Membrane traffic: endocytotic dynamics and regulation

Benjamin J. Nichols and Ludger Johannes

Endocytosis plays a central role in many cell biological processes. Talks at the Minisymposium on “Membrane Traffic: Dynamics and Regulation,” Endocytosis Section, mainly focused on specific mechanistic aspects of endocytosis, addressing the questions of how cargoes are sorted into different endocytic vesicles and how vesicles pinch off from the plasma membrane or bud into multivesicular bodies and move within the cytoplasm.

Making vesicles

Four talks addressed the mechanisms involved in pinching off vesicles. Ludger Johannes (Institut Curie) has previously revealed a mechanism by which lectin-induced extracellular clustering of glycosphingolipids triggers membrane deformation and hence formation of endocytic vesicles without a need for the cytosolic clathrin coat. He reported new data addressing the cellular factors involved in vesicle budding. The BAR-domain protein endophilin has a key role in this process, and a novel mechanism was presented in which scaffolding by endophilin of endocytic invaginations sensitizes them to pulling force-driven scission.

Turning to clathrin-coated vesicles, there has been much debate as to whether these structures form by deformation of a preexisting flat array of clathrin on the plasma membrane or by clathrin recruitment that is directly coupled to the progressive formation of curvature of the nascent vesicle. Ori Avinoam (Kaksonen and Briggs labs, European Molecular Biology Laboratory) presented correlative light and electron microscopy tracking the size and shape of the clathrin lattice at different stages of vesicle invagination and provided compelling evidence that the entire lattice is present on nearly flat membranes at early stages of vesicle formation. The lattice then deforms as the vesicle grows. Emma Evergen (MRC Laboratory of Molecular Biology) showed complementary biochemical and imaging experiments directed at understanding the role of the clathrin adaptor FCHo2. Without FCHo2, the clathrin machinery forms static clusters. This striking result, along with further observations, suggests that FCHo2 acts to provide dynamic instability to the dense network of protein–protein interactions in the forming coated pit.

Budding of intraluminal vesicles away from the cytoplasm has the opposite topology to formation of endocytic vesicles at the plasma membrane and has an important role in late endosomal biogenesis. Aurélien Roux (University of Geneva) presented elegant in vitro experiments using atomic force microscopy and biophysical models to explain how ESCRT-III components form spiral springs to induce membrane curvature away from the cytoplasm.

Sorting of cargoes into vesicles

Determining what gets into a vesicle is clearly important. Vassilis Bitsikas (Nichols laboratory, MRC Laboratory of Molecular Biology) presented data arguing that a surprisingly large proportion of endocytic vesicles arise from budding of clathrin-coated pits at the plasma membrane. Bitsikas’ data also suggested that crowding effects within the coated pit determine the amount of glycosylphosphatidylinositol (GPI)-anchored protein internalized, as cargoes with conventional endocytic sorting signals are usually preferred to GPI-anchored proteins.

Links to the cytoskeleton

Two talks gave new insight into how endocytic vesicles interact with the cytoskeleton. Mirko Messa (de Camilli lab, Yale University) has used both epsin knockout mice and a cell-free assay for endocytosis to show that the clathrin adaptor epsin acts in recruitment of actin to the forming coated pit. This recruitment is likely to provide force important for invagination and then fission of endocytic vesicles. Yoshimitsu Kanai (Hirokawa lab, University of Tokyo) reported data on a different endocytic mechanism, in which caveolae bud from the plasma membrane. Caveolae can recruit a kinesin, KIF13B, which is important for endocytosis of low-density lipoprotein. Consistent with this, KIF13B knockout mice have elevated levels of serum cholesterol. Dynamic caveolar vesicles in the cytoplasm have been reported in several previous studies, and it will be intriguing to see whether these dynamics are KIF13B dependent.