |
| 2 | 3 | ENSG00000277494 | GPIHBP1  | 0.002355 |
| 2 | 3 | ENSG00000118785 | SPP1     | 0.002335 |
| 2 | 3 | ENSG00000013297 | CLDN11   | 0.002240 |
| 2 | 3 | ENSG00000117228 | GBP1     | 0.002201 |
| 2 | 3 | ENSG00000066294 | CD84     | 0.002201 |
| 2 | 3 | ENSG00000159189 | C1QC     | 0.002175 |
| 2 | 3 | ENSG00000172548 | NIPAL4   | 0.002071 |

|   |   |                 |           |          |
|---|---|-----------------|-----------|----------|
| 2 | 3 | ENSG00000271605 | MILR1     | 0.002017 |
| 2 | 3 | ENSG00000162949 | CAPN13    | 0.001996 |
| 2 | 3 | ENSG00000116774 | OLFML3    | 0.001866 |
| 2 | 3 | ENSG00000173253 | DMRT2     | 0.001824 |
| 2 | 3 | ENSG00000127507 | ADGRE2    | 0.001815 |
| 2 | 3 | ENSG00000163823 | CCR1      | 0.001778 |
| 2 | 3 | ENSG00000136867 | SLC31A2   | 0.001714 |
| 2 | 3 | ENSG00000110934 | BIN2      | 0.001664 |
| 2 | 3 | ENSG00000131401 | NAPSB     | 0.001614 |
| 2 | 3 | ENSG00000184574 | LPAR5     | 0.001588 |
| 2 | 3 | ENSG00000129810 | SGO1      | 0.001543 |
| 2 | 3 | ENSG00000142512 | SIGLEC10  | 0.001487 |
| 2 | 3 | ENSG00000158869 | FCER1G    | 0.001305 |
| 2 | 3 | ENSG00000165025 | SYK       | 0.001250 |
| 2 | 3 | ENSG00000100368 | CSF2RB    | 0.001160 |
| 2 | 3 | ENSG00000129465 | RIPK3     | 0.001084 |
| 2 | 3 | ENSG00000122367 | LDB3      | 0.001075 |
| 2 | 3 | ENSG00000132702 | HAPLN2    | 0.000947 |
| 2 | 3 | ENSG00000137869 | CYP19A1   | 0.000921 |
| 2 | 3 | ENSG00000270547 | LINC01235 | 0.000807 |
| 2 | 3 | ENSG00000100292 | HMOX1     | 0.000792 |
| 2 | 3 | ENSG00000197993 | KEL       | 0.000731 |
| 2 | 3 | ENSG00000229140 | CCDC26    | 0.000731 |
| 2 | 3 | ENSG00000012223 | LTF       | 0.000630 |
| 2 | 3 | ENSG00000179178 | TMEM125   | 0.000611 |
| 2 | 3 | ENSG00000011426 | ANLN      | 0.000605 |
| 2 | 3 | ENSG00000006042 | TMEM98    | 0.000563 |
| 2 | 3 | ENSG00000158714 | SLAMF8    | 0.000537 |
| 2 | 3 | ENSG00000228789 | HCG22     | 0.000407 |
| 2 | 3 | ENSG00000168329 | CX3CR1    | 0.000256 |

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|   |   |                 |          |          |
|---|---|-----------------|----------|----------|
| 2 | 3 | ENSG00000167641 | PPP1R14A | 0.000256 |
|---|---|-----------------|----------|----------|

*Table A40. van Rheenen Case-Control SHAP values under each scenario, for each cluster. Scenario 1 refers to all shared genes in the KCL BrainBank case-derived signatures. Scenario 2 removes multicollinearity from the gene signatures.*

| Dataset (McFadden Pseudo R <sup>2</sup> ) | Ensembl ID      | Gene Symbol         | Cluster | Total Dominance | Percentage Relative Importance |
|---|-----------------|---------------------|---------|-----------------|--------------------------------|
| KCL BrainBank (R <sup>2</sup> : 0.788)    | ENSG00000117318 | <i>ID3</i>          | 2       | 0.0906          | 11.495                         |
|   | ENSG00000026508 | <i>CD44</i>         | 3       | 0.0895          | 11.362                         |
|   | ENSG00000010327 | <i>STAB1</i>        | 3       | 0.0711          | 9.018                          |
|   | ENSG00000135842 | <i>NIBAN1</i>       | 2       | 0.0674          | 8.552                          |
|   | ENSG00000047457 | <i>CP</i>           | 2       | 0.0645          | 8.181                          |
|   | ENSG00000187955 | <i>COL14A1</i>      | 2       | 0.0586          | 7.438                          |
|   | ENSG00000161638 | <i>ITGA5</i>        | 2       | 0.0541          | 6.864                          |
|   | ENSG00000151929 | <i>BAG3</i>         | 2       | 0.0477          | 6.059                          |
|   | ENSG00000028137 | <i>TNFRSF1B</i>     | 2       | 0.0438          | 5.556                          |
|   | ENSG00000125810 | <i>CD93</i>         | 2       | 0.0411          | 5.217                          |
|   | ENSG00000105281 | <i>SLC1A5</i>       | 3       | 0.0385          | 4.881                          |
|   | ENSG00000177575 | <i>CD163</i>        | 2       | 0.0358          | 4.545                          |
|   | ENSG00000164692 | <i>COL1A2</i>       | 2       | 0.0342          | 4.344                          |
|   | ENSG00000158714 | <i>SLAMF8</i>       | 3       | 0.0280          | 3.557                          |
|   | ENSG00000174837 | <i>ADGRE1</i>       | 3       | 0.0231          | 2.931                          |
| TargetALS (R <sup>2</sup> : 0.642)        | ENSG00000249307 | <i>LINC01088</i>    | 2       | 0.1142          | 17.783                         |
|   | ENSG00000152049 | <i>KCNE4</i>        | 2       | 0.0583          | 9.088                          |
|   | ENSG00000026508 | <i>CD44</i>         | 3       | 0.0560          | 8.716                          |
|   | ENSG00000187634 | <i>SAMD11</i>       | 2       | 0.0542          | 8.442                          |
|   | ENSG00000160111 | <i>CPAMD8</i>       | 2       | 0.0481          | 7.493                          |
|   | ENSG00000188488 | <i>SERPINA5</i>     | 3       | 0.0435          | 6.769                          |
|   | ENSG00000244682 | <i>FCGR2C</i>       | 3       | 0.0412          | 6.411                          |
|   | ENSG00000047457 | <i>CP</i>           | 2       | 0.0375          | 5.845                          |
|   | ENSG00000149596 | <i>JPH2</i>         | 2       | 0.0336          | 5.231                          |
|   | ENSG00000240583 | <i>AQP1</i>         | 3       | 0.0319          | 4.974                          |
|   | ENSG00000115590 | <i>IL1R2</i>        | 2       | 0.0291          | 4.533                          |
|   | ENSG00000196136 | <i>SERPINA3</i>     | 3       | 0.0285          | 4.436                          |
|   | ENSG00000273259 | <i>Thioesterase</i> | 3       | 0.0240          | 3.741                          |
|   | ENSG00000064886 | <i>CHI3L2</i>       | 3       | 0.0221          | 3.437                          |
|   | ENSG00000125735 | <i>TNFSF14</i>      | 3       | 0.0199          | 3.102                          |
| van Rheenen (R <sup>2</sup> : 0.339)      | ENSG00000074219 | <i>TEAD2</i>        | 2       | 0.0848          | 24.995                         |
|   | ENSG00000110719 | <i>TCIRG1</i>       | 2       | 0.0500          | 14.738                         |
|   | ENSG00000174125 | <i>TLR1</i>         | 3       | 0.0321          | 9.455                          |
|   | ENSG00000105122 | <i>RASAL3</i>       | 3       | 0.0285          | 8.400                          |
|   | ENSG00000101187 | <i>SLCO4A1</i>      | 2       | 0.0233          | 6.885                          |
|   | ENSG00000100504 | <i>PYGL</i>         | 2       | 0.0193          | 5.701                          |
|   | ENSG00000170345 | <i>FOS</i>          | 2       | 0.0163          | 4.798                          |
|   | ENSG00000185885 | <i>IFITM1</i>       | 2       | 0.0159          | 4.679                          |
|   | ENSG00000012124 | <i>CD22</i>         | 3       | 0.0122          | 3.600                          |
|   | ENSG00000225217 | <i>HSPA7</i>        | 3       | 0.0102          | 3.002                          |
|   | ENSG00000112799 | <i>LY86</i>         | 3       | 0.0102          | 3.001                          |
|   | ENSG00000107438 | <i>PDLIM1</i>       | 2       | 0.0102          | 3.001                          |
|   | ENSG00000118503 | <i>TNFAIP3</i>      | 2       | 0.0098          | 2.878                          |
|   | ENSG00000118271 | <i>TTR</i>          | 2       | 0.0092          | 2.713                          |

