Colloquium
2:00PM - CHEM 190
April 9th, 2015

Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee, 3210 North Cramer Street, Milwaukee, WI 53211

Imaging Mass Spectrometry: Molecular Microscopy for Discovery in Biological and Clinical Research

***Richard Caprioli, Ph.D,**
Departments of Biochemistry, Chemistry, Pharmacology and Medicine, and the Mass Spectrometry Research Center, Vanderbilt University School of Medicine, Nashville, TN, U.S.A.

Host: Prof. Leggy A. Arnold

ABSTRACT

MALDI Imaging Mass Spectrometry (IMS) produces molecular maps of peptides, proteins, lipids and metabolites present in intact tissue sections. It employs desorption of molecules by direct laser irradiation to map the location of specific molecules from fresh frozen and formalin fixed tissue sections without the need of target specific reagents such as antibodies. Molecular images of this nature are produced in specific m/z (mass-to-charge) values, or ranges of values. Thus, each specimen gives rise to many hundreds of specific molecular images from a single raster of the tissue. In a complementary approach where only discrete areas within the tissue are of interest, we have developed a histology-directed approach that integrates mass spectrometry and microscopy. Thus, mass spectra are collected from only selected areas of cells within the tissue following laser ablation and analysis.

We have employed IMS in studies of a variety of biologically and medically relevant research projects. One area of interest is the molecular mapping of molecular changes occurring in diabetes in both a mouse model and in the human disease. Major molecular alterations have been recorded in advanced diabetic nephropathy involving both proteins and lipids. Other applications include developmental studies of embryo implantation is mouse, assessment of margins in renal cancers as well as that in other organs, and neurodegenerative disease. Molecular signatures have been identified that are differentially expressed in diseased tissue compared to normal tissue and also in differentiating different stages of disease. These signatures typically consist of 10-20 or more different proteins and peptides, each identified using classical proteomics methods. One such application described is that concerning the differentiation of benign skin lesions from melanomas. In addition, Imaging MS has been applied to drug targeting and metabolic studies both in specific organs and also in intact whole animal sections following drug administration.

This presentation will also describe recent technological advances both in sample preparation and instrumental performance to achieve images at high spatial resolution (1-10 microns) and at high speeds so that a typical sample tissue once prepared can be imaged in just a few minutes. Finally, new biocomputational approaches will be discussed that deals with the high data dimensionality of Imaging MS and our implementation of 'image fusion' in terms of predictive integration of MS images with microscopy and other imaging modalities.