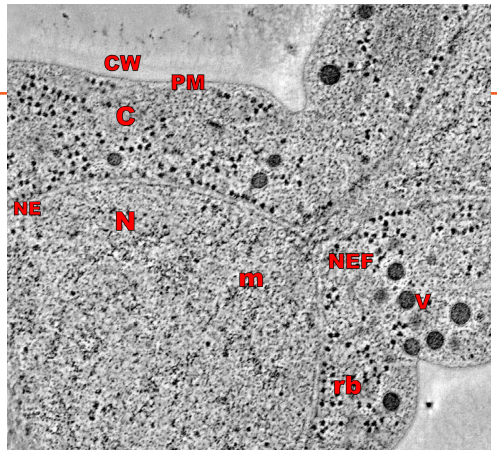


Electron tomography of two mating yeast nuclei reveals multiple steps to fusion.

Text by Mitch Leslie
mitchleslie@comcast.net

Fusion in three easy steps

Mating is complicated for yeast. The nuclei of two cells have to get together, even though both nuclear membranes remain intact. Melloy et al. now nail down how many steps it takes for the cells to combine their nuclei.

Before human gametes fuse, their nuclear membranes break down to allow the nuclear contents to mix. But when yeast mate, the inner and outer membranes of the two nuclei have to join, as do the spindle pole bodies (SPBs). Spanning the inner and outer membranes, SPBs anchor the microtubules that winch the nuclei together. Whether the components merge simultaneously or in three separate steps has been debated, due to the difficulty of catching nuclei in the act.

Melloy et al. used electron tomography to capture 3D images of nuclei at different stages of fusion. They found that nuclei retained separate SPBs even after the inner and outer membranes had joined, indicating that the SPBs are the last to fuse.

To determine which membranes linked up first, the team turned to light microscopy. They filled the nucleus with one marker and the lumen between the inner and outer membranes with another. The lumen marker started moving from one partner to the other about 30 seconds before the nuclear marker, indicating that the outer membranes merge first. Researchers suspect that outer membranes are drawn together by SNARE proteins. The mystery now is which proteins join the inner membranes. JCB

Reference: Melloy, P., et al. 2007. *J. Cell Biol.* 179:659–670.

Cancer cells straighten out

When a cancer cell hangs a left, it needs the protein cofilin. As Sidani et al. report, cofilin helps wandering cancer cells change course by enabling them to turn.

Cofilin is important for cells on the go. As a cell crawls, actin fibers at its front edge polymerize, pushing the membrane forward. Cofilin promotes the elongation of these fibers by breaking them: the fresh ends double the number of attachment points for other actin segments and lure the Arp2/3 complex, which hops on and extends the fibers. Although researchers have worked out some of cofilin's functions, they didn't have a comprehensive picture of how the protein influences cell movement.

Sidani et al. knocked out the protein in a line of aggressive mouse mammary tumor cells. Instead of moving in random directions, the cells crawled straight ahead, rarely turning. The knockout cells sent out fewer lamellipodia, the extensions they use to probe their environment, and the lamellipodia they did produce were stickier, thus inhibiting course changes.

By breaking actin fibers, cofilin draws the Arp2/3 complex to different locations at the cell edge. New lamellipodia sprout at these spots, and the cell shifts direction. Without cofilin, Arp2/3 piles up at the front of the cell, which only goes forward. The researchers have already shown that quashing cofilin activity leashed wandering tumor cells, suggesting that cofilin-blocking drugs will do the same. JCB

Reference: Sidani, M., et al. 2007. *J. Cell Biol.* 179:777–791.

When cargos jump tracks

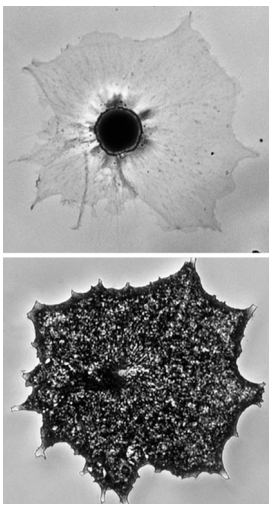
As organelles cruise around the cell, they can travel on microtubules or actin fibers. Slepchenko et al. report the first measurements of how often cargos jump from one type of fiber to the other.

In the cell's transportation system, microtubules are highways for long-distance journeys, whereas actin fibers are local roads for short trips. Cargos can switch fibers, but researchers haven't been able to observe these transfers because so many filaments crisscross the cytoplasm.

To determine how often switching occurs, Slepchenko et al. combined measurements of organelle movement in fish melanophores, or pigment cells, with mathematical models. The researchers tracked pigment granules traveling toward either the cell center or the periphery on actin and microtubules, including in cells with only one filament type. The team used the data to devise models that describe movement on each kind of cellular road. They then merged the models and applied them to cells with both types of filaments to estimate how often cargos transfer.

On the outward trip, granules were likely to jump from microtubules to actin but rarely did the opposite. As granules moved away from the cell's edge, however, they usually diverted from actin onto microtubules. The researchers concluded that cells dictate which track a cargo takes by changing only the rate of switching from actin to microtubules. This value is 10^4 times higher for the inbound trip, meaning relatively more cargos make it to microtubules. Cells might draw cargos onto microtubules by boosting the activity of dynein motors, which haul organelles toward the cell center, or by modifying the filaments to make them more available to motors. JCB

Reference: Slepchenko, B.M., et al. 2007. *J. Cell Biol.* 179:635–641.



Moving pigment granules switch from actin to microtubules more often when they are congregating (top) than dispersing (bottom).