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|  |                 |         |   |        |       |
|--|-----------------|---------|---|--------|-------|
|  | ENSG00000187955 | COL14A1 | 2 | 0.0073 | 2.153 |
|--|-----------------|---------|---|--------|-------|

*Table A41. Results of dominance analysis for Cluster 1 vs Clusters 2 and 3. The top 15 predictors were obtained from each dataset, or fewer if there were not at least 15 dominant genes identified. For each dataset, the McFadden's Pseudo  $R^2$  is shown, which is the proportion of variance in the model explained by these predictor genes, with a value of 0.2-0.4 indicating good model fit, and values beyond indicating excellent model fit. For each gene identified as a key predictor, their original cluster assignment is shown, along with their total dominance, which summarises the contributions of each predictor to all of the combinatory models, and percentage relative dominance, which describes the relative importance of each predictor.*

| Dataset (McFadden Pseudo R <sup>2</sup> ) | Ensembl ID      | Gene Symbol               | Cluster | Total Dominance | Percentage Relative Importance |
|---|-----------------|---------------------------|---------|-----------------|--------------------------------|
| KCL BrainBank (R <sup>2</sup> : 0.888)    | ENSG00000161638 | <i>ITGA5</i>              | 2       | 0.1395          | 16.623                         |
|   | ENSG00000107796 | <i>ACTA2</i>              | 2       | 0.0815          | 9.717                          |
|   | ENSG00000206538 | <i>VGLL3</i>              | 2       | 0.0793          | 9.456                          |
|   | ENSG00000112499 | <i>SLC22A2</i>            | 2       | 0.0774          | 9.222                          |
|   | ENSG00000168542 | <i>COL3A1</i>             | 2       | 0.0625          | 7.447                          |
|   | ENSG00000175084 | <i>DES</i>                | 2       | 0.0575          | 6.858                          |
|   | ENSG00000149591 | <i>TAGLN</i>              | 2       | 0.0506          | 6.031                          |
|   | ENSG00000108821 | <i>COL1A1</i>             | 2       | 0.0504          | 6.008                          |
|   | ENSG00000163017 | <i>ACTG2</i>              | 2       | 0.0427          | 5.086                          |
|   | ENSG00000101335 | <i>MYL9</i>               | 2       | 0.0419          | 4.993                          |
|   | ENSG00000187955 | <i>COL14A1</i>            | 2       | 0.0408          | 4.862                          |
|   | ENSG00000131471 | <i>AOC3</i>               | 2       | 0.0391          | 4.660                          |
|   | ENSG00000133392 | <i>MYH11</i>              | 2       | 0.0382          | 4.551                          |
|   | ENSG00000164692 | <i>COL1A2</i>             | 2       | 0.0376          | 4.486                          |
| TargetALS (R <sup>2</sup> : 0.693)        | ENSG00000166523 | <i>CLEC4E</i>             | 2       | 0.0867          | 12.505                         |
|   | ENSG00000112499 | <i>SLC22A2</i>            | 2       | 0.0829          | 11.950                         |
|   | ENSG00000163017 | <i>ACTG2</i>              | 2       | 0.0782          | 11.283                         |
|   | ENSG00000184058 | <i>TBX1</i>               | 2       | 0.0777          | 11.201                         |
|   | ENSG00000229926 | <i>IL9RP1</i>             | 2       | 0.0462          | 6.670                          |
|   | ENSG00000109758 | <i>HGFAC</i>              | 2       | 0.0396          | 5.706                          |
|   | ENSG00000115590 | <i>IL1R2</i>              | 2       | 0.0391          | 5.643                          |
|   | ENSG00000278130 | <i>FAM166A Pseudogene</i> | 2       | 0.0365          | 5.268                          |
|   | ENSG00000170577 | <i>SIX2</i>               | 2       | 0.0338          | 4.878                          |
|   | ENSG00000258676 | <i>Lnc-ST8SIA2-1</i>      | 2       | 0.0332          | 4.792                          |
|   | ENSG00000226390 | <i>KCNQ2-AS1</i>          | 2       | 0.0329          | 4.743                          |
|   | ENSG00000173421 | <i>IHO1</i>               | 2       | 0.0317          | 4.573                          |
|   | ENSG00000279821 | None                      | 2       | 0.0304          | 4.389                          |
|   | ENSG0000015520  | <i>NPC1L1</i>             | 2       | 0.0266          | 3.837                          |
| ENSG00000187922                           | <i>LCN10</i>    | 2                         | 0.0178  | 2.561           |                                |
| van Rheenen (R <sup>2</sup> : 0.375)      | ENSG00000133321 | <i>PLAAT4</i>             | 3       | 0.0632          | 16.868                         |
|   | ENSG00000166927 | <i>MS4A7</i>              | 3       | 0.0410          | 10.957                         |
|   | ENSG00000101335 | <i>MYL9</i>               | 2       | 0.0365          | 9.746                          |
|   | ENSG00000187955 | <i>COL14A1</i>            | 2       | 0.0327          | 8.726                          |
|   | ENSG00000163565 | <i>IFI16</i>              | 3       | 0.0286          | 7.647                          |
|   | ENSG00000096696 | <i>DSP</i>                | 2       | 0.0268          | 7.142                          |
|   | ENSG00000166923 | <i>GREM1</i>              | 3       | 0.0234          | 6.237                          |
|   | ENSG00000118271 | <i>TTR</i>                | 2       | 0.0209          | 5.581                          |
|   | ENSG00000128652 | <i>HOXD3</i>              | 3       | 0.0181          | 4.825                          |
|   | ENSG00000160221 | <i>GATD3A</i>             | 1       | 0.0172          | 4.583                          |
|   | ENSG00000101187 | <i>SLCO4A1</i>            | 2       | 0.0171          | 4.572                          |
|   | ENSG00000161638 | <i>ITGA5</i>              | 2       | 0.0166          | 4.426                          |
|   | ENSG00000225217 | <i>HSPA7</i>              | 3       | 0.0158          | 4.213                          |



