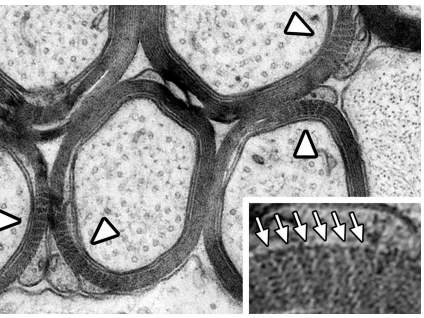
In This Issue



Claudin 11 tight junctions (arrowheads) in a radial cross section of an axon.

Claudin 11 stops the leaks

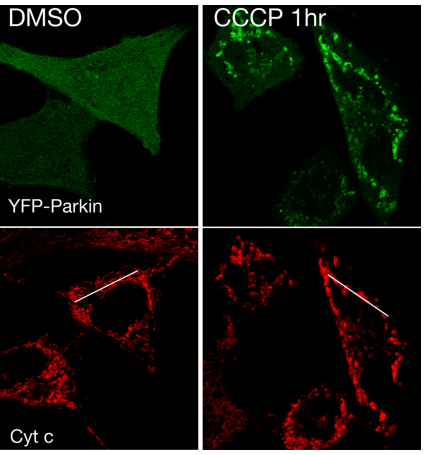
Devaux and Gow demonstrate how a tight junction protein called claudin 11 makes the neuronal myelin sheath a snug fit.

Like the rubber coating on a copper wire, the myelin sheath—a membrane extension of glial cells that spirals around the axons of neurons—creates an insulation layer that prevents current leakage from axons and aids electrical conduction along the length of the axon.

Claudin 11 forms tight junctions between successive spiral layers of the myelin sheath, but it was unknown whether it was required for myelin to act as a good insulator. To examine this question, Devaux and Gow compared electrical recordings from the optic nerve of wild-type and claudin 11 knockout mice. They found that although claudin 11 deficiency caused no gross defects in the appearance of the myelin sheath, it slowed electrical signals—at least in neurons with small-diameter axons.

Using a computer model that incorporates the resistive and capacitive properties of axons (and their myelin sheaths), the authors showed that claudin 11 adds to the electrical resistance of myelin by preventing leakage of charged ions (and electrical current) through the spiral space between myelin layers. The reduced resistance in the absence of claudin 11 affects small-diameter axons most severely because such axons have thinner myelin sheaths and thus less insulation to begin with. Because neurons with small-diameter axons are mostly found in the CNS, the authors speculate that defects in claudin 11 could be associated with deficits in cognition and perception, like those found in schizophrenia or neurodegenerative diseases.

Devaux, J., and A. Gow. 2008. *J. Cell Biol.* doi:10.1083/jcb.200808034.



Parkin (green) goes to mitochondria (Cyt c labeling, red) when these organelles are depolarized by the drug CCCP.

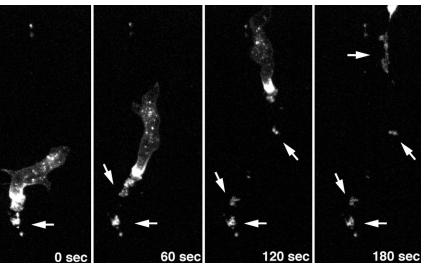
Parkin cleans house

A study by Narendra et al. suggests that Parkin, the product of the Parkinson's disease-related gene Park2, prompts neuronal survival by clearing the cell of its damaged mitochondria.

Loss-of-function mutations in the gene Park2, which encodes an E3 ubiquitin ligase (Parkin), are implicated in half the cases of recessive familial early-onset Parkinson's disease. Several lines of evidence suggest that Parkin loss is associated with mitochondrial dysfunction, but exactly how was unknown. To learn more about Parkin's role in cells, Narendra et al. examined the protein's subcellular location. They found that Parkin was present in the cytoplasm of most cells, but translocated to mitochondria in cells that had undergone mitochondrial damage such as membrane depolarization.

Damaged mitochondria can trigger cell death pathways; indeed, dysregulation of mitochondrial health was already thought to be a possible cause of the neuronal cell death associated with Parkinson's disease. The relocation of Parkin to damaged mitochondria, the team showed, sends these defunct organelles to autophagosomes for degradation. Parkin may thus prevent the damaged mitochondria from triggering cell death. Because neurons are not readily replicable, disposing of damaged mitochondria may be especially important in the adult brain.

Narendra, D., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200809125.



Dictyostelium leave ACA-containing vesicles (arrows) behind them as they crawl.

Dictyostelium cells lay a breadcrumb trail

When starved of their food source and then presented with a chemoattractant signal like cAMP, individual *Dictyostelium* cells acquire a polarized morphology and aggregate to form a migrating stream. This is the first step in a developmental program that culminates in the formation of a multicellular organism. Kriebel et al. show how this streaming response is coordinated at a single-cell level.

Besides acquiring a polarized morphology and beginning to chemotax, *Dictyostelium* cells respond to cAMP signals by making their own cAMP, thereby recruiting yet more cells to join the parade. The team previously discovered that ACA—the enzyme that makes cAMP—is highly enriched at the back of migrating cells. They thus proposed that the attractant is released mainly from the rear of cells, which prompts fellow cells to align and generate head-to-tail streaming structures. Kriebel et al. now show that ACA is packaged into intracellular vesicles that cluster at the rear of cells in a process that is dependent on actin and microtubule networks. They also show that de novo protein synthesis is required to maintain the asymmetrical distribution of the ACA vesicles.