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Mass Spectrometry & Purification Techniques

Commentary

The History and Applications of Protein Mass Spectrometry

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ABOUT THE STUDY

Protein mass spectrometry is the use of mass spectrometry to investigate proteins. Mass spectrometry is an important approach for accurately determining and characterizing the mass of proteins, and a range of procedures and instruments have been developed to accommodate its many applications. Its uses include protein identification and post-translational modification, elucidation of protein complexes, subunits, and functional relationships, and global protein measurement in proteomics. It can also be used to localize proteins to different organelles and to detect interactions between proteins and membrane lipids. Electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI) are the two basic methods for ionising proteins in mass spectrometry. These ionization techniques work in tandem with mass analyzers like tandem mass spectrometry. In general, proteins are analyzed using either a "top-down" technique, in which proteins are analyzed intact, or a "bottom-up" approach, in which proteins are digested into fragments first. An intermediate "middle-down" approach in which larger peptide fragments are analyzed may also sometimes be used. Recent advances in protein mass spectrometry have paved the way for the identification of autoantibody targets in a variety of renal disorders. Researchers go over what readers should know about protein mass spectrometry in order to comprehend the technology and new discoveries as they emerge. In recent years, mass spectrometry has seen increased application in identifying endogenous antigens that are autoantibody targets. For example, identifying two podocyte cell surface proteins that bind autoantibodies in membranous nephropathy (the PLA2 receptor and Thrombospondin type-1 domain-containing 7A) was a huge accomplishment. A member of the protein DnaJ homolog subfamily was recently discovered as a probable target antigen in fibrillary glomerulonephritis, according to a study published in the Journal of the American Society of Nephrology. Similarly, megalin, a proximal tubule protein that acts as an albumin clearance receptor, has been identified as a target antigen in anti-brush border antibody illness, a newly discovered form of Acute Kidney Injury (AKI).

Mass spectrometer speed and mass resolution advancements, together with improved quantification procedures and bioinformatic methods, have catalyzed progress. Studies forecast new discoveries related to the molecular underpinnings of kidney disease based on present accomplishments and anticipated progress. What should readers know to assess the validity of future papers on the use of protein mass spectrometry to find disease biomarkers? Here, the article a fundamental "how it works" overview of protein mass spectrometry as it is often performed, as well as some basic data analysis principles applicable to quantification and false-positive result reduction.

History of mass spectrometry

Following the invention of MALDI and ESI, the use of mass spectrometry to investigate proteins became widespread in the 1980s. These ionization techniques have been crucial in the characterization of proteins. Franz Hillenkamp and Michael Karas invented the term matrix-assisted laser desorption ionization (MALDI) in the late 1980s. Hillenkamp, Karas, and their colleagues were able to ionize the amino acid alanine by combining it with the amino acid tryptophan and exposing it to a 266 nm pulse laser. Despite its significance, the breakthrough did not occur until 1987. Koichi Tanaka used the "ultra fine metal plus liquid matrix method" to ionize 34,472 Da protein carboxypeptidase-A biomolecules in 1987.

Malcolm Dole published the first study on the use of electrospray ionization with mass spectrometry in 1968. John Bennett Fenn was credited with developing electrospray ionisation at the same time MALDI became popular. Koichi Tanaka, John Fenn, and Kurt Wüthrich shared the 2002 Nobel Prize in Chemistry for "the development of methods for the identification and structure analyses of biological macromolecules." These ionization procedures have substantially aided the mass spectrometric investigation of proteins. As a result, protein mass spectrometry has taken the lead in protein characterization.

Applications of protein mass spectrometry

MS is also recommended over other methodologies, such as antibody-based methods, for identifying post-translational changes

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in proteins. Typically, *de novo* peptide sequencing for mass spectrometry is performed without knowledge of the amino acid sequence. It is the technique of attributing amino acids to protein peptide fragment weights. *De novo* sequencing has been shown to be effective for confirming and expanding on database search results. The initial stage in teaching the immune system to recognize new infections is antigen presentation. To that goal, antigen-presenting cells disclose protein fragments to the immune system *via* MHC molecules. However, not all protein fragments bind to a specific individual's MHC molecules. The true spectrum of chemicals exposed to the immune system can be determined using mass spectrometry. Laser-induced covalent labelling is another intriguing route in protein structural investigations. Hydroxyl radicals are used in this technique to modify protein solvent-exposed regions. Protein folding research have made use of its conjunction with fast mixing. Peptides discovered by mass spectrometry are used to improve gene annotations (for example, gene start locations) and protein annotations in what is now known as proteogenomics. When comparing several species, parallel study of the genome and proteome enables the finding of post-translational modifications and proteolytic processes.