|  |                 |       |   |        |       |
|--|-----------------|-------|---|--------|-------|
|  | ENSG00000108823 | SGCA  | 2 | 0.0108 | 2.875 |
|  | ENSG00000074219 | TEAD2 | 2 | 0.0060 | 1.598 |

*Table A42. Results of dominance analysis for Cluster 2 vs Clusters 1 and 3. The top 15 predictors were obtained from each dataset, or fewer if there were not at least 15 dominant genes identified. For each dataset, the McFadden's Pseudo  $R^2$  is shown, which is the proportion of variance in the model explained by these predictor genes, with a value of 0.2-0.4 indicating good model fit, and values beyond indicating excellent model fit. For each gene identified as a key predictor, their original cluster assignment is shown, along with their total dominance, which summarises the contributions of each predictor to all of the combinatory models, and percentage relative dominance, which describes the relative importance of each predictor.*

| Dataset (McFadden Pseudo R <sup>2</sup> ) | Ensembl ID      | Gene Symbol                                 | Cluster | Total Dominance | Percentage Relative Importance |
|---|-----------------|---|---------|-----------------|--------------------------------|
| KCL BrainBank (R <sup>2</sup> : 0.822)    | ENSG00000152689 | <i>RASGRP3</i>                              | 3       | 0.1380          | 16.796                         |
|   | ENSG00000131401 | <i>NAPSB</i>                                | 3       | 0.1205          | 14.663                         |
|   | ENSG00000283431 | <i>Novel Zinc Finger Protein Pseudogene</i> | 3       | 0.1002          | 12.199                         |
|   | ENSG00000042493 | <i>CAPG</i>                                 | 3       | 0.0985          | 11.984                         |
|   | ENSG00000173988 | <i>LRRC63</i>                               | 3       | 0.0860          | 10.469                         |
|   | ENSG00000175785 | <i>PRIMA1</i>                               | 3       | 0.0629          | 7.655                          |
|   | ENSG00000279223 | None  | 3       | 0.0473          | 5.761                          |
|   | ENSG00000128652 | <i>HOXD3</i>                                | 3       | 0.0446          | 5.434                          |
|   | ENSG00000174837 | <i>ADGRE1</i>                               | 3       | 0.0422          | 5.134                          |
|   | ENSG00000188488 | <i>SERPINA5</i>                             | 3       | 0.0410          | 4.990                          |
|   | ENSG00000125735 | <i>TNFSF14</i>                              | 3       | 0.0404          | 4.916                          |
| TargetALS (R <sup>2</sup> : 0.803)        | ENSG00000064886 | <i>CHI3L2</i>                               | 3       | 0.1756          | 21.857                         |
|   | ENSG00000080031 | <i>PTPRH</i>                                | 3       | 0.0607          | 7.556                          |
|   | ENSG00000173988 | <i>LRRC63</i>                               | 3       | 0.0586          | 7.297                          |
|   | ENSG00000172548 | <i>NIPAL4</i>                               | 3       | 0.0586          | 7.288                          |
|   | ENSG00000231840 | <i>TMEM139-AS1</i>                          | 3       | 0.0494          | 6.148                          |
|   | ENSG00000101049 | <i>SGK2</i>                                 | 3       | 0.0468          | 5.820                          |
|   | ENSG00000187908 | <i>DMBT1</i>                                | 3       | 0.0454          | 5.650                          |
|   | ENSG00000139292 | <i>LGR5</i>                                 | 3       | 0.0449          | 5.595                          |
|   | ENSG00000127412 | <i>TRPV5</i>                                | 3       | 0.0441          | 5.483                          |
|   | ENSG00000250072 | <i>SH3TC2-DT</i>                            | 3       | 0.0436          | 5.426                          |
|   | ENSG00000287538 | None  | 3       | 0.0416          | 5.183                          |
|   | ENSG00000259104 | <i>PTCSC3</i>                               | 3       | 0.0367          | 4.564                          |
|   | ENSG00000258342 | <i>LINC00609</i>                            | 3       | 0.0362          | 4.502                          |
|   | ENSG00000231427 | <i>LINC01445</i>                            | 3       | 0.0326          | 4.054                          |
|   | ENSG00000286569 | None  | 3       | 0.0287          | 3.575                          |
| van Rheenen (R <sup>2</sup> : 0.408)      | ENSG00000074219 | <i>TEAD2</i>                                | 2       | 0.0643          | 15.748                         |
|   | ENSG00000166927 | <i>MS4A7</i>                                | 3       | 0.0599          | 14.671                         |
|   | ENSG00000101187 | <i>SLCO4A1</i>                              | 2       | 0.0425          | 10.402                         |
|   | ENSG00000187955 | <i>COL14A1</i>                              | 2       | 0.0386          | 9.463                          |
|   | ENSG00000166923 | <i>GREM1</i>                                | 3       | 0.0345          | 8.456                          |
|   | ENSG00000161638 | <i>ITGA5</i>                                | 2       | 0.0252          | 6.161                          |
|   | ENSG00000232560 | <i>LINC01549</i>                            | 3       | 0.0210          | 5.143                          |
|   | ENSG00000225217 | <i>HSPA7</i>                                | 3       | 0.0188          | 4.601                          |
|   | ENSG00000101335 | <i>MYL9</i>                                 | 2       | 0.0188          | 4.595                          |
|   | ENSG00000128652 | <i>HOXD3</i>                                | 3       | 0.0164          | 4.024                          |
|   | ENSG00000118271 | <i>TTR</i>                                  | 2       | 0.0162          | 3.956                          |
|   | ENSG00000012124 | <i>CD22</i>                                 | 3       | 0.0155          | 3.797                          |
|   | ENSG00000107438 | <i>PDLIM1</i>                               | 2       | 0.0154          | 3.779                          |
|   | ENSG00000138964 | <i>PARVG</i>                                | 3       | 0.0107          | 2.622                          |

|  |                 |               |   |        |       |
|--|-----------------|---------------|---|--------|-------|
|  | ENSG00000185885 | <i>IFITM1</i> | 2 | 0.0105 | 2.582 |
|--|-----------------|---------------|---|--------|-------|

