**In Brief**

**Transport, Not Capture, for Myo2p**
Budding yeast uses actin and a myosin, M yo2p, to accomplish polarized secretion. The simplest model for this process, which Schott et al. confirm on page 791, is based on transport: the M yo2p head walks along actin to growth sites, with vesicle cargoes attached to its tail. The alternative is a capture model. In this scenario, the M yo2p tail targets the protein to the growth site, where it can organize and polarize actin.

The transport model was in doubt because the original myo2 mutant had severe cytoskeletal disorganization, suggesting an indirect effect on polarity. In more recent experiments, a tail region alone localized to polarized sites, but Schott et al. show that this occurs by transport. It requires a vesicle targeting factor and normal M yo2p, which presumably carries the extra tails attached to vesicle cargoes.

Schott et al. isolate seven new myo2 alleles, all mutant in the tail region. According to the transport model, these proteins should be competent for their own localization, but incapable of moving other proteins. Consistent with this theory, a shift to high temperatures rapidly delocalizes a secretory vesicle marker, but mutant M yo2p is still localized as long as actin cables are intact. One tail mutant isolated in another study fails to localize, suggesting that even after transport there may be a mechanism for tethering M yo2p to the polarization site.

**Finding a Receptor in cis**
On page 707, Zeng et al. report an association between contactin, a glycosylphosphatidylinositol (GPI)-linked receptor involved in neurite extension and neuronal differentiation, and the extracellular domain of PTPα, a receptor protein tyrosine phosphatase (RPTP). PTPα may link contactin to the intracellular kinase fyn. Contactin and PTPα associate when expressed in the same cell, but not when they are expressed in two different cell lines that are then mixed. This cis mode of association “shows a whole new way of looking at PTPs as receptors,” says senior author Catherine Pallen. “Finding the extracellular signals [for PTPs] has really stalled the field. But besides looking for the ligand on other cell surfaces we should be considering [PTPs] as key components of known receptor complexes.”

**A New Golgi to ER Transport Pathway**
ER proteins are recycled from the Golgi using the K DEL or K KXX motifs and vesicles formed with the COP1 coat-protein complex. On page 743, and in the November issue of Nature Cell Biology (Girod, A., B. Storrie, J.C. Simpson, L. Johannes, B. Goud, L.M. Roberts, J.M. Lord, T. Nilsson, and R. Pepperkok. 1999. Nat. Cell Biol. 1:423-430), two groups report that some bacterial toxins and Golgi proteins move from the Golgi to the ER using a different, COP1-independent, but Rab6-dependent, pathway.

White et al. visualize the Rab6 GTPase as cells internalize the Shiga toxin B-fragment. The proteins colocalize in transport structures that move from the Golgi to the cell periphery, before the toxin fragment disperses into the ER. This trafficking is unaffected by antibodies to COP1 that inhibit K DEL-mediated transport, but a Rab6 mutant reduces toxin delivery to the ER and, therefore, toxicity. Girod et al. report similar trafficking results with both Shiga-like toxin and a Golgi-resident glycosylation enzyme. The Rab6 pathway may use delivery to the ER to weed out misfolded Golgi proteins or to recycle excess lipids from the trans-Golgi network.

**Assembling snRNPs in Cajal Bodies**
The spinal muscular atrophy disease gene product (SMN) has been implicated in the assembly of spliceosomal small nuclear ribonucleoproteins (snRNPs). In previous studies, snRNPs were localized to nuclear structures called coiled, or Cajal, bodies, and SMN was found in neighboring gems. How the two ever got together was a mystery.

On page 715, Carvalho et al. report that, in most cell types, SMN is found predominantly in Cajal bodies, further strengthening the idea that Cajal bodies are a site for assembly or processing of spliceosome components. Gems appear to be SMN aggregates, present only in a subset of cells, and their function remains unclear.

Most snRNA s are exported to the cytoplasm after transcription. They then assemble with Sm proteins and re-enter the nucleus. Carvalho et al. use leptomycin to block snRNA export, which leads to a gradual depletion of snRNPs from the Cajal bodies. This transient association with Cajal bodies is consistent with the findings of Sleeman and Lamond (Sleeman, J.E., and A.I. Lamond. 1999. Curr. Biol. 9:1065-1074), who see a pulse of labeled Sm proteins move from the cytoplasm to the Cajal bodies, and then on to nuclear speckles, which are reservoirs from which splicing factors are recruited to splicing sites. Thus, the Cajal body seems to be a transit site where a particular (and, as yet, unidentified) spliceosome biogenesis step takes place.

**The Point of No Return for Apoptosis**
Some cells, such as neurons, can recover from the mitochondrial release of cytochrome c that normally initiates apoptosis. On page 809, Kluck et al. identify a permeability enhancing factor (PEF) which may ensure that other cells fully commit to apoptosis.

Kluck et al. find that mitochondria in frog extract release cytochrome c and two other proteins from the mitochondrial intermembrane space, suggesting that any channel for cytochrome c is not specific to that protein. But, proteins are not released from the matrix compartment, which shows no signs of swelling or visible damage.
The apoptosis-initiating proteins, Bid and Bax, produce similar effects. However, only extract treatment opens up mitochondria enough so that large amounts of exogenous cytochrome c can re-enter mitochondria and gain access to oxidizing or reducing complexes. Kluck et al. name this extract factor PEF. A PEF-treated mitochondrion’s ability to re-admit cytochrome c may be an indicator of a more extensive and permanent opening of mitochondrial channels. “PEF might ensure that the mitochondria can’t recover,” says senior author Donald Newmeyer.

PEF does not consist of, but is, in fact, destroyed by, the cell death proteases or caspases. Thus, therapeutic inhibition of caspase activity may have the unintended consequence of increasing PEF activity and reinforcing cell death. Newmeyer is now testing to see if neurons (which can recover from cytochrome c release) lack PEF activity and if PEF activity is generally higher in cells that are readily replaceable.

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