Calcium signals from outside

Calcium just got a promotion. Findings by Caroppo et al. (page 111) reveal that in addition to its many roles inside the cell, Ca\(^{2+}\) has a distinct extracellular purpose: it acts via a Ca\(^{2+}\)-receptor (CaR) to regulate the function of gastric epithelial cells.

It has been known for some time that extracellular Ca\(^{2+}\) can be sensed by the CaR. The team noted that a Ca\(^{2+}\) gradient was generated outside gastric cells after cholinergic stimulation with carbachol, which mimics a signal received during digestion processes. Ca\(^{2+}\) levels increased on the apical side and decreased on the basolateral side, and prompted secretion of pepsinogen. Proteolytic cleavage of pepsinogen yields the digestive enzyme pepsin. It is well known that carbachol boosts intracellular Ca\(^{2+}\) in gastric cells, and a resultant increase in extracellular Ca\(^{2+}\) is no surprise. But the authors found that extracellular Ca\(^{2+}\) was both necessary and sufficient for the induction of pepsinogen secretion.

Perhaps cells economize by using a single messenger, calcium, both inside and outside of the cell. In this way, the authors speculate, cells can use the raised Ca\(^{2+}\) levels that are present outside cells during intracellular Ca\(^{2+}\) signaling events to control necessary functions.

Orbit(ing) the furrow

Two distinct populations of spindle microtubules provide signals that initiate and complete cytokinesis, according to a proposition from Inoue et al. (page 49).

During interphase, microtubules radiate from centrosomes in all directions. But after chromosome segregation a structure called the central spindle forms. It provides the signals that place the actin-based cytokinetic furrow in the right place and then orchestrates its actions.

The authors take a close look at the central spindle in living fly spermatozoa and find that this structure, previously thought to be uniform, is composed of two populations of microtubules. These peripheral and interior microtubules were both graphically and biochemically distinct, with only the interior microtubules associated with the Orbit/Mast protein.

In mutants with reduced levels of Orbit protein, formation of the interior bundle of central spindle microtubules was defective. As in wild-type cells, peripheral microtubules still probed the actin-rich cortex leading to cleavage furrow initiation, but the furrows in mutants eventually snapped back. This failure in cleavage was accompanied by the mislocalization of several proteins thought to be involved in generating the cytokinesis signal.

Orbit helps to stabilize microtubule plus ends. This stabilization may not be favorable for the highly dynamic peripheral microtubules but may be essential for the maintenance of the more stable interior microtubules. As is clear from mutants with less Orbit, a full description of cytokinesis may have to account for the coordination not only of myelin movement

Myelin movement

Like the hard candy shell around an M&M, oligodendrocytes swathe axons with a sheath of myelin for protection. Now, Edgar et al. (page 121) show that the myelin casing may do more than just provide shelter and stability; it may also set up conditions necessary for fast axonal transport.

The team noticed multiple organelles amassed within optic nerve axons in mice with a null mutation of the Plp gene, which encodes two major proteins of the myelin sheath. These organelle traffic jams implied that there might be problems with transport in these cells. So Edgar et al. looked at movement of labeled tracers in fast anterograde and retrograde transport. There were minor defects in fast forward transport that took some time to accumulate, and severe defects in fast backward transport. A closer look at motor proteins revealed that levels of the retrograde motor dynein and associated dynactin were elevated, possibly due to the accumulation of proteins on stalled vesicles. Anterograde motors were unaffected.

The primary function of myelin is to insulate nerves and thus speed transduction of nerve impulses. But it has also been shown to affect mitochondrial placement and cytoskeleton function in the underlying neuron. Exactly how the oligodendrocyte is communicating with the neuron to achieve such tasks, and which of these events are necessary for fast axonal transport, remains uncertain.