*Table A43. Results of dominance analysis for Cluster 3 vs Clusters 1 and 2. The top 15 predictors were obtained from each dataset, or fewer if there were not at least 15 dominant genes identified. For each dataset, the McFadden's Pseudo  $R^2$  is shown, which is the proportion of variance in the model explained by these predictor genes, with a value of 0.2-0.4 indicating good model fit, and values beyond indicating excellent model fit. For each gene identified as a key predictor, their original cluster assignment is shown, along with their total dominance, which summarises the contributions of each predictor to all of the combinatory models, and percentage relative dominance, which describes the relative importance of each predictor.*

| Ensembl ID      | Gene Symbol         | Cluster | Importance |
|-----------------|---------------------|---------|------------|
| ENSG00000138316 | <i>ADAMTS14</i>     | 3       | 0.1293     |
| ENSG00000106366 | <i>SERPINE1</i>     | 2       | 0.1093     |
| ENSG00000129465 | <i>RIPK3</i>        | 3       | 0.1080     |
| ENSG00000106624 | <i>AEBP1</i>        | 2       | 0.1067     |
| ENSG00000099994 | <i>SUSD2</i>        | 2       | 0.1040     |
| ENSG00000107438 | <i>PDLIM1</i>       | 2       | 0.0973     |
| ENSG00000249307 | <i>LINC01088</i>    | 2       | 0.0933     |
| ENSG00000106211 | <i>HSPB1</i>        | 2       | 0.0893     |
| ENSG00000160111 | <i>CPAMD8</i>       | 2       | 0.0893     |
| ENSG00000011426 | <i>ANLN</i>         | 3       | 0.0867     |
| ENSG00000167851 | <i>CD300A</i>       | 3       | 0.0867     |
| ENSG00000051523 | <i>CYBA</i>         | 3       | 0.0827     |
| ENSG00000110852 | <i>CLEC2B</i>       | 2       | 0.0827     |
| ENSG00000173597 | <i>SULT1B1</i>      | 2       | 0.0813     |
| ENSG00000171860 | <i>C3AR1</i>        | 3       | 0.0813     |
| ENSG00000111057 | <i>KRT18</i>        | 2       | 0.0800     |
| ENSG00000163739 | <i>CXCL1</i>        | 2       | 0.0800     |
| ENSG00000174837 | <i>ADGRE1</i>       | 3       | 0.0747     |
| ENSG00000270640 | <i>Lnc-BABAM2-2</i> | 2       | 0.0747     |
| ENSG00000086730 | <i>LAT2</i>         | 3       | 0.0720     |
| ENSG00000261997 | None                | 3       | 0.0720     |
| ENSG00000120708 | <i>TGFBI</i>        | 2       | 0.0707     |
| ENSG00000162444 | <i>RBP7</i>         | 3       | 0.0707     |
| ENSG00000131747 | <i>TOP2A</i>        | 3       | 0.0693     |
| ENSG00000166482 | <i>MFAP4</i>        | 2       | 0.0693     |
| ENSG00000173421 | <i>IHO1</i>         | 2       | 0.0693     |
| ENSG00000152766 | <i>ANKRD22</i>      | 3       | 0.0680     |
| ENSG00000256618 | <i>MTRNR2L1</i>     | 3       | 0.0680     |
| ENSG00000286810 | None                | 1       | 0.0667     |

|                 |                              |   |        |
|-----------------|------------------------------|---|--------|
| ENSG00000286558 | None                         | 3 | 0.0667 |
| ENSG00000145708 | <i>CRHBP</i>                 | 1 | 0.0653 |
| ENSG00000204389 | <i>HSPA1A</i>                | 2 | 0.0640 |
| ENSG00000287593 | Antisense to<br><i>ADTRP</i> | 1 | 0.0640 |
| ENSG00000129757 | <i>CDKN1C</i>                | 3 | 0.0627 |
| ENSG00000139629 | <i>GALNT6</i>                | 3 | 0.0627 |
| ENSG00000204482 | <i>LST1</i>                  | 3 | 0.0627 |
| ENSG00000073792 | <i>IGF2BP2</i>               | 2 | 0.0587 |
| ENSG00000125735 | <i>TNFSF14</i>               | 3 | 0.0587 |
| ENSG00000129667 | <i>RHBDF2</i>                | 3 | 0.0587 |
| ENSG00000136235 | <i>GPNMB</i>                 | 3 | 0.0587 |
| ENSG00000140379 | <i>BCL2A1</i>                | 3 | 0.0587 |
| ENSG00000160183 | <i>TMPRSS3</i>               | 2 | 0.0587 |
| ENSG00000276317 | <i>Lnc-GATA5-10</i>          | 2 | 0.0573 |
| ENSG00000277918 | <i>RNVU1-28</i>              | 1 | 0.0573 |
| ENSG00000155629 | <i>PIK3AP1</i>               | 3 | 0.0573 |
| ENSG00000163823 | <i>CCR1</i>                  | 3 | 0.0573 |
| ENSG00000167641 | <i>PPP1R14A</i>              | 3 | 0.0560 |
| ENSG00000174123 | <i>TLR10</i>                 | 3 | 0.0560 |
| ENSG00000254362 | <i>Lnc-PPP2R2A-2</i>         | 2 | 0.0560 |
| ENSG00000000971 | <i>CFH</i>                   | 2 | 0.0547 |
| ENSG00000011422 | <i>PLAUR</i>                 | 2 | 0.0547 |
| ENSG00000042493 | <i>CAPG</i>                  | 3 | 0.0547 |
| ENSG00000101335 | <i>MYL9</i>                  | 2 | 0.0547 |
| ENSG00000143546 | <i>S100A8</i>                | 2 | 0.0547 |
| ENSG00000152804 | <i>HHEX</i>                  | 3 | 0.0547 |
| ENSG00000173068 | <i>BNC2</i>                  | 2 | 0.0547 |
| ENSG00000185201 | <i>IFITM2</i>                | 2 | 0.0547 |
| ENSG00000253924 | <i>Lnc-NPBWR1-8</i>          | 3 | 0.0547 |

