

## What has lipidomics done for me lately: insights, advances and limitations in the application of lipidomics to the study of lipid metabolism in health and disease

T.W. Mitchell, School of Medicine, Illawarra Health and Medical Research Institute, University of Wollongong, Wollongong, NSW 2522, Australia.

The level of interest in lipids has grown rapidly in the past decade, which is due in no small part to the emergence of lipidomics. The lofty aim of lipidomics is “the full characterization of lipid molecular species and of their biological roles with respect to expression of proteins involved in lipid metabolism and function, including gene regulation” (Spener *et al.*, 2003). While achieving this aim is some way off, rapid advances in lipidomics technology and methodology over the past decade have greatly enhanced our understanding of lipids and their functions.

Recent breakthroughs in technology, *e.g.* high-resolution and imaging mass spectrometry have seen the field expand at a rapid rate. While several recent discoveries, *e.g.* phospholipid biomarkers of memory impairment (Mapstone *et al.*, 2014) and the regulation of dopamine uptake at the synaptic cleft by 1-oleoyl-2-palmitoyl-sn-glycerophosphocholine (Kuge *et al.*, 2014) have highlighted the power of lipidomics and the importance of lipid metabolism in health and disease. Nevertheless, significant challenges remain, particularly the inability of lipidomic technologies to identify isomeric lipids that differ in the position of double bonds, the stereochemistry of double bonds and the attachment site of fatty acids to glycerol backbones (*sn* position). New methods, such as differential ion mobility (Shvartsburg *et al.*, 2011), ozone-induced dissociation (Thomas *et al.*, 2008) and radical-directed dissociation (Pham *et al.*, 2012) are showing some promise but require further development. Given that even subtle changes in lipid molecular structure will affect their biochemical and biophysical properties (Brown *et al.*, 2012), development of these tools is essential if we wish to fully elucidate the roles of lipids in cellular function.

Brown SH, Mitchell TW, Oakley AJ, Pham H & Blanksby SJ. (2012). Time to face the fats: what can mass spectrometry reveal about the structure of lipids and their interactions with proteins? *J Am Soc Mass Spectrom* **23**, 1441-1449.

Kuge H, Akahori K, Yagyu K-I & Honke K. (2014). Functional compartmentalization of the plasma membrane of neurons by a unique acyl chain composition of phospholipids. *J Biol Chem* **289**, 26783-26793.

Mapstone M, Cheema AK, Fiandaca MS, Zhong X, Mhyre TR, Macarthur LH, Hall WJ, Fisher SG, Peterson DR, Haley JM *et al.* (2014). Plasma phospholipids identify antecedent memory impairment in older adults. *Nature Med* **20**, 415-418.

Pham HT, Ly T, Trevitt AJ, Mitchell TW & Blanksby SJ. (2012). Differentiation of complex lipid isomers by radical-directed dissociation mass spectrometry. *Anal Chem* **84**, 7525-7532.

Shvartsburg AA, Isaac G, Leveque N, Smith RD & Metz TO. (2011). Separation and classification of lipids using differential ion mobility spectrometry. *J Am Soc Mass Spectrom* **22**, 1146-1155.

Spener F, Lagarde M, G  lo  n A & Record M. (2003). Editorial: What is lipidomics? *Euro J Lipid Sci Technol* **105**, 481-482.

Thomas MC, Mitchell TW, Harman DG, Deeley JM, Nealon JR & Blanksby SJ. (2008). Ozone-Induced Dissociation: Elucidation of Double Bond Position within Mass-Selected Lipid Ions. *Anal Chem* **80**, 303-311.