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COMMENTARY (see article on p. 378)

Check for updates

ActaDV Acta Dermato-Venereologica ActaDV Advances in dermatology and venereology

Matrix-Assisted Laser Desorption/Ionisation Time-Of-Flight Mass Spectrometry in Dermatology

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Until recently the laboratory diagnosis of infections has depended on the use of cultural identification, often coupled with biochemical tests. Increasingly, this process has been changed and refined with the development of rapid and accurate molecular methods. Most attention has focused on the detection of identifying genetic material, RNA or DNA; nucleic acid amplification techniques provide a rapid and sensitive method for microbial detection. However a new approach using Matrix-Assisted Laser Desorption/Ionisation Time-Of-Flight (MALDI-TOF) Mass Spectrometry (MS) has emerged as a powerful tool for microbial identification and research. Mass spectrometry involves the ionisation of chemical compounds into charged molecules and measurement of their mass to charge (m/z) ratio. The development of 'soft ionisation' methods such as MALDI has widened the application of MS to the detection of large biological molecules, including polypeptides, glycoproteins and complex carbohydrates. The process involves mixing the microbiological sample with an energy-absorbent matrix; constituents are ionised by laser energy and separated, based on the time taken to travel along a flight tube that depends on their mass-to-charge ratio. These data are used to construct a mass spectrum or peptide mass fingerprint (PMF) that is compared against a database of reference spectra, identifying the organism to genus, species or strain level. Highly abundant microbial proteins, mostly ribosomal proteins in the mass range 2-20 kDa, are the main contributors to the PMF for an individual organism and results can be generated in seconds and with a minimum of material.

MALDI-TOF MS is a sensitive and very rapid technique for analysing a wide range of microbial products. In addition to the identification of organisms it can provide useful information, for instance, on antibiotic susceptibility, through the detection of resistance-associated proteins (e.g. beta-lactamases). The potential for rapid, high-throughput analysis of protein products from complex mixtures makes MALDI-TOF MS an important technology in studying pathogenetic mechanisms. It can also be used to image proteins directly from intact tissue sections, a process known as imaging mass spectrometry (IMS). This can provide information on the relative concentration and spatial distribution of proteins within different areas of tissue (healthy and diseased). It is a cost-effective method for microbial detection, compared with molecular and immunological methods, however high setup costs may be a barrier to initial implementation and sometimes there can be difficulty in distinguishing genetically very similar organisms.

The literature contains many examples of the benefits of using MALDI-TOF MS, for both clinical diagnosis and as a research tool in dermatology. The accurate classification of strains of *Propionibacterium acnes* at the proteomic level has provided a foundation for further molecular investigation to characterise the role of this organism in the pathogenesis of acne (1, 2). Numerous case reports highlight the utility of MALDI-TOF MS (often supported by DNA/RNA sequencing) in the identification of new and rare organisms in clinical specimens, which might not otherwise be detected using conventional methods. Baran et al. (3) recently described a case of chronic lower leg wound infection with *Kerstersia gyiorum* (diagnosed by MALDI-TOF MS) in a patient with Buerger's disease. They draw attention to the likelihood of misdiagnosis of this organism using biochemical methods in isolation. The use of this technique is not restricted to bacteria and is finding wide acceptance as a rapid method for identifying fungi such as dermatophytes and yeasts isolated from clinical material (4, 5).

In this issue Del Giudice and colleagues (6) report the first case of cellulitis caused by an emerging pathogen, *Streptococcus halichoeri*. They highlight the usefulness of MALDI-TOF for microbial identification in comparison to conventional methods. Results obtained from microbiological samples using biochemical methods were discordant. Subsequent evaluation with MALDI-TOF mass spectrometry identified the organism as *S. halichoeri*. The use of MALDI-TOF MS in this case (supported by 16S rRNA gene sequencing) confirmed the cause of cellulitis.

The increasing use of modern molecular tools such as MALDI-TOF MS will result in the detection of more unusual and unfamiliar microorganisms; but communication between clinicians and laboratory scientists will remain important in order to determine their pathogenic relevance as well as resistance patterns. Maintaining, and adding to, reference data bases where comparative information on the mass fingerprints is stored is key to the future success and application of this method.

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