|                 |                     |   |        |
|-----------------|---------------------|---|--------|
| ENSG00000279821 | None                | 2 | 0.0547 |
| ENSG00000268758 | <i>ADGRE4P</i>      | 3 | 0.0533 |
| ENSG00000108798 | <i>ABI3</i>         | 3 | 0.0533 |
| ENSG00000019582 | <i>CD74</i>         | 3 | 0.0520 |
| ENSG00000105383 | <i>CD33</i>         | 3 | 0.0520 |
| ENSG00000117228 | <i>GBP1</i>         | 3 | 0.0520 |
| ENSG00000197747 | <i>S100A10</i>      | 3 | 0.0520 |
| ENSG00000129810 | <i>SGO1</i>         | 3 | 0.0507 |
| ENSG00000277117 | <i>LOC102723996</i> | 3 | 0.0507 |
| ENSG00000106034 | <i>CPED1</i>        | 2 | 0.0493 |
| ENSG00000125731 | <i>SH2D3A</i>       | 2 | 0.0493 |
| ENSG00000156463 | <i>SH3RF2</i>       | 2 | 0.0493 |
| ENSG00000174607 | <i>UGT8</i>         | 3 | 0.0493 |
| ENSG00000180353 | <i>HCLS1</i>        | 3 | 0.0493 |
| ENSG00000244682 | <i>FCGR2C</i>       | 3 | 0.0493 |
| ENSG00000134531 | <i>EMP1</i>         | 2 | 0.0480 |
| ENSG00000138678 | <i>GPAT3</i>        | 1 | 0.0480 |
| ENSG00000164867 | <i>NOS3</i>         | 2 | 0.0480 |
| ENSG00000172005 | <i>MAL</i>          | 3 | 0.0467 |
| ENSG00000172548 | <i>NIPAL4</i>       | 3 | 0.0467 |
| ENSG00000110077 | <i>MS4A6A</i>       | 3 | 0.0453 |
| ENSG00000145287 | <i>PLAC8</i>        | 3 | 0.0453 |
| ENSG00000112303 | <i>VNN2</i>         | 2 | 0.0440 |
| ENSG00000115956 | <i>PLEK</i>         | 3 | 0.0440 |
| ENSG00000130635 | <i>COL5A1</i>       | 2 | 0.0440 |
| ENSG00000149573 | <i>MPZL2</i>        | 2 | 0.0440 |
| ENSG00000025708 | <i>TYMP</i>         | 3 | 0.0427 |
| ENSG00000131401 | <i>NAPSB</i>        | 3 | 0.0427 |
| ENSG00000133392 | <i>MYH11</i>        | 2 | 0.0427 |
| ENSG00000169403 | <i>PTAFR</i>        | 3 | 0.0427 |

|                 |                        |   |        |
|-----------------|------------------------|---|--------|
| ENSG00000185885 | <i>IFITM1</i>          | 2 | 0.0427 |
| ENSG00000196954 | <i>CASP4</i>           | 2 | 0.0427 |
| ENSG00000237424 | <i>FOXD2-AS1</i>       | 2 | 0.0427 |
| ENSG00000275713 | <i>H2BC9</i>           | 3 | 0.0427 |
| ENSG00000128340 | <i>RAC2</i>            | 3 | 0.0413 |
| ENSG00000169896 | <i>ITGAM</i>           | 3 | 0.0413 |
| ENSG00000171840 | <i>NINJ2</i>           | 3 | 0.0413 |
| ENSG00000185499 | <i>MUC1</i>            | 2 | 0.0413 |
| ENSG00000250771 | <i>TLR2 Pseudogene</i> | 3 | 0.0413 |
| ENSG00000000938 | <i>FGR</i>             | 2 | 0.0400 |
| ENSG00000012779 | <i>ALOX5</i>           | 3 | 0.0400 |
| ENSG00000105641 | <i>SLC5A5</i>          | 2 | 0.0400 |
| ENSG00000117322 | <i>CR2</i>             | 1 | 0.0400 |
| ENSG00000125430 | <i>HS3ST3B1</i>        | 2 | 0.0400 |
| ENSG00000159216 | <i>RUNX1</i>           | 3 | 0.0400 |
| ENSG00000258227 | <i>CLEC5A</i>          | 3 | 0.0400 |
| ENSG00000100292 | <i>HMOX1</i>           | 3 | 0.0387 |
| ENSG00000127507 | <i>ADGRE2</i>          | 3 | 0.0387 |
| ENSG00000280109 | <i>PLAC4</i>           | 2 | 0.0387 |
| ENSG00000112299 | <i>VNN1</i>            | 2 | 0.0373 |
| ENSG00000163191 | <i>S100A11</i>         | 3 | 0.0373 |
| ENSG00000254415 | <i>SIGLEC14</i>        | 3 | 0.0373 |
| ENSG00000281383 | <i>Lnc-KCNE1B-157</i>  | 1 | 0.0373 |
| ENSG00000285938 | <i>BCL6-AS1</i>        | 2 | 0.0373 |
| ENSG00000286522 | <i>H3C2</i>            | 3 | 0.0373 |
| ENSG00000105122 | <i>RASAL3</i>          | 3 | 0.0360 |
| ENSG00000154188 | <i>ANGPT1</i>          | 2 | 0.0360 |
| ENSG00000155926 | <i>SLA</i>             | 3 | 0.0360 |
| ENSG00000173530 | <i>TNFRSF10D</i>       | 2 | 0.0360 |
| ENSG00000004939 | <i>SLC4A1</i>          | 2 | 0.0347 |

