The importance of catastrophe

For microtubule asters, just as with life in general, sometimes you get stuck in a corner. And, say Cendrine Faivre-Moskalenko and Marileen Dogterom (FOM Institute for Atomic and Molecular Physics, Amsterdam, Netherlands), it can take a catastrophe to get things moving again.

Dogterom has been trying to reproduce aster behavior in the minimal environment of a microfabricated chamber. Her beads, which are coated with cross-linked tubulin seeds to direct the growth of microtubules, are nudged to the chamber’s center as microtubules push on the chamber walls.

But Dogterom realized that, in live cells, asters move and reposition constantly during mitosis. She mimicked these events by grabbing the beads with a laser trap. Beads placed in a corner stayed put, because the established, long microtubules bent around the chamber walls.

But if Dogterom added Op18 protein to induce catastrophic microtubule shortening, the number of lengthy microtubules was reduced. Growing microtubules once again encountered the chamber walls head-on, allowing them to push the aster around.

In the smaller cells of fission yeast, a microtubule that hits the cell surface might induce its own catastrophe. The force upon contact slows growth rate, and thus increases the likelihood that the microtubule will lose its protective cap. But in larger cells, the longer microtubules will buckle more readily. Here, peripheral motors may help pull asters to a central position. Dogterom hopes to test such a model by tethering motors to the walls of her chambers.■


Cohesin resolves to let go

A chromosomal glue needs to get out of the way so that sister chromatids can resolve into two distinct entities, say Ana Losada, Michiko Hirano, and Tatsuya Hirano (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY). Cohesin sticks sister chromatids together from the moment of their replication.

During interphase this may aid in homology-based DNA repair. But when it is time to compact chromosomes in mitosis, all that glue could confuse matters. Up to 95% of the cohesin disperses, with the rest remaining in place until chromosome pairs finally split during anaphase.

Hirano and his colleagues found that two kinases—polo-like kinase (Plx1) and aurora B—were necessary for the initial dispersal. Plx1 probably operates via its direct phosphorylation of cohesin, whereas aurora B seems to hit another target such as histone H3.

Cohesin was no longer lost from chromosomes when frog extracts were depleted of both kinases. But, to the team’s surprise, this had no effect on either the loading of condensin or its ability to condense the chromosomes. Based on temporal correlation, some had predicted that cohesin had to leave to make way for the incoming condensin.

Instead, cohesin’s persistence resulted in a failure of sister chromatid resolution. Pairs of sister chromatids formed single rod-shaped structures. In this circumstance, says Hirano, “the condensin is not smart enough to recognize that there are two double helices.”

But in normal cells, with cohesin out of the way, Hirano predicts that the condensin operates on only a single DNA molecule. Condensin’s compacting activity should reel in a single DNA molecule, while allowing topoisomerases to untangle the strands that have not yet been packed away.■


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**Oscillating wildly**

Bacterial cell division is restricted to the middle of the cell. This, say Kyoko Suefuji, Regina Valluzzi, and Debabrata Ray-Chaudhuri (Tufts University, Boston, MA), can be explained by polymerization events that oscillate between the two ends of the cell.

The polymerization process forms filaments of MinD at one end of the cell, which sequester MinC from the middle of the cell, thus leaving the bacterial cell division protein FtsZ to do its job. An additional component, MinE, forms a cap on the MinCD crescent so that the inhibitor, MinC, cannot reach the central FtsZ.

These proteins must inhibit division at both ends, and they do so by oscillating from one end of the cell to the other every 50 seconds. In several existing models, self-assembly is a key part of this oscillation. Joe Lutkenhaus (University of Kansas, Kansas City, KS) has recently seen self-assembly of MinD on lipid vesicles, with diffraction patterns suggesting a regular structure.

But the Tufts team is the first to visualize MinD filaments directly. Assembly was dependent on ATP (MinD is an ATPase), and filaments were much longer and thicker when vesicles were added. MinE bound to the filaments and increased their length and width even further, but also led to bundle disassembly that was dependent on ATP hydrolysis. As the bundles disassembled, they frayed preferentially at one end.

“MinE is clearly doing two things at one time—bundling the MinD filaments and turning them over,” says Ray-Chaudhuri. In its negative role, MinE may both halt the progression of polymerization toward the cell center and begin chewing away at the existing filaments. As MinD is liberated from one end, it may polymerize at the only MinE-free site: the other end of the cell. These new MinD polymers then attract MinE, and the cycle begins again.

Although MinD is not quite a bacterial version of the microtubule, Ray-Chaudhuri can see parallels. He plans to use motor-like assays to test whether MinE’s depolymerization activity is polar. And he says that, like microtubules, “this system clearly evolved as a mechanism to search and explore cellular space.”


**A trigger for myelination**

Some cells can induce the production of their own protective blanket. The signal comes from active neurons in the central nervous system (CNS), and triggers the differentiation of oligodendrocyte precursor cells (OPCs)—thus yielding the cells that cover the neurons with a protective sheath of myelin.

Now, Beth Stevens, Douglas Fields, and colleagues (National Institutes of Health, Bethesda, MD) have shown that the neurons accomplish this task by releasing a simple metabolite, adenosine.

The finding could be critical for possible stem cell treatments for the myelinating disease multiple sclerosis. “The problem [with stem cell treatments] is not getting the stem cells; the problem is getting the cells to differentiate at the right stage,” says Fields. Adenosine looks like a promising stop signal for OPCs. And, as a further enticement, Fields showed that a brief exposure to adenosine might be enough to set cells on the right path.

Fields added a wide variety of biomolecules to OPCs and found that adenosine alone could reduce proliferation and induce everything from differentiation markers to a differentiated morphology and myelination. Adenosine receptor antagonists, meanwhile, prevented the changes in OPC proliferation and morphology normally caused by active neurons.

These results contrasted with the group’s earlier findings with Schwann cells, which provide myelination for the peripheral nervous system (PNS). For Schwann cells it is ATP that is active but with an opposite effect: the ATP arrests maturation. This may give the PNS axons time to mature before they are surrounded by myelin.

The regulation of the two systems will take some time to decipher. ATP and adenosine not only have different effects on OPCs and Schwann cells, but one metabolite can be converted to the other via extracellular enzymes. Fields thinks the decoding effort will be worthwhile.

“As neuroscientists we are all focused on rapid communication,” he says, “but all cells communicate, and this is one of the most ancient systems.”