In This Issue

No vacuolar reunion

On page 401, LaGrassa and Ungermann show that divided vacuolar membranes are kept apart by a kinase that disables their tethering complexes. Similar tethers may be the regulatory center of fission/fusion cycles at various membranes.

Yeast vacuoles divide, or fragment, during budding or in response to salt stress. Mutants have been isolated that are unable to fragment, but the new article identifies a regulatory mutant whose vacuoles, although initially fragmented correctly, reassemble prematurely.

This mutant lacks the Yck3 casein kinase. In vitro and in vivo, abundant Yck3 inhibited vacuole fusion, whereas its absence improved it. The authors find that the effects are tied to Yck3’s ability to inhibit tethering, which brings two membranes in close enough proximity for their SNAREs to zip them together.

On vacuoles, tethering is controlled by a Rab GTPase and the HOPS complex. The authors show that a HOPS component is phosphorylated during salt stress and that this modification requires Yck3. Phosphorylation increased HOPS dynamics and may interfere with tethering by loosening its association with the Rab. But without Yck3, unphosphorylated HOPS was tightly bound to vacuole membranes, allowing membranes to snap back together.

Tethering complexes may be a common target for inhibiting fusion. Phosphorylation of GM130 tethering protein prevents refusion of Golgi fragments. Tethering complexes of other organelles, such as the exocyst, may be similarly targeted by kinases—to slow protein secretion, for example. JCB

BiP chaperones ER entry

A gate that guards the translocon is opened and closed by ATP cycles that also give the same protein chaperone activity, as shown on page 389 by Alder et al.

The translocon is an aqueous pore in the ER membrane through which secreted proteins pass during translation. To prevent the unwanted passage of ions, unused pores are plugged on the lumen side by the action of BiP. Within the ER, BiP is also an Hsp70-like chaperone. Alder et al. now find that the ATP-dependent changes in substrate affinity that make BiP an efficient chaperone also give it its translocon gating ability.

ADP-bound Hsp70 chaperones bind tightly to their substrates, whereas ATP induces a conformational change that opens the substrate-binding pocket. Cycles of binding and release allow BiP to help its substrates fold properly.

For its gating activity, BiP’s “substrate” appears to be an as-yet-unidentified translocon component. Only ADP-bound BiP was able to seal the translocon pore. Pore opening, conversely, required ATP-induced conformational changes, presumably to release the translocon protein from BiP’s substrate-binding pocket.

Interactions with a protein containing a J-domain are also required for both its chaperone and gating activities. Perhaps the translocon-associated J-domain protein binds to a regulator that suppresses nucleotide exchange on BiP, thus keeping the door shut until the translocating protein needs to enter. JCB

Yeast warfare

Inside knowledge of the enemy’s weaknesses can help yeast to kill their enemy—other yeast cells—report Reiter et al. on page 353. They show that yeast activate the self-destruct mechanism in their yeast foes.

Self-destruction, or apoptosis, is thought to be a common outcome in yeast cells exposed to environmental stresses, such as peroxide or UV light, or internal stresses, such as aging. Suicide of a unicellular organism is thought to benefit the healthier, surviving members of the population by conserving limited nutrients.

But some members of the yeast populace are far less altruistic—they harbor toxin-producing viral sequences that eliminate other yeast in two ways. At high concentrations, the toxins bring about necrotic death in other cells via several strategies: some make holes in the plasma membrane; others inhibit DNA synthesis. In natural environments, however, the toxins rarely accumulate to such high levels.

The new results show that low toxin concentrations are still deadly because they trigger apoptosis in the enemy cells. As with other stresses, toxins required a caspase-like enzyme and reactive oxygen species to induce apoptosis. Because the killer cells are resistant to the toxins, these cells would probably dominate over time in the wild. JCB