In This Issue

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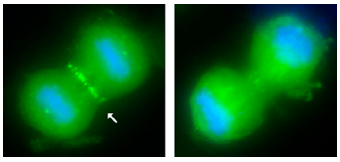
KIF4A knows its own limits



PP2A-B56γ (green) accumulates at the central spindle (arrow) of a control anaphase cell (left) but remains cytosolic in a cell lacking KIF4A (right).

Nunes Bastos et al. describe how the kinesin motor KIF4A restricts its own activity during anaphase by recruiting the phosphatase PP2A-B56 to the central spindle.

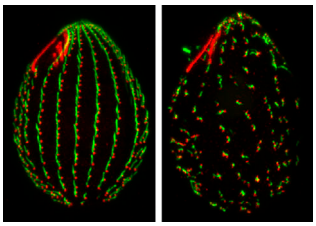
During mitosis, KIF4A limits the size of the central spindle by suppressing the growth of microtubules in the spindle midzone. The kinase Aurora B phosphorylates KIF4A to promote the kinesin's localization and motor activity, but a phosphatase must reverse this modification so that the central spindle can extend and push sister chromatids apart at the later stages of anaphase. The PP2A–B56 phosphatase family opposes Aurora B's functions in other mitotic processes, so Nunes Bastos et al. examined whether any of the five family members regulated KIF4A.

The researchers found that two PP2A–B56 isoforms, γ and ε, dephosphorylated KIF4A in vitro and localized to the central spindle in anaphase cells. The phosphatases accumulated at the spindle midzone by binding to KIF4A itself, indicating that the kinesin's localization and activity is restricted by a negative feedback loop. In the absence of B56γ and B56ε, increased amounts of active KIF4A accumulated at the central spindle, which therefore failed to completely extend during anaphase.

Other members of the PP2A–B56 family localize elsewhere in the cell or, in the case of B56β, localize to the central spindle but fail to bind or dephosphorylate KIF4A. Senior author Francis Barr now wants to understand the basis of these different specificities.

Nunes Bastos, R., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201409129.

Understanding the DisAp-pearance of cilia orientation



Kinetodesmal fibers (green) are shorter and basal bodies less organized in a disA-1 mutant Tetrahymena cell (right) compared with a wild-type cell (left).

Galati et al. identify a protein that helps cilia basal bodies (BBs) respond to mechanical force so that they maintain their organization in multiciliated *Tetrahymena* cells.

Cilia are organized by BBs docked at the cell cortex. In order to swim efficiently, *Tetrahymena* align their BBs into arrays that run from the front to the back of the cell, and each BB is oriented so that its attached cilium beats in the same direction as all the others. This organization is lost in *disA-1* mutant cells, but the identity of the mutated gene and the function of the protein that it encodes are unknown.

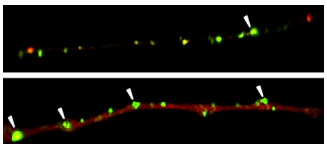
Galati et al. used next-generation sequencing to identify the *disA-1* mutation and found that it results in a truncated version of a protein the researchers called DisAp. DisAp localized to the kinetodesmal fibers (KFs) that protrude from the anterior side of BBs and control the structures' positioning and orientation. Galati et al. found that KFs grew when cilia experienced more mechanical force (either because they were beating faster or were pushing against a more viscous medium). KFs were shorter in *disA-1* cells and didn't elongate in response to increased force. This reduced the fibers' contacts with the cell cortex, which might otherwise prevent BBs from reorienting.

The researchers also discovered that newly assembled BBs dock in the correct position by moving along the KF of the mother BB from which they formed. The shorter KFs of *disA-1* cells likely inhibit this process as well.

DisAp is not conserved in vertebrates, but structures analogous to KFs, known as striated rootlets, orient BBs in multiciliated vertebrate cells. Senior author Chad Pearson now wants to investigate if these structures also elongate in response to increased mechanical force.

Galati, D.F., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201409123.

Ankyrin aweigh for axonal transport



AnkB (red) is present in synaptic vesicles (green) in a control axon (top) but absent in an axon lacking PIK3C3 and PI(3)P (bottom).

The adaptor protein ankyrin-B (AnkB) promotes the axonal transport of multiple organelles by linking the dynein motor accessory factor dynactin to membrane phospholipids, Lorenzo et al. reveal.

Ankyrin proteins are best known for their role in assembling spectrin–actin networks at the plasma membrane. Mice lacking AnkB develop severe brain abnormalities, but the reason for these defects is unclear. Lorenzo et al. found that AnkB-deficient neurons grew shorter axons than wild-type neurons, even though their axonal spectrin networks remained intact.

Instead, the researchers found, knocking out AnkB impaired axonal growth by inhibiting the transport of various organelles along axonal microtubules. Synaptic vesicles, mitochondria, endosomes, and lysosomes all showed reduced motility in the absence of AnkB, particularly in the retrograde direction toward the cell body. AnkB localized to all of these organelles by binding to the phospholipid PI(3)P. Knocking out the PI(3)P-generating kinase PIK3C3 inhibited both AnkB localization and organelle transport.

Retrograde axonal transport is driven by the dynein–dynactin motor complex, and AnkB promotes the formation of skeletal muscle costameres by binding to the dynactin subunit p62. Lorenzo et al. therefore wondered whether AnkB recruits dynactin to axonal cargoes and found that the motor complex was lost from organelles in AnkB-deficient neurons. Moreover, an AnkB mutant unable to bind p62 failed to restore organelle transport and axonal growth.

Mutations in the gene encoding AnkB—including ones affecting a large, axon-specific isoform of the protein—have recently been linked to autism. Senior author Vann Bennett is now interested in investigating whether any of these mutations affect axonal transport.

Lorenzo, D.N., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201407063.