

This special issue of BBA Lipids originated with an invitation from Rudi Zechner (former Executive Editor, BBA Molecular and Cell Biology of Lipids) to flesh out ideas that had been presented in recent short reviews by Bigay and Antonny (2012) and Holthuis and Menon (2014). These reviews described the biosynthesis of lipids in biogenic compartments, mechanisms by which they were distributed throughout the cell, and crucially how organelles acquired their distinct lipid character such that – simply - the early secretory pathway could be described as having thin membranes, relatively loosely packed, cholesterol-poor, displaying very little formal charge on the cytoplasmic side, whereas late secretory membranes, including the plasma membrane were thick, cholesterol-rich, structured and strongly negatively charged when seen from the cytoplasm. The gradients of charge, bilayer thickness and structure are essentially due to lipids, and so the term ‘lipid landscape’ was coined and associated with the corresponding biogenic and barrier functions of these membranes. In this issue we take these ideas to greater level of detail and conceptual depth through individual reviews that address distinct features of the lipid landscape - its properties and genesis. We begin with lipid biosynthesis and turnover, membrane bilayer assembly and the lateral organization of lipids in the membrane. Next, we discuss how proteins sense the membrane - its thickness and composition. Then we move to a series of articles describing the role of membrane contact sites in determining the lipid landscape, and this is followed by descriptions of key players proposed to act at contacts.

Chauhan et al. update a key review article from the early 1980s, highlighting new discoveries about lipid biosynthesis especially recent progress in the structural biology of phospholipid biosynthetic enzymes (Chauhan et al., 2016). Montigny et al. then review the transbilayer movement of lipids, a process that is not only required for the assembly of membrane bilayers but is also a key determinant of the lipid landscape through the establishment of transbilayer lipid asymmetry (Montigny et al., 2015). Olson et al. and Wang complete the set of introductory review articles by describing sphingolipid biosynthesis and homeostasis (Olson et al., 2015), and the biology of lipid droplets (Wang, 2015). The next set of articles focuses on the properties of membranes themselves and how they are sensed by cytoplasmic proteins. Malinsky et al. highlight lateral heterogeneities in membrane structure (Malinsky et al., 2016), Kishimoto et al. review technologies for detecting these heterogeneities (Kishimoto et al., 2016), and Holowka and Baird consider the role of lateral heterogeneity in the context of signaling receptors (Holowka and Baird, 2016). Finally, Saita et al. and Cornell discuss how membrane thickness and curvature are sensed (Saita et al., 2016; Cornell, 2015)

Next we move to the topic of membrane contact sites, starting with a review by Chang and Liou on the many links between ER and the plasma membrane that maintain the signalling lipid PI(4,5)P<sub>2</sub> during PLC activation (Chang and Liou, 2016). This brings up themes of lipid and Ca<sup>2+</sup> traffic that are then taken up by Eden in a review of contacts between the ER and the endo-/lyso-somal system (Eden,

2016). In their review, Daniele and Schiaffino consider the relation of these contacts to those made with mitochondria both by lysosomes and other organelles (Daniele and Schiaffino, 2016). Lipid transport facilitated by contact site formation is a theme that also applies to the intracellular parasites, and insights from the development of the chlamydial parasitophorous vacuole are reviewed by Dumoux and Hayward (Dumoux and Hayward, 2016). Next we move to the molecular composition of contact sites, with a phylogenetic analysis by Wideman and Munoz-Gomez of many of the complexes and proteins implicated in ER-mitochondrial communication (Wideman and Munoz-Gomez, 2016).

With so many discoveries linking intracellular trafficking pathways to membrane contact sites, we end with articles that describe specific components of these sites that are implicated in determining the lipid landscape. First there are two articles on the TUBular LIPid binding protein (TULIP) family, starting with a phylogenetic analysis by Alva and Lupas, who show how remote sequence homologies stress an early division between these proteins and their extracellular counterparts (Alva and Lupas, 2016). This is followed by a review from Reinisch and de Camilli of structural studies by themselves and others of these domains, and how they might function *in situ* (Reinisch and De Camilli, 2015). Next are two articles on the family of proteins related to OxySterol Binding Protein (OSBP). Im and colleagues focus particularly on the structural aspects of ligand binding by different OSBP related proteins (Tong et al., 2016), while Mesmin and Antonny describe the roles of multiple ligand binding both in physiological and pathological settings (Mesmin and Antonny, 2016). Finally, Murphy and Levine review the literature vesicle-associated membrane protein-associated protein (VAP), a common player at many contact sites (Murphy and Levine, 2016).

#### **Legend for cover illustration:**

A cut away view of a model of a yeast cell generated from images acquired by FIB-SEM (focused ion beam – scanning electron microscopy). Purple, plasma membrane (PM); green, endoplasmic reticulum (ER); yellow, nucleus. Other intracellular structures are not shown. The image highlights the close proximity of the ER to the PM such that 40-50% of the PM in yeast is closely apposed to ER. Image courtesy Yves Y. Sere (Weill Cornell Medical College), William J. Rice (Simons Electron Microscopy Center at New York Structural Biology Center) and Anant K. Menon (Weill Cornell Medical College).

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