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Lipidomics

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Lipidomics is the large scale identification and quantitation of the diverse repertoire of lipids in biologic systems that play critical roles in cellular function. The purpose of this Virtual Issue on Lipidomics is to highlight recent articles in *Analytical Chemistry* that have developed innovative strategies and technologies that have and will continue to greatly impact progress in the field. Although the field of lipidomics using mass spectrometry has been practiced for over 30 years, recent robust advances in multiple integrated technologies have greatly expanded the scope and penetrance of the field. Through the synergistic utilization of a wide array of technological advances in ionization, fragmentation, high mass accuracy analysis, and robust increases in resolution, the power of lipidomics-based investigations has greatly expanded facilitating the identification of biomarkers of disease, disease mechanisms, and the efficacy of therapeutic approaches for disease entities.

Lipids serve pleiotropic roles in cellular functions. The most obvious is the formation of interfacial boundaries that are critical for the physiologic maintenance of cellular integrity and subcellular compartments. The lipid composition of cellular membranes is a critical determinant of the biophysical characteristics of discrete membrane compartments and domains that serve as prominent regulators of transmembrane protein activities such as ion channels and receptors. Furthermore, recent lipidomic studies have demonstrated specialized domains in cellular membranes that provide the nidus for supramolecular assemblies that are critical for cellular function. Moreover, many hundreds to thousands of lipids serve a wide variety of signaling functions that orchestrate appropriate cellular responses to external perturbations during health but precipitate pathologic changes in metabolic networks initiating disease processes.

The field of lipidomics has developed using three main approaches that involve various degrees of sample preparation/separation prior to mass spectrometric analysis. These include shotgun lipidomics where lipid extracts of biological samples are directly infused into the mass spectrometer and analyzed using a variety of fragmentation strategies,

Notes

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chromatographic separation of lipid extracts prior to tandem mass spectrometric analysis (LC–MS/MS), and MALDI-based methods for high-throughput analysis of lipids as well as imaging of biological tissues. In addition, the development of specialized derivatization methodologies either for the targeted identification and extremely sensitive quantification of lipids or for the differentiation of various types of isobaric lipid molecules, such as double bond positional isomers, cis/trans geometrical isomers, regioisomers, and enantiomers is a prominent area of growth in the lipidomics field. Each of these approaches has its own advantages and limitations which are cell type and context dependent. The judicious choice of method(s) utilized will allow facile access to mechanisms underlying the biologic questions of interest. Finally, the importance of stable isotopes for analysis of metabolic flux in interwoven metabolic networks will lead to new insights into the mechanisms of multiple disease processes. Through development of innovative approaches using informative stable isotopes in conjunction with novel bioinformatic analyses, the mechanisms underlying alterations in the lipidome can be identified and high yield pharmacologic targets can be identified.

Recently, the application of MALDI-based imaging mass spectrometry has enabled the identification of the anatomic sites of specific lipids that has led to an increased understanding of the roles of discrete lipids in cellular function. Presently, imaging with MALDI-based methods can reach a spatial resolution of 5 μm while SIMS can resolve moieties below 1 μm which allows unprecedented access to lipid alterations in subcellular compartments and membrane domains. The importance of separating changes in bulk lipid content in extracts of biologic tissues comprised of multiple cell types from alterations in specifically affected cells and subcellular organelles in understanding the pathogenesis of disease processes cannot be overstated. To this end, it is anticipated that further innovation in mass spectrometry imaging will lead to novel mechanistic insights into the roles of lipids in specific cell types and subcellular compartments in disease processes.

This “Virtual Issue” on lipidomics focuses on benchmark papers which have driven the field and represent the foundations of future advances in lipidomics. Given the pleiotropic roles of lipids in disease processes and the technology driven increases in metabolic network analysis, the understanding of the roles of lipids in disease processes will continue to fuel the rapid growth of lipidomics.