p115 untethered

Sometimes the simplest, most elegant hypothesis is correct. And sometimes it is not. On page 227, Puthenveedu and Linstedt poke holes in a hypothesis that has been used to explain how the Golgi is vesiculated for distribution during mitosis. In the process they invoke a new, essential function for the p115 protein in the earliest steps of Golgi formation.

The p115 protein forms part of a tether that leads from GRASP65 on Golgi membranes, through GM130 and then p115, and finally to the integral membrane protein giantin on vesicles. Loss of this link in the presence of continued vesicle formation could lead to vesiculation of the Golgi, and indeed during mitosis GM130 is phosphorylated, such that it no longer binds p115.

Consistent with this theory, Puthenveedu and Linstedt find that the injection of p115 antibodies results in Golgi fragmentation. Anti-GM130 does not prevent Golgi formation after mitosis.

In contrast, a p115 function that is independent of giantin and GM130 is essential. This essential function may involve loading of p115 at the ER by interaction with COPII coats (used for ER to Golgi transport). This p115 could then serve as a target for the docking of Golgi-derived vesicles, which might effect the maturation of an intermediate compartment into a cis-Golgi compartment. As for mitosis, inhibition of this essential p115 function, and perhaps other vesicle events, may cause mitotic vesiculation.

Exchanging clathrin

Wu et al. (page 291) find that clathrin in the existing lattices of clathrin-coated pits can exchange. This ATP-dependent process may play a part in converting hexagonal, flat clathrin lattices to curved lattices that are a mixture of hexagons and pentagons.

Although Wu et al. see no clathrin exchange in an in vitro system, the exchange is rapid after photobleaching of GFP–clathrin produced in vivo. The recovery could be a function of new clathrin coats forming at the membrane, but inhibition of endocytosis (which also inhibits formation of new clathrin coats) has no effect on the recovery of clathrin fluorescence. And clathrin coats in the bleached areas are not being replaced by clathrin coats flowing in from unbleached areas, as there is no visible gradient of recovery from the outside of the bleached area inwards, and the recovering fluorescent spots are in the same positions as were the spots before bleaching.

The protein mediating the exchange of clathrin may be Hsc70, which can form a tight complex with clathrin that can transiently rebind stripped vesicles. Confirmation of this hypothesis, and a study of possible regulation, will have to wait for future work.

Bind and bend

Farsad et al. report on page 193 that recombinant endophilin has an intrinsic ability to tubulate membranes. The tubulation appears to help during synaptic vesicle endocytosis in nerve terminals.

Endophilin joins dynamin and amphiphysin in the league of endocytic proteins with lipid-deforming properties. All three proteins can act alone to deform membranes, and both amphiphysin and endophilin interact with dynamin, but the mode of action of the proteins remains obscure. Others had suggested that endophilin acts as an acyl transferase to modify the shape of inner leaflet phospholipids, and thus the membrane curvature. But Farsad et al. find that endophilin can tubulate membranes during an incubation that is either on ice or lacking the substrates for the relevant acyl transfer reaction.

The authors find that amphiphysin and endophilin share a short stretch of homology, essential for endophilin action, that may form an amphipathic helix. Such a helix could interact with both charged head groups and hydrophobic tails of membrane lipids, thus inserting into the membrane. The lipid-stimulated oligomerization of endophilin observed by the authors could then impose a new spacing on the membrane lipids of one leaflet of the membrane, thus inducing curvature and creating tubules. The different functions of endophilin, amphiphysin, and dynamin during this process are yet to be established.