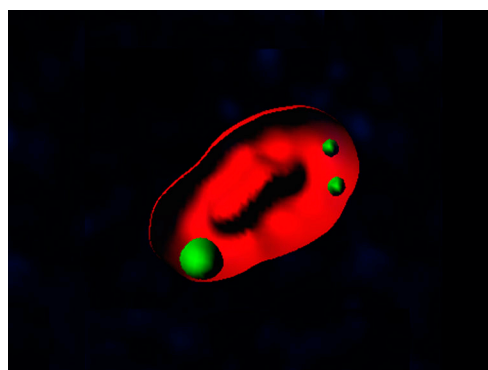




Cytoplasmic bodies (red) latch onto HIV particles (green).

Proteins gang up on HIV

It takes teamwork to defeat HIV, as Campbell et al. reveal. The researchers show that clusters of defensive proteins inside cells capture viral invaders and promote their destruction.

Defensive TRIM5 proteins have a narrow but important job: fending off retroviruses that normally attack other species. Human

versions trap certain mouse viruses, for example, and those from rhesus monkeys take on HIV. The proteins seem to halt a retrovirus before it can recopy its RNA genome into DNA. But how TRIM5 proteins prevent infection remains unclear. In cells, the proteins form clusters known as cytoplasmic bodies. Campbell et al. investigated whether these clusters are important for stopping infection.

The researchers followed HIV particles that invaded HeLa cells modified to produce rhesus monkey TRIM5 α . Cytoplasmic bodies and HIV particles cozied up, the team found. These asso-

ciations were only detectable for a short time after the virus entered the cell. However, HIV remained stuck in the cytoplasmic bodies if the researchers added a drug that shuts down the proteasome—the cellular garbage disposal that chops up worn-out or damaged proteins.

The team then observed interactions between labeled HIV particles and TRIM5 α clusters in living cells. The viruses sometimes hooked onto an existing cytoplasmic body and traveled along with it. Sometimes a virus broke away, but it had a coat of TRIM5 α . And sometimes a new cytoplasmic body formed around a virus particle.

The researchers conclude that shortly after viral entry, TRIM5 α ensnares HIV particles and then collaborates with the proteasome to destroy them. The mechanism of destruction is obscure, since an individual virus is too large to fit into the proteasome. But as several TRIM5 α proteins that have latched onto an HIV particle get drawn into the proteasome, their pulling might tear the virus to pieces, “like sharks eating a dead whale,” says senior author Thomas Hope. **JCB**

Reference: Campbell, E.M., et al. 2008. *J. Cell Biol.* 180:549–561.

Stuck on the membrane

Like pain relievers, vesicles in neurons come in slow-release and fast-release varieties. Hammarlund et al. reveal that the two varieties differ in how they attach to the cell membrane.

One reason that impulses can zip through the nervous system is that vesicles filled with neurotransmitters are attached to the membrane, ready to spill their contents into the synapse when a neuron is stimulated. But neurons also release peptides that can increase or reduce the sensitivity of nerve cells. These peptides reside in so-called dense core vesicles, which require multiple, rapid stimuli before they disgorge their contents. Dense core vesicles might be slower because they aren't hitched to the membrane and have to travel there after stimulation. But at least some of these vesicles are docked, researchers have found, so another possibility is that dense core vesicles and neurotransmitter vesicles are attached to the membrane in different ways.