|                 |                |   |        |
|-----------------|----------------|---|--------|
| ENSG00000054598 | <i>FOXC1</i>   | 2 | 0.0347 |
| ENSG00000137801 | <i>THBS1</i>   | 2 | 0.0347 |
| ENSG00000187554 | <i>TLR5</i>    | 3 | 0.0347 |
| ENSG00000198467 | <i>TPM2</i>    | 2 | 0.0347 |
| ENSG00000066336 | <i>SPI1</i>    | 3 | 0.0333 |
| ENSG00000105281 | <i>SLC1A5</i>  | 3 | 0.0333 |
| ENSG00000140682 | <i>TGFB111</i> | 2 | 0.0333 |
| ENSG00000163736 | <i>PPBP</i>    | 2 | 0.0333 |
| ENSG00000188536 | <i>HBA2</i>    | 2 | 0.0333 |
| ENSG00000198019 | <i>FCGR1BP</i> | 3 | 0.0333 |
| ENSG00000129450 | <i>SIGLEC9</i> | 3 | 0.0320 |
| ENSG00000173988 | <i>LRRC63</i>  | 3 | 0.0320 |
| ENSG00000182885 | <i>ADGRG3</i>  | 2 | 0.0320 |
| ENSG00000196154 | <i>S100A4</i>  | 2 | 0.0320 |
| ENSG00000204252 | <i>HLA-DOA</i> | 3 | 0.0320 |
| ENSG00000012124 | <i>CD22</i>    | 3 | 0.0307 |
| ENSG00000111341 | <i>MGP</i>     | 2 | 0.0307 |
| ENSG00000161638 | <i>ITGA5</i>   | 2 | 0.0307 |
| ENSG00000185561 | <i>TLCD2</i>   | 2 | 0.0307 |
| ENSG00000197405 | <i>C5AR1</i>   | 2 | 0.0307 |
| ENSG00000224397 | <i>PELATON</i> | 3 | 0.0307 |
| ENSG00000081237 | <i>PTPRC</i>   | 3 | 0.0293 |
| ENSG00000100368 | <i>CSF2RB</i>  | 3 | 0.0293 |
| ENSG00000115604 | <i>IL18R1</i>  | 2 | 0.0293 |
| ENSG00000130592 | <i>LSP1</i>    | 3 | 0.0293 |
| ENSG00000184730 | <i>APOBR</i>   | 3 | 0.0293 |
| ENSG00000239672 | <i>NME1</i>    | 1 | 0.0293 |
| ENSG00000100060 | <i>MFNG</i>    | 2 | 0.0280 |
| ENSG00000170458 | <i>CD14</i>    | 3 | 0.0280 |
| ENSG00000041982 | <i>TNC</i>     | 3 | 0.0267 |

|                 |                 |   |        |
|-----------------|-----------------|---|--------|
| ENSG00000150337 | <i>FCGR1A</i>   | 3 | 0.0267 |
| ENSG00000159403 | <i>C1R</i>      | 2 | 0.0267 |
| ENSG00000167772 | <i>ANGPTL4</i>  | 2 | 0.0267 |
| ENSG00000171631 | <i>P2RY6</i>    | 3 | 0.0267 |
| ENSG00000187912 | <i>CLEC17A</i>  | 3 | 0.0267 |
| ENSG00000237082 | <i>COX5BP6</i>  | 3 | 0.0267 |
| ENSG00000077420 | <i>APBB1IP</i>  | 3 | 0.0253 |
| ENSG00000136286 | <i>MYO1G</i>    | 3 | 0.0253 |
| ENSG00000148908 | <i>RGS10</i>    | 3 | 0.0253 |
| ENSG00000149591 | <i>TAGLN</i>    | 2 | 0.0253 |
| ENSG00000173391 | <i>OLR1</i>     | 3 | 0.0253 |
| ENSG00000175567 | <i>UCP2</i>     | 3 | 0.0253 |
| ENSG00000198848 | <i>CES1</i>     | 2 | 0.0253 |
| ENSG00000074219 | <i>TEAD2</i>    | 2 | 0.0240 |
| ENSG00000090339 | <i>ICAM1</i>    | 2 | 0.0240 |
| ENSG00000104974 | <i>LILRA1</i>   | 3 | 0.0240 |
| ENSG00000117595 | <i>IRF6</i>     | 2 | 0.0240 |
| ENSG00000126860 | <i>EVI2A</i>    | 3 | 0.0240 |
| ENSG00000137462 | <i>TLR2</i>     | 3 | 0.0240 |
| ENSG00000182718 | <i>ANXA2</i>    | 2 | 0.0240 |
| ENSG00000229140 | <i>CCDC26</i>   | 3 | 0.0240 |
| ENSG00000244734 | <i>HBB</i>      | 2 | 0.0240 |
| ENSG00000166927 | <i>MS4A7</i>    | 3 | 0.0227 |
| ENSG00000173110 | <i>HSPA6</i>    | 2 | 0.0227 |
| ENSG00000176046 | <i>NUPR1</i>    | 2 | 0.0227 |
| ENSG00000200959 | <i>SNORA74A</i> | 1 | 0.0227 |
| ENSG00000251429 | <i>AIDAP2</i>   | 3 | 0.0227 |
| ENSG00000128016 | <i>ZFP36</i>    | 2 | 0.0213 |
| ENSG00000158865 | <i>SLC5A11</i>  | 3 | 0.0213 |
| ENSG00000158869 | <i>FCER1G</i>   | 3 | 0.0213 |

|                 |                 |   |        |
|-----------------|-----------------|---|--------|
| ENSG00000160791 | <i>CCR5</i>     | 3 | 0.0213 |
| ENSG00000162747 | <i>FCGR3B</i>   | 2 | 0.0213 |
| ENSG00000197471 | <i>SPN</i>      | 3 | 0.0213 |
| ENSG00000163220 | <i>S100A9</i>   | 2 | 0.0200 |
| ENSG00000180739 | <i>S1PR5</i>    | 3 | 0.0200 |
| ENSG00000186081 | <i>KRT5</i>     | 1 | 0.0200 |
| ENSG00000221869 | <i>CEBPD</i>    | 2 | 0.0200 |
| ENSG00000011600 | <i>TYROBP</i>   | 3 | 0.0187 |
| ENSG00000026508 | <i>CD44</i>     | 3 | 0.0187 |
| ENSG00000122025 | <i>FLT3</i>     | 1 | 0.0187 |
| ENSG00000170345 | <i>FOS</i>      | 2 | 0.0187 |
| ENSG00000171051 | <i>FPR1</i>     | 3 | 0.0187 |
| ENSG00000235750 | <i>KIAA0040</i> | 2 | 0.0187 |
| ENSG00000090104 | <i>RGS1</i>     | 3 | 0.0173 |
| ENSG00000101049 | <i>SGK2</i>     | 3 | 0.0173 |
| ENSG00000101336 | <i>HCK</i>      | 3 | 0.0173 |
| ENSG00000149257 | <i>SERPINH1</i> | 2 | 0.0173 |
| ENSG00000279320 | None            | 2 | 0.0173 |
| ENSG00000115602 | <i>IL1RL1</i>   | 2 | 0.0160 |
| ENSG00000143858 | <i>SYT2</i>     | 1 | 0.0160 |
| ENSG00000148826 | <i>NKX6-2</i>   | 3 | 0.0160 |
| ENSG00000082074 | <i>FYB1</i>     | 3 | 0.0147 |
| ENSG00000107099 | <i>DOCK8</i>    | 3 | 0.0147 |
| ENSG00000138061 | <i>CYP1B1</i>   | 2 | 0.0147 |
| ENSG00000169429 | <i>CXCL8</i>    | 2 | 0.0147 |
| ENSG00000171049 | <i>FPR2</i>     | 2 | 0.0147 |
| ENSG00000204287 | <i>HLA-DRA</i>  | 3 | 0.0147 |
| ENSG00000225217 | <i>HSPA7</i>    | 3 | 0.0147 |
| ENSG00000006747 | <i>SCIN</i>     | 3 | 0.0133 |
| ENSG00000014257 | <i>ACP3</i>     | 3 | 0.0133 |

