PLENARY LECTURE P1
Sponsored by: Waters

Molecular profiling and imaging of tissues by mass spectrometry: assessing spatial and temporal factors

Richard Caprioli

Vanderbilt University School of Medicine, Nashville, TN, USA

The spatial and temporal aspects of molecular processes in cells and tissues play an enormous part in the biology that defines living systems. Profiling and Imaging MALDI MS provides an effective means to measure and assess those dimensions on a molecular basis, including peptides, proteins, lipids, metabolite as well as others. The technology is extraordinarily high throughput with high molecular specificity and is an excellent discovery tool. It provides the capability of mapping the location of specific molecules such as drugs, lipids, peptides and proteins directly from fresh frozen tissue sections. For example, utilization of this technology provides spatial information across a tissue section for a target protein expression or for a signature of multiple proteins and can be used to correlate changes in expression levels with specific disease states or drug response. Protein patterns can be directly correlated to known histological regions within the tissue, allowing for the direct monitoring of proteins specific to these regions within a tissue sample. Profiling and imaging MS have been used to characterize many tissue types, including human gliomas and lung cancers, as well as tumor response to specific therapeutics, suggesting the use of proteomic information in assessing disease progression as well as predicting patient response to specific treatments.

Frozen tissues specimens are sectioned (~10 μm thick), thaw-mounted on flat metallic target plates, and matrix automatically deposited. This can be done in a histology-directed manner to bring into play the expertise and experience of pathologists to obtain molecular profiles from discrete areas of tissue. This represents a profiling approach where only specific areas of interest are being interrogated. In the imaging mode, high density laser ablation of an ordered array of spots over the entire tissue gives rise to a 2-dimensional ion density map (or image) with 30-80 μm lateral resolution in which location and relative abundance of a given analyte is displayed. From the analysis of a single section, images at virtually any molecular weight may be obtained. In addition to MALDI ToF MS and MS/MS instrumentation, the capabilities of ion mobility MS and FTICR MS for profiling and imaging of tissues will be discussed.

This presentation will discuss several biological applications of this technology, including examples of discovery in mouse developmental models and the profiling of human tumors, characterizing protein differences between tumor grades, and monitoring protein changes due to drug therapy. We have applied this technology for the creation of 3-D protein images of substructures of mouse brain, to drug targeting and metabolic studies and the measurement of concomitant protein changes in specific tissues after systemic drug administration. Finally, we explore the correlation of lipid and protein changes in several systems in both health and disease.