Hammarlund et al. tested this hypothesis by comparing the two vesicle types in

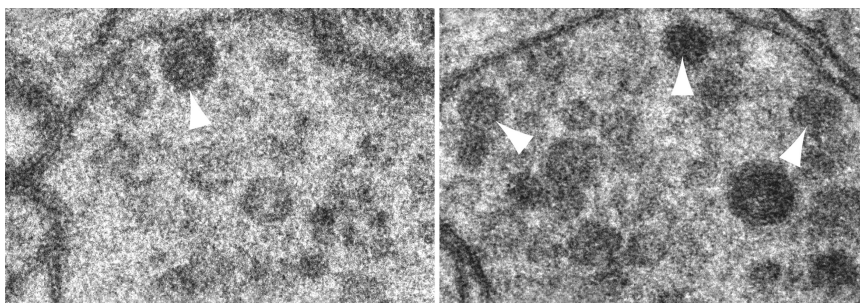
C. elegans neurons. The scientists determined that neurotransmitter-filled vesicles cluster at the synapse, whereas dense core vesicles disperse around the axon. Dense core vesicles remain aloof from the membrane if the protein CAPS is lacking, the team found. However, CAPS isn't necessary for neurotransmitter vesicles to dock. Instead, these vesicles need a related protein called UNC-13.

Previous work suggests that UNC-13 promotes docking by interacting with a membrane protein called syntaxin. Syntaxin can double over on itself, and UNC-13

probably pries open syntaxin to allow attachment. The results from Hammarlund et al. suggest that CAPS also opens up syntaxin. Their findings also suggest that CAPS and UNC-13 might help docked vesicles fuse with the membrane after stimulation.

Dense core vesicles and neurotransmitter vesicles thus appear rely on unique mechanisms to hook onto the membrane. Nailing down how these differences translate into changes in release speed will require further research. **JCB**

Reference: Hammarlund, M., et al. 2008. *J. Cell Biol.* 180:483–491.



Dense core vesicles dock at the membrane (left) or hang back (right).

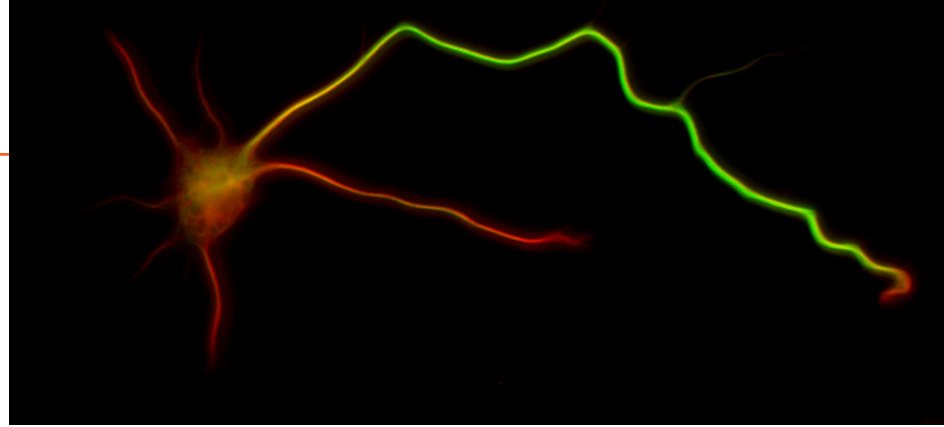
Helping an axon go long

A developing neuron has to decide where to grow its axon. Witte et al. show that the choice requires an overlooked ingredient: stable microtubules.

As a neuron matures, it sprouts several projections, or neurites. One neurite continues to lengthen and becomes an axon, while the others become dendrites. Although researchers have probed how actin promotes this process, they don't understand microtubules' role.

Witte et al. gauged microtubule dynamics in cultured hippocampal neurons. They found that microtubules in the axon were more stable than those in other neurites. If the researchers added the microtubule-stabilizing drug taxol to cells that were just extending neurites, multiple axons resulted.

The team then exposed cells at the neurite-



Stable microtubules (green) mark the axon of a neuron, while dynamic ones (red) occur in the axon tip and in neurites.

sprouting stage to a light-activated form of taxol. When they shone UV light on one of the neurites, it would usually become the axon. By dosing taxol-treated cells with a marker for growing microtubules, the scientists also found that taxol shifted the polymerizing microtubules from the neurite shaft to the tip.