|                 |                  |   |        |
|-----------------|------------------|---|--------|
| ENSG00000114013 | <i>CD86</i>      | 3 | 0.0133 |
| ENSG00000125733 | <i>TRIP10</i>    | 2 | 0.0133 |
| ENSG00000145779 | <i>TNFAIP8</i>   | 2 | 0.0133 |
| ENSG00000152689 | <i>RASGRP3</i>   | 3 | 0.0133 |
| ENSG00000165025 | <i>SYK</i>       | 3 | 0.0133 |
| ENSG00000169894 | <i>MUC3A</i>     | 2 | 0.0133 |
| ENSG00000174348 | <i>PODN</i>      | 2 | 0.0133 |
| ENSG00000185585 | <i>OLFML2A</i>   | 2 | 0.0133 |
| ENSG00000185905 | <i>C16orf54</i>  | 3 | 0.0133 |
| ENSG00000188511 | <i>MIR3667HG</i> | 2 | 0.0133 |
| ENSG00000155307 | <i>SAMSN1</i>    | 3 | 0.0120 |
| ENSG00000229391 | <i>HLA-DRB6</i>  | 3 | 0.0120 |
| ENSG00000096696 | <i>DSP</i>       | 2 | 0.0107 |
| ENSG00000105967 | <i>TFEC</i>      | 3 | 0.0107 |
| ENSG00000122012 | <i>SV2C</i>      | 1 | 0.0107 |
| ENSG00000142102 | <i>PGGHG</i>     | 2 | 0.0107 |
| ENSG00000158715 | <i>SLC45A3</i>   | 3 | 0.0107 |
| ENSG00000003436 | <i>TFPI</i>      | 2 | 0.0093 |
| ENSG00000101187 | <i>SLCO4A1</i>   | 2 | 0.0093 |
| ENSG00000118640 | <i>VAMP8</i>     | 3 | 0.0093 |
| ENSG00000160255 | <i>ITGB2</i>     | 3 | 0.0093 |
| ENSG00000186431 | <i>FCAR</i>      | 2 | 0.0093 |
| ENSG00000235568 | <i>NFAM1</i>     | 3 | 0.0093 |
| ENSG00000047457 | <i>CP</i>        | 2 | 0.0080 |
| ENSG00000070190 | <i>DAPP1</i>     | 3 | 0.0080 |
| ENSG00000135842 | <i>NIBAN1</i>    | 2 | 0.0080 |
| ENSG00000143226 | <i>FCGR2A</i>    | 3 | 0.0080 |
| ENSG00000163563 | <i>MNDA</i>      | 3 | 0.0080 |
| ENSG00000172243 | <i>CLEC7A</i>    | 3 | 0.0080 |
| ENSG00000231246 | <i>LINC02884</i> | 2 | 0.0080 |

|                 |                     |   |        |
|-----------------|---------------------|---|--------|
| ENSG00000243323 | <i>PTPRVP</i>       | 1 | 0.0080 |
| ENSG00000271605 | <i>MILR1</i>        | 3 | 0.0080 |
| ENSG00000275395 | <i>FCGBP</i>        | 3 | 0.0080 |
| ENSG00000277775 | <i>H3C7</i>         | 3 | 0.0080 |
| ENSG00000010327 | <i>STAB1</i>        | 3 | 0.0067 |
| ENSG00000117318 | <i>ID3</i>          | 2 | 0.0067 |
| ENSG00000120875 | <i>DUSP4</i>        | 1 | 0.0067 |
| ENSG00000150048 | <i>CLEC1A</i>       | 2 | 0.0067 |
| ENSG00000160593 | <i>JAML</i>         | 2 | 0.0067 |
| ENSG00000164342 | <i>TLR3</i>         | 3 | 0.0067 |
| ENSG00000183508 | <i>TENT5C</i>       | 2 | 0.0067 |
| ENSG00000261170 | <i>LOC107984827</i> | 2 | 0.0067 |
| ENSG00000066294 | <i>CD84</i>         | 3 | 0.0053 |
| ENSG00000137752 | <i>CASP1</i>        | 3 | 0.0053 |
| ENSG00000146192 | <i>FGD2</i>         | 3 | 0.0053 |
| ENSG00000148773 | <i>MKI67</i>        | 3 | 0.0053 |
| ENSG00000158859 | <i>ADAMTS4</i>      | 3 | 0.0053 |
| ENSG00000163565 | <i>IFI16</i>        | 3 | 0.0053 |
| ENSG00000165507 | <i>DEPP1</i>        | 2 | 0.0053 |
| ENSG00000172578 | <i>KLHL6</i>        | 3 | 0.0053 |
| ENSG00000173372 | <i>C1QA</i>         | 3 | 0.0053 |
| ENSG00000177575 | <i>CD163</i>        | 2 | 0.0053 |
| ENSG00000246363 | <i>LINC02458</i>    | 1 | 0.0053 |
| ENSG00000100336 | <i>APOL4</i>        | 2 | 0.0040 |
| ENSG00000107796 | <i>ACTA2</i>        | 2 | 0.0040 |
| ENSG00000110934 | <i>BIN2</i>         | 3 | 0.0040 |
| ENSG00000118503 | <i>TNFAIP3</i>      | 2 | 0.0040 |
| ENSG00000148926 | <i>ADM</i>          | 2 | 0.0040 |
| ENSG00000153551 | <i>CMTM7</i>        | 3 | 0.0040 |
| ENSG00000162511 | <i>LAPTM5</i>       | 3 | 0.0040 |

|                 |                 |   |        |
|-----------------|-----------------|---|--------|
| ENSG00000169385 | <i>RNASE2</i>   | 3 | 0.0040 |
| ENSG00000242574 | <i>HLA-DMB</i>  | 3 | 0.0040 |
| ENSG00000060138 | <i>YBX3</i>     | 2 | 0.0027 |
| ENSG00000090382 | <i>LYZ</i>      | 3 | 0.0027 |
| ENSG00000134061 | <i>CD180</i>    | 3 | 0.0027 |
| ENSG00000167613 | <i>LAIR1</i>    | 3 | 0.0027 |
| ENSG00000175489 | <i>LRRC25</i>   | 3 | 0.0027 |
| ENSG00000203710 | <i>CR1</i>      | 3 | 0.0027 |
| ENSG00000028137 | <i>TNFRSF1B</i> | 2 | 0.0013 |
| ENSG00000157227 | <i>MMP14</i>    | 3 | 0.0013 |

