In Brief

Movement by Cable or Capture

Secrecy is polarized into the yeast bud so that the bud grows in preference to the mother cell. Pruyne et al. (page 1931) report that this actin-based process is directed by actin fibers that extend into the bud, and not by the actin patches that are clustered near the bud tip.

Most perturbations to the actin system depolarize both patches and cables, but Pruyne et al. find that the combination of a temperature-sensitive tropomyosin 1 mutation and a tropomyosin 2 deletion can be used to selectively rid the cell of cables. Tropomyosin is found on, and stabilizes, actin cables but is not present in actin patches.

Actin cables disappear just one minute after shifting the double mutant to a restrictive temperature; another minute later two other molecules are no longer concentrated at the bud tip. These proteins—Sec4, a secretory vesicle GTPase, and Myo2p, an unconventional myosin V implicated in targeted secretion—become diffuse several minutes before actin patches begin to delocalize.

When the mutant is shifted back to the permissive temperature, tropomyosin-containing cables are reformed, and Sec4p and Myo2p localization are reestablished within one to two minutes. Repolarization of actin patches takes 15–20 min.

The tropomyosin double mutant should help identify the yeast cell polarity marker. Of the proteins that are localized to the bud tip, only those that remain localized in the tropomyosin mutant, and that are necessary for regeneration of polarized cables, will remain as the leading candidates.

This work and previous studies with Myo2p establish actin cable–based transport as the key event in yeast polarized secretion. Transport of mammalian melanosomes was also thought to be an actin-dependent process. But in mouse melanocytes, Wu et al. (page 1899) find that these organelles also undergo rapid, bidirectional, microtubule-dependent movements between the cell center and the periphery. A myosin V isoform encoded by the dilute locus is necessary for peripheral accumulation of melanosomes, but it functions primarily by capturing these organelles in the cell periphery.

The striking difference between these two papers may reflect the different dimensions of the two cell types. Smaller yeast cells may preferentially use actin-based transport, whereas larger vertebrate cells use both short-range actin-based transport and longer-range microtubule-based transport.

Gathering Together Unfolded Proteins

When faced with unmanageable quantities of unfolded proteins, bacteria and yeast make inclusion bodies. Now Johnston et al. (page 1883) find that mammalian cells react by actively gathering the protein together into an aggregate that the researchers name the aggresome.

Johnston et al. use a poorly folding mutant of cystic fibrosis transmembrane conductance regulator (CFTR) as their model protein. Overproduction of the protein, or inhibition of the proteolytic activities of the proteasome, leads to formation of the aggresome. Formation of these stable structures requires microtubules; in the absence of microtubules unfolded protein is found throughout the cytoplasm in roughly spherical, membrane-free particles 60–80 nm in diameter. Aggresomes appear to be an aggregate of these particles wrapped in bundles of filamentosous material that includes the intermediate filament vimentin.

Vimentin forms a similar cage around the spindle during mitosis, and its participation in aggresome formation may be a byproduct of this mitotic role. The tangled and ubiquitinated protein in aggresomes is probably a potent proteasome inhibitor, as substrates of the proteasome must be unfolded before they are destroyed. Inhibition of the proteasome may disrupt the cell cycle and lead to the vimentin phosphorylation that, in mitosis, causes it to coalesce around the spindle.

Gathering together unfolded proteins may limit their interference with membranes and partially folded protein intermediates. But aggresomes form around the centrosome, so they may disrupt microtubule-dependent trafficking in neurons, or cell division in other cells. Johnston et al. suggest that aggresomes are a general response to unfolded proteins, as they detect similar structures after expressing the Alzheimer’s disease protein presenilin-1. The relation of aggresomes to the protein aggregates found in many neurodegenerative disorders remains to be established.

Not All Sarcoglycans Are Equal

Of the three subcomplexes in the dystrophin–glycoprotein complex, the function of the sarcoglycan subcomplex is the least well described. The dystrophins link to actin and the dystroglycans link to the dystrophins and the extracellular matrix, so theoretically these two subcomplexes could be sufficient to anchor muscle cells. But mutations in sarcoglycan and dystrophin genes cause similar muscular dystrophy syndromes.

