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Editorial overview: Cell organelles

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Organelles compartmentalize cells, allowing the regulation of the numerous processes that occur within them. Early studies of cells using microscopy and fractionation revealed that organelles have characteristic sizes, shapes, compositions, and positions within cells. Later, as more advanced techniques were developed it became clear that organelles are also highly dynamic and that complex mechanisms are used to form and maintain organelles. Central to these processes are the sorting of proteins and lipids into vesicles and domains of organelle membranes, protein quality control and import, and the regulation of organelle dynamics. This issue highlights some of the most exciting recent developments in the study of these processes and their role in organelle biogenesis.

Vesicles are the principle means of transport of proteins within the secretory and endocytic pathways. While we understand a considerable amount about the biogenesis of some classes of endocytic vesicles — most notably the formation of clathrin-coated vesicles at the cell surface — considerably less is understood about the machinery and mechanisms employed by alternate endocytic pathways. [Shvets et al.](#) bring us up-to-date on one such alternate pathway with their review on the formation and function of caveolae. While [Jackson](#) provides a perspective on recent advances in our understanding of the mechanisms of protein cargo selection in the biogenesis of Golgi-derived COPI vesicles.

Following vesicle biogenesis, transport vesicles must be recognized by their target compartment before membrane fusion — in a process broadly termed tethering. Distinct tethering complexes are found on a variety of organelles and vesicle-tethering specificity is central to organelle biogenesis. [Kümmel and Ungermann](#) review our current understanding of the mechanisms of membrane tethering and fusion in the biogenesis of endosomes and lysosomes, and provide their perspective on the fields outstanding questions.

In order for the compositional integrity of an organelle to be preserved it is crucial that the cell be able to regulate the transport of transient proteins and at the same time ensure the retention of its unique protein and membrane constituents. Understanding how the compositional identity of an endomembrane compartment is established and preserved is particularly challenging when it comes to the Golgi. The Golgi is the cell's protein sorting hub and this organelle is comprised of a number of sub-compartments defined by their compositional and biochemically distinct features. Attempts to understand the biogenesis of the Golgi have relied heavily on the formulation of transport models that best reconcile a

diversity of experimental findings. [Papanikou and Glick](#) describe a three-stage model for the Golgi and posit how this model may best be able to account for the biogenesis of this organelle.

We are perhaps somewhat more cognizant of the transport of correctly folded and processed proteins, however the cell is also tasked with dealing with proteins that have not obtained a transport-competent state, become damaged *in situ*, or have simply fulfilled their functional expectations. [MacGurn](#) reviews what we currently understand about the mechanisms cells employ to remove aberrant proteins from the plasma membrane and target them for degradation. While [Nakatsukasa et al.](#) provide an update on recent technical advances that will likely provide deeper mechanistic insight into the mechanisms cells employ to degrade misfolded proteins in the endoplasmic reticulum.

Shaping membranes is critical for organelle biogenesis and many cellular membranes are highly curved. Although a number of protein-mediated membrane bending mechanisms have been identified, which ones are primarily employed in cells has remained controversial. [Kozlov et al.](#) summarize the proposed mechanisms and provide quantitative estimates of the efficiency of each of them.

The ER plays an important role in the biogenesis of some organelles — one of which is the peroxisome. Peroxisomes were once thought to be semi-autonomous organelles but about a decade ago it became clear that the ER was necessary for some aspects of peroxisome biogenesis. The precise role the ER plays, and the machinery responsible for the ER contribution to peroxisome biogenesis, has remained somewhat obscure. [Hettema et al.](#) summarize recent progress in our understanding of the role of the ER in *de novo* peroxisome biogenesis as well as the growth and division of pre-existing peroxisomes. The ER plays a similarly complex but incompletely understood role in lipid droplet (LD) biogenesis. It has been long known that *de novo* LD biogenesis begins at the ER and that most lipids stored in LDs are synthesized in the ER — however the mechanisms of lipid transfer to growing LDs remains poorly understood. [Wilfling et al.](#) discuss our current understanding of *de novo* LD biogenesis in the ER and as well as how LDs grow and fuse.

The biogenesis of autophagosomes has been another exciting and sometimes controversial subject in the last few years. [Ge et al.](#) summarize our current understanding of this fast moving field. Work from a number of groups is beginning to provide a mechanistic understanding of the formation of the phagophore, the double membrane that encloses cytoplasmic organelles during autophagy.

It has long been known that some organelles are transferred between cells, though in most cases the mechanism remains poorly defined. One such organelle is the melanosome, pigment-containing vesicles produced by melanocytes that must be transferred to keratinocytes, and are necessary for photo-protection by skin. [Wu and Hammer](#) summarize recent developments and highlight the remaining controversies about how this intercellular organelle transfer occurs.

Work in the last few years has also uncovered enigmas about the biogenesis of organelles that were thought to be relatively well understood. For example, we have learned a great deal

about the targeting and translocation of many proteins into the ER. However, [Aviram and Schuldiner](#) highlight recent genomic studies, which reveal novel but still poorly understood mechanisms that may target and translocate a significant number of proteins into the ER. Similarly, [Wong et al.](#) summarize recent work showing that the ER, despite being composed of one continuous membrane, is actually divided into more domains than had been previously appreciated. They also discuss growing evidence that diffusion barriers may separate ER regions from one another. Such compartmentalization of organellar membranes is not unique to the ER, and [Rao and Mayor](#) provide both an historical account as well as a compelling perspective of the limiting membrane of cells as a dynamic multifaceted membrane domain.

Regions of the ER that have been increasingly studied in recent years are zones of close contacts between the ER and mitochondria, which are thought to mediate signaling. This contact is the subject of a review by [Hajnóczky et al.](#) They focus on the role of contacts in calcium signaling between these organelles, particularly on a family of calcium-binding proteins. [Hoppins](#) focuses on the emerging connection between mitochondrial the dynamics of mitochondrial fission and fusion and intra-cellular signaling.

Finally, the study of so-called conventional secretory pathways has had a long and august history. By contrast, and despite the first description of exocytic vesicles more than 40 years ago, precisely how exocytic carriers are generated, and the mechanisms that facilitate the release of such vesicles from cells remains a matter of considerable debate. [Kowal et al.](#) highlight what is currently understood about the origin of exosomal proteins, the biogenesis of exocytic vesicles and their mode of secretion from cells. While [Ding et al.](#) highlight our current understanding of what may be a closely related process — unconventional protein secretion — in plants.

Biographies

David K Banfield received his PhD in Biochemistry from the University of British Columbia and completed is postdoctoral training with Sir Hugh Pelham at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK. David moved to the Hong Kong University of Science and Technology in 1995 where is currently a Professor in the Division of Life Science. His laboratory investigates mechanisms of membrane protein retention in the Golgi using yeast as a model system.

Will Prinz received his PhD in Microbiology from Harvard University and was a post-doc with Tom Rapoport, who is also at Harvard. Will moved to the National Institutes of Health in Bethesda, MD in 2001, where he is currently a Senior Investigator. His laboratory studies organelle biogenesis, with an emphasis on intracellular lipid trafficking.