## School of Medicine

## **Neuroscience Center of Excellence**

## Chancellor's Award Lecture in Neuroscience



Lipids are a diverse class of molecules that play critical roles in the biochemistry of all living organisms. Lipids are relatively low molecular weight molecules with both hydrophobic and hydrophilic properties that impart unique biophysical attributes. Certain types of lipids serve as chemical communicators coordinating biochemical events between cells and even within a cell, while other lipids have physical roles of providing a semipermeable barrier (bilayer). Recently, the world of lipids has been redefined as composed of seven different classes that emphasize the diversity of structure as well as function, yet interestingly there are only two biochemical pathways by which lipids can be synthesized, namely the carbanion (CoA dependent pathway) and the carbocation pathway of prenyl phosphates. The analysis of lipids by mass spectrometry has expanded greatly due to the development of electrospray ionization and matrix assisted laser desorption. Furthermore, the development of a tandem mass spectrometer has resulted in several powerful techniques of specific ion detection including precursor ion scanning, product ion scanning, constant neutral loss, and selective reaction monitoring experiments. These scanning features which are implemented only in the triple guadrupole mass spectrometer are particularly relevant for complex lipid analysis. Using these techniques it is now possible to gain a detailed understanding of the biochemical events taking place within cells related to lipid substances. One of the important challenges in lipid biochemistry is having sufficiently sensitive and precise tools that enable localization of specific lipids in their natural habitat within tissues, and hopefully within the individual cell. Imaging mass spectrometry has developed as an immensely powerful tool particularly suited for the analysis of lipids in tissues, although its origins originated an interest in elucidating the regional location of proteins and peptides in tissue. Several examples of the use of IMS for brain lipids will be given where unique information has been obtained relevant to specific lipid biochemical studies. These imaging techniques can also be used when implemented on a tandem mass spectrometer to structurally characterize the lipids because of the unique ion chemistry that many of the lipid substances have. The regional localization of specific lipid molecular species from sphingolipids, phospholipids, as well as glycerol lipids (and other neutral lipids) is now possible.



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