Foci of decay

Cytoplasmic structures are sites of active mammalian mRNA decay, according to Cougot et al. (page 31).

The group had previously identified cytoplasmic foci that included two human mRNA decapping enzymes. They now add subunits of a deadenylase, exonuclease, and possible helicase to the list of proteins found at these sites. After inhibition of a 5’-3’ exonuclease, poly(A)+ RNA accumulates at these sites, further suggesting that these are locations for active degradation of RNA rather than passive storage centers for degradation factors. The foci almost completely disappear after addition of either translational inhibitors that are known to stabilize RNAs or transcriptional inhibitors that deplete the cytoplasm of all mRNA.

Similar structures have been seen in yeast, although these structures were fewer in number and only visible under certain nutrient conditions. Both findings suggest that the cytoplasm is more structured than previously thought. The regulation of foci formation remains a subject for future studies.

Brain construction goes straight

Brains of mice lacking the cell adhesion molecule L1 are a mess. Failures in neural migration, pathfinding, morphogenesis, and fasciculation result in shortages of cells in various regions and aberrant architecture. But now Itoh et al. (page 145) report that homophilic binding of L1 is not necessary for axonal guidance and neuronal migration in the central nervous system (CNS).

L1 was one of the first neural cell adhesion molecules to be discovered, and its binding partners have been proliferating ever since. Many of those binding partners contact several of L1’s many domains, making individual contributions difficult to tease apart. Itoh et al., however, succeed in ablating only a subset of L1’s binding interactions via a deletion of L1’s sixth Ig domain.

The resulting protein does not bind either to itself or to α5β1 integrin. And yet mice expressing only this variant have brains and spinal cords that look normal. Thus, it seems that L1 homophilic binding, earlier found to mediate neurite outgrowth in vitro, is not needed for this function in the CNS.

When the L1 variant is backcrossed into another mouse strain, the progeny get hydrocephalus. This swelling of the brain results when cerebrospinal fluid is not correctly cleared from the brain ventricles. The link between L1 mutation and hydrocephalus has been noted before, in humans, but its mechanistic basis remains unclear.

Form a shmoo

Matheos et al. (page 99) define a new step in this polarization dance—a step that may link the extracellular yeast pheromone signal to the intracellular establishment of polarized actin cables.

The proposed link involves phosphorylation of Bni1p, a cable-generating formin protein, by Fus3p, a MAP kinase. Fus3p got its name because cells lacking this kinase could not fuse during mating. Sure enough, activated Fus3p was long ago found to lead to transcription of fusion genes. Then Fus3p was found to help arrest the cell cycle of mating cells. But replacement of both of these functions did not restore fusion to cells lacking Fus3p.

Now Matheos et al. find that Fus3p is also needed for polarization of the cell and localization of Bni1p to the tips of shmoo, or mating projections. Overexpression of Bni1p overcomes the need for Fus3p, but multiple actin-containing projections replace the normal single shmoo.

All of this activity is set in motion when pheromone binds its receptor, liberating two G protein activities: a βγ complex that turns on both Fus3p and Cdc42-mediated actin polymerization, and an α subunit that helps localize the Fus3p that activates Bni1p. The need for both pathways may be a failsafe mechanism. Or perhaps it is related to the very different types of actin networks that the pathways make. Cdc42 is good at making actin meshworks that push out the cell membrane, but Bni1p is better at making cables that facilitate transport to the site of mating.