Table A44. Results of permutation importance of the Zucca dataset. The analysis was performed with 50 iterations.



| Cell Type        | Statistics | Cluster 1 | Cluster 2 | Cluster 3 | Shapiro-Wilk (W, p-value) | ANCOVA (F statistic, p-value) | Tukey p-value   |
|------------------|------------|-----------|-----------|-----------|---------------------------|-------------------------------|-----------------|
| Neurons          | Mean       | 0.767     | 0.686     | 0.629     | 0.878, 3.82E-08           | 9.87, 1.161E-04               | 1 vs 2 0.0136   |
|                  | Median     | 0.779     | 0.744     | 0.681     |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.0574    | 0.167     | 0.121     |                           |                               | 2 vs 3 0.507    |
|                  | IQR        | 0.0591    | 0.199     | 0.155     |                           |                               |                 |
| Astrocytes       | Mean       | 0.155     | 0.223     | 0.192     | 0.912, 1.83E-06           | 6.05, 3.241E-03               | 1 vs 2 6.37E-03 |
|                  | Median     | 0.152     | 0.181     | 0.181     |                           |                               | 1 vs 3 0.0471   |
|                  | SD         | 0.0498    | 0.12      | 0.0653    |                           |                               | 2 vs 3 0.836    |
|                  | IQR        | 0.0521    | 0.14      | 0.0815    |                           |                               |                 |
| Microglia        | Mean       | 0.00149   | 0.00755   | 0.0245    | 0.542, < 2.2E-16          | 33.0, 3.37E-11                | 1 vs 2 < 0.001  |
|                  | Median     | 0.000579  | 0.0062    | 0.0121    |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.00215   | 0.00568   | 0.0436    |                           |                               | 2 vs 3 0.135    |
|                  | IQR        | 0.00192   | 0.00662   | 0.0112    |                           |                               |                 |
| Endothelial      | Mean       | 0.0139    | 0.0518    | 0.0306    | 0.747, 1.32E-12           | 36.8, 7.006E-13               | 1 vs 2 < 0.001  |
|                  | Median     | 0.013     | 0.0347    | 0.0212    |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.00887   | 0.0408    | 0.0212    |                           |                               | 2 vs 3 0.0147   |
|                  | IQR        | 0.0103    | 0.0301    | 0.0304    |                           |                               |                 |
| Oligodendrocytes | Mean       | 0.0627    | 0.0317    | 0.124     | 0.935, 3.64E-05           | 28.8, 3.67E-10                | 1 vs 2 < 0.001  |
|                  | Median     | 0.058     | 0.0252    | 0.129     |                           |                               | 2 vs 3 < 0.001  |
|                  | SD         | 0.0371    | 0.0255    | 0.0497    |                           |                               | 1 vs 3 0.0162   |
|                  | IQR        | 0.0348    | 0.0292    | 0.055     |                           |                               |                 |

Table A45. Cell deconvolution results of KCL BrainBank cases using MuSiC. Overall differences in cell type composition between the three clusters were assessed using ANCOVA corrected for age of death and sex assigned at birth, with Tukey's test used for post-hoc comparison of cell composition between clusters. A p-value of < 0.05 denotes significance. Any cell types that were not normally distributed, as assessed with the Shapiro-Wilk test was log transformed before running ANCOVA.

| Cell Type        | Statistics | Cluster 1 | Cluster 2 | Cluster 3 | Shapiro-Wilk (W, p-value) | ANCOVA (F statistic, p-value) | Tukey p-value   |
|------------------|------------|-----------|-----------|-----------|---------------------------|-------------------------------|-----------------|
| Neurons          | Mean       | 0.742     | 0.629     | 0.545     | 0.932, 5.51E-07           | 34.0, 5.24E-13                | 1 vs 2 6.74E-03 |
|                  | Median     | 0.753     | 0.668     | 0.606     |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.0704    | 0.137     | 0.165     |                           |                               | 2 vs 3 2.52E-03 |
|                  | IQR        | 0.0802    | 0.151     | 0.2       |                           |                               |                 |
| Astrocytes       | Mean       | 0.177     | 0.264     | 0.2       | 0.872, 1.27E-10           | 12.6, 8.21E-06                | 1 vs 2 < 0.0001 |
|                  | Median     | 0.174     | 0.248     | 0.171     |                           |                               | 1 vs 3 0.404    |
|                  | SD         | 0.0453    | 0.0917    | 0.0958    |                           |                               | 2 vs 3 1.45E-03 |
|                  | IQR        | 0.0511    | 0.11      | 0.0511    |                           |                               |                 |
| Microglia        | Mean       | 0.00468   | 0.0103    | 0.0227    | 0.817, 4.82E-13           | 28.7, 3.67E-11                | 1 vs 2 9.59E-03 |
|                  | Median     | 0.00384   | 0.00673   | 0.0165    |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.00478   | 0.0088    | 0.0171    |                           |                               | 2 vs 3 0.0125   |
|                  | IQR        | 0.00603   | 0.0139    | 0.0153    |                           |                               |                 |
| Endothelial      | Mean       | 0.00763   | 0.0441    | 0.024     | 0.797, 8.38E-14           | 30.3, 1.15E-11                | 1 vs 2 < 0.0001 |
|                  | Median     | 0.00554   | 0.0232    | 0.0179    |                           |                               | 1 vs 3 < 0.001  |
|                  | SD         | 0.00873   | 0.0431    | 0.0208    |                           |                               | 2 vs 3 0.105    |
|                  | IQR        | 0.0089    | 0.0369    | 0.0264    |                           |                               |                 |
| Oligodendrocytes | Mean       | 0.068     | 0.0526    | 0.208     | 0.888, 8.12E-10           | 49.7, < 2.2E-16               | 1 vs 2 0.288    |
|                  | Median     | 0.0566    | 0.0384    | 0.179     |                           |                               | 1 vs 3 < 0.0001 |
|                  | SD         | 0.0453    | 0.0362    | 0.107     |                           |                               | 2 vs 3 < 0.0001 |
|                  | IQR        | 0.0603    | 0.0524    | 0.109     |                           |                               |                 |

Table A46. Cell deconvolution results of TargetALS cases using MuSiC. Overall differences in cell type composition between the three clusters were assessed using ANCOVA corrected for age of death and sex assigned at birth, with Tukey's test used for post-hoc comparison of cell composition between clusters. A p-value of < 0.05 denotes significance. Any cell types that were not normally distributed, as assessed with the Shapiro-Wilk test was log transformed before running ANCOVA

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