The results suggest that microtubule stabilization helps dictate which neurite will specialize into an axon. The team hypothesizes that stabilizing the fibers within the axon directs microtubule extension toward the tip, thus pushing the end of the projection forward. **JCB**

Reference: Witte, H., et al. 2008. *J. Cell Biol.* 180:619–632.

When cilia lose the beat

Like a rower who stops midstroke, cilia lacking a particular protein slack off too soon, Lechtreck et al. report. The results could lead to new ways of identifying patients prone to fluid buildup in the brain.

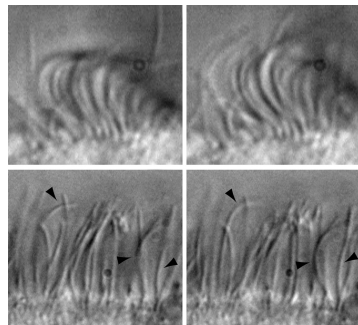
Beating cilia circulate cerebrospinal fluid through the brain. If they falter, fluid can accumulate, causing the brain-damaging condition hydrocephalus. Mice carrying mutations in the gene for the protein hydin develop hydrocephalus, but it wasn't known why. Last year, the researchers discovered a clue by finding that the absence of hydin caused flagella in the protist *Chlamydomonas* to freeze up. Now the team has observed a similar effect in the cilia of mice.

Cilia from mice with *Hydin* mutations beat abnormally. Instead of showing a smooth back-and-forth movement, the cilia merely vibrated. They also beat more slowly and often stopped. Though the precise function of the hydin protein is unclear, it is known to be part of the cilia's axoneme. Indeed, the *Hydin* mice also had a subtle structural defect in their cilia—a knob on one of the central microtubules was absent.

The authors believe that this defect might cause a lack of coordination among the dynein motors that move cilia. Normally, motors on one side of the shaft kick into gear to produce the forward stroke. Then they flip off and motors on the opposite side turn on,

producing the return stroke. But the researchers suspect that this switch doesn't occur in hydin-lacking cilia, causing the shaft to relax prematurely. The results predict that humans with defects in hydin will develop hydrocephalus and primary ciliary dyskinesia, an inherited disorder caused by defective airway cilia. **JCB**

Reference: Lechtreck, K.-F., et al. 2008. *J. Cell Biol.* 180:633–643.



Normal cilia beat smoothly (top), but hydin-lacking cilia (bottom) are stiff.

Supersized lipid droplets

When we get plump, so do the lipid storage droplets in our cells. By screening mutant yeast, Fei et al. identify the first gene that controls the size of these lipid droplets. A similar human gene is involved in a rare fat storage disorder.

Lipid droplets serve as containers for triacylglycerols and sterol esters. The structures might perform other functions as well, such as shuttling lipids between organelles and housing hydrophobic proteins. Wild-type budding yeast contain on average three to seven lipid droplets per cell, each somewhere between 0.5–1.5 μm in diameter. But how cells set the number and size of their lipid droplets is a mystery.

Fei et al. screened some 4,700 yeast mutants and identified 17 mutations that result in too few lipid droplets and more than 100 that result in too many. One gene, which the researchers dubbed *FLD1*, caught their attention because cells lacking it produced mammoth droplets 50 times the normal volume.

From in vitro and in vivo observations, the researchers discovered that the lipid droplets from the mutant yeast grow so large because they fuse promiscuously. It appears that *FLD1* is involved in the synthesis of the phospholipids that encircle the droplets, as the *FLD1* mutant yeast cells used shorter fatty acids to fashion these phospholipids. This effect might explain why the droplets can fuse more easily and thus can grow to monstrous proportions.

The human equivalent of *FLD1*, *BSCL2*, is defective in some forms of the rare Berardinelli-Seip congenital lipodystrophy, in which patients lack fat-storing adipocytes and often develop type II diabetes as teenagers. This connection might provide clues about how our bodies control fat production and storage. **JCB**

Reference: Fei, W., et al. 2008. *J. Cell Biol.* 180:473–482.