RESEARCH HIGHLIGHTS

Sorting lipids at the Golgi

The trans-Golgi network (TGN) is the main hub in the secretory pathway for sorting proteins. Now, Simons and colleagues report that in *Saccharoymyces cerevisiae*, the TGN can also sort lipids (*J. Cell Biol*. **185,** 601–612).

The authors purified TGN-derived secretory vesicles bearing a raft marker. These vesicles were found to contain other raft proteins destined for the plasma membrane but lacked soluble secreted proteins that are delivered in different vesicles. Comparative lipidomics between secretory vesicles, TGNs and endosomes revealed that ergosterol and sphingolipids — lipids typical of raft domains — were enriched in the vesicles, whereas other lipids were under-represented. Moreover, the authors found that the vesicle membrane was more ordered relative to the TGN, potentially reflecting the coalescence of lipid raft domains in the vesicles.

These findings demonstrate not only that lipids can be sorted at the TGN, but also that sorting may rely on a raft-based clustering mechanism during the biogenesis of secretory vesicles at the TGN. Identifying factors that facilitate raft clustering at the TGN will be the next important step in understanding how rafts may assist in cargo sorting. SS

Pom1 sets size limit

Two studies in *Nature* from the groups of Sophie Martin and Paul Nurse find that the polarized distribution of the kinase Pom1 functions as a cell size sensor that controls mitotic entry through the Wee1-inhibitory kinase Cdr2 (*Nature,* doi:10.1038/nature08074 and doi:10.1038/nature08054).

Pom1 regulates polarized cell growth at the tips of *Schizosaccharomyces pombe* cells. Both groups noticed that *pom1* mutants divide at a smaller size than wild-type cells do and found that Pom1 acts as a dose-dependent inhibitor of mitotic entry. It localizes Cdr2 medially and negatively regulates Cdr2, perhaps through direct phosphorylation.

The gradient of Pom1 levels emanating from cell tips only reaches the cell centre to overlap with Cdr2 in small cells. When cells reach a threshold size, Pom1 no longer inhibits Cdr2, resulting in Wee1 inhibition and hence mitotic entry. Consistent with this, both groups found that expressing Pom1 at higher levels in the middle of the cell can trigger a delay in mitotic entry.

Thus, these studies provide an elegant example of how the intracellular gradient of a polarity protein can regulate a cell size checkpoint. AS

oskar moved by myosin V

In *Drosophila* oocytes, posterior accumulation of *oskar* mRNA is required for embryonic development. *oskar* localization requires the microtubule-based motor kinesin, but the precise mechanism is unclear. Ephrussi and colleagues now demonstrate that the actin-based motor myosin V has two functions in oocyte polarization: it directly modulates kinesin activity and it targets *oskar* mRNA to the posterior cortex (*Curr. Biol.,* doi:10.1016/j.cub.2009.04.062). A previous screen identified mutants with anterior–posterior patterning defects, which are now shown to be due to mutations in the myosin V gene, *didium*. Both *oskar* mRNA and Staufen, which mediates posterior oskar localization, are mislocalized in *didium*-mutant oocytes, or when dominant-negative myosin V peptides are expressed. Genetic experiments suggest that kinesin activity is upregulated when myosin V is deficient, which may cause accumulation of *oskar* mRNA in the middle of the oocyte. Consistent with the direct regulation of kinesin, myosin V is found to interact with kinesin, confirming data from mammalian cells. Myosin V also colocalizes with *oskar* mRNA at the posterior cortex, biochemically interacts with *oskar* mRNA and is required for the cortical localization of *oskar* mRNA and protein. Thus, in addition to the microtubule-based and kinesin-dependent cytoplasmic transport mechanism, *oskar* mRNA is translocated to the posterior cortex in an actin-based and myosin V-dependent manner. CKR

Chemical iPS cocktails

Overexpression of the transcription factors Oct4, Sox2 and either Klf4, c-Myc or Nanog, Lin28 is sufficient to reprogram somatic cells into embryonic stem (ES) cell-like induced pluripotent stem (iPS) cells. Whereas fine-tuning culture conditions has obviated the requirement for c-Myc, the other potentially oncogenic factors still have to be overexpressed from viral vectors, limiting clinical applications. Transient transfection and excisable vectors also represent viable approaches, albeit less efficient ones. A number of recent studies have identified small-molecule compounds that allow efficient iPS induction with only Oct4 and either Klf4 or Sox2, raising the possibility that a chemical cocktail can be derived that allows iPS induction in a more clinically relevant setting. The laboratories of Jaenisch and Schultz now report the results of a screen of 500,000 compounds designed to select for replacements for Klf4 (*Proc. Natl Acad. Sci. USA* **106,** 8912–8917; 2009). The broad-spectrum kinase inhibitor kenpaullone in combination with Oct4, Sox2 and c-Myc yielded iPS cells that were indistinguishable from ES cells. siRNA depletion of combinations of known kenpaullone targets did not reproduce the effect. Although the compound is less efficient and does not completely recapitulate the role of Klf4 overexpression, future screens to replace Oct4 may provide a chemical protocol for iPS generation. BP

Viral-induced polyadenylation mediates decay

mRNA polyadenylation usually correlates with increased mRNA stability in metazoan eukaryotes, but has been linked to mRNA decay in *Escherichia coli* and yeast. Herpesviruses induce a global shut-off of their hosts transcriptome to evade immune surveillance and the Kaposi's herpesviral protein SOX (shut off and exonuclease) mediates global mRNA decay in eukaryotic cells, although it has no homology to ribonucleases. Glaunsinger and colleagues now show that SOX induces aberrant mRNA polyadenylation to stimulate transcriptome turnover (*PLoS Biol.,* doi:10.1371/journal.pbio.1000107).

The authors observed that SOX expression in cells triggers polyadenylation and rapid turnover of the *GFP* (green fluorescent protein) mRNA reporter. Knockdown of polyA polymerase (PAPII) by siRNA impairs *GFP* mRNA hyperadenylation and SOX-induced decay. In addition, SOX promotes the relocation of the cytoplasmic polyA-binding protein PAPBC to the nucleus, correlating with the destabilization of the cytoplasmic *GFP* mRNA, and siRNA silencing of *PAPBC* prevents SOX action.

Thus, the Kaposi herpesvirus uses a new mechanism based on aberrant polyadenylation to trigger host transcriptome shut-off. How exactly SOX regulates PAPBC relocation and how viral mRNA escapes this process will be the focus of future studies. NLB

By Nathalie Le Bot, Bernd Pulverer, Christina Karlsson Rosenthal, Alison Schuldt and Sowmya Swaminathan