In This Issue

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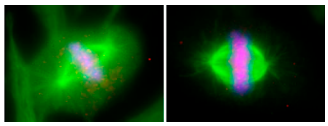
Ran's downhill slide during mitosis



RCC1 (red), which generates RanGTP on mitotic chromosomes (blue), is reduced in HFF-1 fibroblasts (left) relative to HeLa cells (right).

Hasegawa et al. clarify the role of RanGTP in the formation of the mitotic spindle.

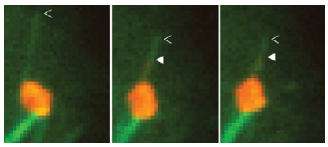
Because RanGTP is prevalent in the cell, its job during spindle assembly has been difficult to nail down. One possibility is that RanGTP promotes construction of the spindle by liberating spindle assembly factors from the importins that carry them. Previous studies of *Xenopus* egg extracts and fast-dividing cells have discovered a precipitous RanGTP gradient surrounding mitotic chromosomes, which might ensure that the protein triggers the spindle to coalesce near the chromosomes. However, researchers weren't sure if other, slower-growing cell types showed this steep dropoff in RanGTP levels.

To find out, Hasegawa et al. measured RanGTP gradients in an assortment of mitotic cells. Whereas some cell types, such as highly proliferative HeLa cells, showed steep gradients, other cell types had shallower gradients, and slow-growing HFF-1 fibroblasts exhibited no gradient at all.

The team then altered the slope of the RanGTP gradient in different cells. HeLa cells with a shallower-than-normal gradient spent more time in prometaphase, the stage when spindle microtubules transport the chromosomes to the cell center. This suggests that a steep RanGTP gradient helps orchestrate assembly of a working spindle during prometaphase. The researchers also found that they could make the gradient steeper by fusing HFF-1 cells, forcing them to carry extra chromosomes, which might help explain why aneuploid cancer cells divide more rapidly.

Hasegawa, K., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201206142.

Fly chromosomes don't just ride the tips



A NOD motor (red) linked to chromatin contacts and ascends (filled arrowhead) a microtubule (green).

The motor protein NOD works harder during cell division than researchers thought, Cane et al. show. NOD not only tows chromosomes, it also helps them hitchhike on microtubules.

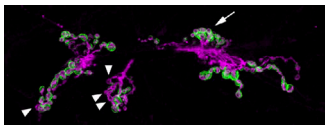
Polar ejection forces push mitotic chromosomes away from the spindle poles. One source for these forces, researchers think, are motor proteins that drag chromosomes along the spindle microtubules. In vertebrates, the motor protein KID, a member of the kinesin-10 family, hauls chromosomes along microtubules. NOD, the *Drosophila* homologue of KID, appears to be immobile. However, the molecular motor can link to the ends of microtubules, leading to the model that fly chromosomes are instead pushed away from the poles by the tips of polymerizing microtubules.

Cane et al. found that NOD takes a more active role in *Drosophila* cells. The researchers noticed that NOD-coated chromatin stretched in two ways as it interacted with microtubules. If a microtubule rammed head-on into chromosomes, the chromatin extended rapidly and then recoiled. The speed at which the chromatin stretched matched the growth rate of microtubules during mitosis, suggesting that this event represents a push from a growing microtubule. But the researchers also observed lingering interactions in which the chromatin appeared to stretch along a microtubule, as if the NOD motors were tugging the chromosome along the filament.

The researchers then replaced NOD's motor domain with a segment that only attaches to microtubule tips or with a motor domain from another kinesin that readily slides on microtubules. Both altered versions generated polar ejection forces. The work suggests that NOD performs double duty, pulling chromosomes along microtubules as well as enabling them to ride on elongating filaments.

Cane, S., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201211119.

Spreading around a Wnt protein



In a fly lacking Trol, arrows and arrowheads mark the extra boutons in a neuromuscular junction stained for pre- (purple) and postsynaptic (green) markers.

A proteoglycan helps disperse Wnt proteins during development of the neuromuscular junction, Kamimura et al. reveal.

Wnt proteins help shape many parts of a developing embryo, including neuromuscular junctions where nerves connect to muscles. In fruit flies, the Wnt protein Wingless (Wg) stimulates the presynaptic side of the junction, spurring the growth of synaptic boutons. Wg also prompts differentiation of the postsynaptic side of the junction. However, researchers don't know how the hydrophobic Wg is parceled out to the presynaptic and postsynaptic membranes. One possible mechanism involves heparan sulfate proteoglycans, which latch onto Wg and help set up concentration gradients of the protein.

To determine whether proteoglycans help distribute Wg, Kamimura et al. scrutinized fly larvae with mutated versions of Trol, a gene that codes for the proteoglycan perlecan. The insects showed defects on both sides of their neuromuscular junctions. Wg built up on the presynaptic side, which sprouted extra boutons. Postsynaptic flaws included puny muscles and an undersized subsynaptic reticulum (SSR), a highly folded region on the muscle membrane. Stimulating the nerve provoked a weak current, indicating that the neuromuscular junctions in the mutants malfunctioned.

Trol normally gathers at the SSR, the researchers found. Whether Trol helps transport Wg across the synapse isn't clear, but it ensures that an ample supply of Wg reaches the postsynaptic side. Without Trol, excess Wg accumulates on the presynaptic side and triggers the growth of extraneous synaptic boutons.

Kamimura, K., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201207036.

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