Kicking MiD51 out of the enzyme club

A key protein that helps mitochondria divide is a non-functional enzyme, Richter et al. show. Mitochondria are continually fusing and breaking apart. The protein Drp1 cleaves the organelles. After attaching to a mitochondrion, Drp1 polymerizes to form a molecular noose that tightens and cuts the organelle in two. Two related proteins, MiD49 and MiD51, serve as Drp1’s receptors on the mitochondrial surface. The sequences of MiD49 and MiD51 show few similarities to those of other proteins, and they lack any telling domains or motifs that might reveal how they function.

Richter et al. determined the crystal structure of the cytosolic portion of MiD51 and identified a fold that places the protein in the nucleotidyltransferase superfamily. Members of this clan latch onto nucleotides such as GTP and pass them to a substrate.

Polarity proteins duel in Drosophila

Gamblin et al. reveal how two proteins grapple to control polarity in epithelial cells. During Drosophila development, the protein Yurt initially settles on the sides of an epithelial cell, preventing the cell’s lateral membranes from acquiring apical traits. Later in development, the protein relocates to the apical end of the cell and stops this part of the membrane from growing too large and disrupting tissues. As Yurt moves, it sheds some of its phosphates, suggesting that a kinase helps hold it in place. A likely candidate for this task is aPKC, which enables the apical membrane to retain its characteristics.

Ndc1 catches the shuttle

The amount of Ndc1 (green) binding to the spindle pole body (SPB) is lower in mutant cells (right) than in controls (left). The protein Ndc1 commutes between jobs in yeast cells. Chen et al. pinpoint a nuclear membrane protein that might give it a ride.

In budding yeast, Ndc1 helps insert nuclear pore complexes (NPCs) and the spindle pole body (SPB), the yeast equivalent of the centrosome, into the nuclear envelope.

To better understand how Ndc1 completes its diverse tasks, Chen et al. gauged the effects of several mutant versions of the protein. They identified a variant, ndc1-L562S, that was able to attach to components of the NPCs and the SPB. They expected that this mutated protein wouldn’t affect the cells’ survival, but it was lethal because the cells couldn’t replicate the SPB. That finding suggested that Ndc1 might have another binding partner.

The team discovered that Ndc1 normally latches onto a nuclear membrane SUN protein, Mps3, to which ndc1-L562S attached only weakly. Line-scanning fluorescence cross-correlation spectroscopy revealed that the two proteins link up at nuclear membrane locations distinct from NPCs and the SPB. Reducing ndc1-L562S’s association with NPCs increased the protein’s localization to SPBs and rescued the growth of mutant cells. Chen et al. therefore suspect that Mps3 distributes Ndc1 between NPCs and the SPB to ensure that both structures are correctly inserted into the nuclear envelope.

Because Drp1 is a GTPase, the researchers wondered whether MiD51 was handing off GTP to its partner. However, neither GTP nor ATP bound to MiD51.

On the other hand, the researchers found that MiD51 could bind GDP and ADP, yet these interactions weren’t necessary for mitochondrial fission. Nucleotidyltransferases carry a characteristic stretch of amino acids in their active site. All but one of these amino acids is missing from MiD51, indicating that the protein does not catalyze reactions. Instead, a region in MiD51 that is not usually found in other nucleotidyltransferases helps assemble the Drp1 molecular noose. When Richter et al. mutated this region, MiD51 was unable to connect to Drp1 and promote mitochondrial fission.

The results suggest that MiD51 is a pseudoenzyme that reuses its nucleotidyltransferase fold as an assembly platform. Why MiD51 binds GDP and ADP is unclear, but one possibility is that they regulate the GTPase activity of Drp1.

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