Bridging the gap between atlastin conformations

Morin-Leisk et al. describe how a salt bridge drives a conformational change in the atlastin GTPase to promote membrane fusion and ER branching.

Atlastins are membrane-anchored members of the dynamin family of GTPases that tether and fuse ER tubules together in order to maintain the organelle’s branched morphology. Crystal structures suggest that atlastin molecules in opposing ER membranes initially dimerize head-on to tether the membranes together. GTP hydrolysis is then thought to trigger a rotation in the dimer’s conformation that brings the two membranes close enough to fuse with each other.

Morin-Leisk et al. identified several mutations in atlastin that prevented the GTPase from maintaining a branched ER network.

For Myo4p, two heads are better than one

Myo4p and She3p form elongated, single-headed structures on their own (left), but they assemble into two-headed, V-shaped complexes in the presence of She2p (right).

S. cerevisiae. Myo4p links to its cargo by pairing up with the adaptor protein She3p, which, in turn, binds the mRNA-binding protein She2p. In vitro, however, Myo4p and She3p fail to move continuously along actin tracks because, unlike many other class V myosins, the motor doesn’t homodimerize and therefore only has one ATPase head domain, which can’t take processive steps along the filament on its own.

A new spin on radial spokes

Pigino et al. describe the three-dimensional structure of radial spokes, key regulatory complexes that determine how cilia and flagella move.

Radial spokes connect the central pair of microtubules in cilia and flagella axonemes to the nine outer microtubule doublets and are thought to regulate how dynein motors slide these microtubules to generate movement. Each spoke contains at least 23 proteins, with two or three spokes (depending on the species) clustering together at regular intervals along the axoneme. How the spokes function is unclear, however, so Pigino et al. used cryoelectron tomography to observe their structure in various cilia and flagella.

Two of these mutations affected either the glutamate or the lysine residue of an ionic salt bridge that forms when atlastin assumes its “postfusion” conformation. Altering the charge on either of these polar amino acids had no effect on GTP binding or hydrolysis but inhibited the assembly of “postfusion” atlastin dimers. Restoring the salt bridge by reversing the charge on both residues rescued atlastin dimerization and ER branching.

The salt bridge therefore promotes ER tubule fusion by stabilizing atlastin’s postfusion conformation. Surprisingly, Morin-Leisk et al. found that GTP hydrolysis wasn’t required for the transition to this conformation, at least for soluble versions of atlastin lacking the GTPase’s transmembrane domain. Senior author Tina Lee now wants to determine whether the same is true for full-length atlastin and, if so, to investigate which part of atlastin’s fusion mechanism is dependent on nucleotide hydrolysis.