Chan et al. (page 2033) take a first step in analyzing sarcoglycans by dividing the subcomplex into a core of β- and δ-sarcoglycan, with γ- and then α-sarcoglycan more loosely associated. Only δ-sarcoglycan cross-links to the α/β-dystrophin unit. The definition of a core complex explains why human patients with β- or δ-sarcoglycan mutations show a complete loss or drastic reduction in all sarcoglycan proteins, whereas patients with α- or γ-sarcoglycan mutations often retain some sarcoglycan expression.
Intramolecular disulfide bonds are present in β-, δ-, and γ-sarcoglycan, and the protein sequences suggest that the disulfides may form a structure resembling the ligand-binding pocket of growth factor receptors. Sarcoglycans might be involved in mechanochemical signaling, but candidate ligands have not been defined.

**Nuclear Pore Complexes and Spindle Pole Bodies Share a Component**

Until now we knew of only one attribute shared by the spindle pole body (SPB) and the nuclear pore complex (NPC) of budding yeast: they are both inserted in the nuclear envelope. Now Chial et al. (page 1789) report that the SPB (yeast’s version of the centrosome) and the NPC both contain a protein called Ndc1p.

Mutants in ndc1 fail to insert the nascent SPB into the nuclear envelope, but Chial et al. do not find a similar defect in NPC insertion. It is possible that the SPB insertion defect is secondary to a specific defect in nuclear transport, but senior author Mark Winey favors an alternative. “Our favorite model is that the two organelles share at some level the same mechanism for membrane insertion,” he says. The extreme version of the model, he says, is that the two organelles could have a shared ancestry.

In support of the insertion model, Ndc1p localizes to the periphery of NPCs and the edges of the SPB central plaques. The localization data suggests that Ndc1p has a direct role in SPB insertion (contrary to previous assumptions), and may provide the first real handle on this process.

**Early Functions for Desmosomes**

Many desmosomal components are at least partially redundant, making it difficult to completely ablate desmosomal function. The surprising exception seems to have been found in a desmoplakin knockout mouse described by Gallicano et al. (page 2009).

Desmoplakin was thought to operate solely as a linker to intermediate filaments, and indeed there are few if any intermediate filaments associated with the desmosomes in the knockout. But these desmosomes are also 10-fold fewer in number and 2-fold smaller than in wild-type embryos. Thus, it appears that desmoplakin is not only important in attaching intermediate filaments to desmosomes, but also necessary for desmosome assembly or stabilization. The loss of attachment to intermediate filaments does not by itself lead to a loss of desmosome integrity, as intact desmosomes are found in knockout mouse cells that lack keratin networks.

The desmoplakin knockout mice successfully progress past the implantation stage, suggesting that E-cadherin linkages can withstand the forces inherent in forming a blastocoel cavity. By embryonic day 6, ectoderm proliferation and elongation of the central egg cylinder begin to fail. At this stage desmosomes are normally present only in the extraembryonic tissues, such as the endoderm that encases the ectoderm. This mutant endoderm must be failing either to protect or to send a signal to the ectoderm. This failure, and the breaking apart of the surrounding endoderm in response to the stresses of ectodermal proliferation and remodeling, lead to embryonic lethality within the next day.

**A Sex-specific Homeodomain Protein in Algae**

On page 1971, Kurvari et al. describe GSP1, the first homeodomain protein to be discovered in an alga, and the first protein with sex-limited expression to be discovered in *Chlamydomonas*. GSP1 was identified as a cDNA specific to *Chlamydomonas* gametes of the mt+ mating type after a screen involving subtractive hybridization. The GSP1 protein is absent in mt− mating type cells, but unlike other genes for mating type–specific proteins, the gsp1 gene is present in both mating types. The gsp1 gene is turned off in mt− gametes, directly or indirectly, by the MID repressor. Based on expression profiles, GSP1 may be turning on mating functions in mt+ gametes or regulating early expression patterns in the zygote.

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