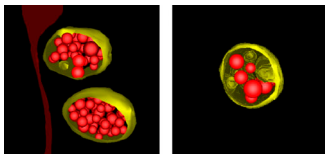
In This Issue

Text by Mitch Leslie
mitchleslie@comcast.net

ESCRT-III has an escort



More intralumenal vesicles (red) break away from the endosome membrane in control cells (left) than in cells that overexpress a domain of Bro1 (right).

The protein Bro1 lives up to its name, Wemmer et al. show. Like a big brother, Bro1 protects a protein complex that helps pinch off vesicles.

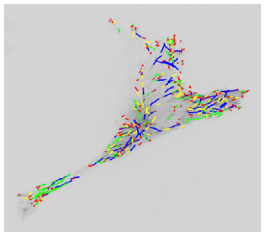
The ESCRT-III complex serves as a pair of molecular scissors that cuts cell membranes, helping to separate dividing cells and enabling viruses such as HIV to bud from the cell surface. The complex also helps endosomes fashion intralumenal vesicles (ILVs), which hold worn-out membrane proteins scheduled for destruction in lysosomes. ESCRT-III snips the nascent vesicles from the endosome membrane. How ESCRT-III promotes membrane scission and how cells manage its activity remain unclear.

Previous work has shown that the ATPase Vps4 breaks up the ESCRT-III complex. Wemmer et al. found that Bro1, which latches onto the Snf7 subunit of ESCRT-III, stands up to Vps4. In yeast cells and in vitro, Bro1's attachment to Snf7 boosted the complex's stability. And ESCRT-III complexes containing a mutant version of Snf7 that rebuffs Bro1 were prone to falling apart. ILVs often remained attached to the endosome membrane in cells expressing extra amounts of Bro1, which might indicate that Vps4's disassembly of the ESCRT-III complex helps snip off the vesicles.

Cells are continually assembling and disassembling ESCRT-III, and Bro1 might allow the subunits to remain together long enough to perform their task. How Bro1 shields ESCRT-III isn't known, but the team suggests that the protein prevents Vps4 from reaching a vulnerable site on the complex. Still uncertain is what keeps Bro1 under control.

Wemmer, M., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201007018.

Stiff ECM puts the brakes on microtubule growth



Enclosed in a stiff material, this cell shows numerous slow-growing, long-lasting microtubules (green).

For cells that build new blood vessels, a big life choice is whether to branch. Myers et al. reveal how the extracellular matrix (ECM) influences this decision by altering the cell's microtubule dynamics.

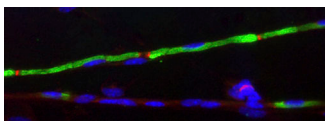
A blood vessel starts to grow when a chain of endothelial cells sets off for a new location. The lead cell guides the others and changes direction by sending out a branch. The researchers previously discovered that whether endothelial cells send out offshoots depends on the stiffness of the ECM—spongy ECM promotes branching. ECM characteristics might affect branching by altering microtubule (MT) dynamics, as MTs are known to influence this process in neurons.

In this study, Myers et al. designed software to track the growth rate and longevity of MTs. Endothelial cells migrating on a stiff surface tended to have slow-growing, long-lasting MTs. By contrast, when the cells sat atop a flexible ECM, MTs grew faster and broke down more often. The researchers found that branching correlated with MT growth rate. Although MT persistence did not correlate with the formation of new branches, it might help existing ones elongate.

Another factor besides stiffness was important. The team's previous study revealed that cells are less likely to branch when they are on a two-dimensional surface than when their surroundings are three-dimensional. Myers et al. found that MTs grew faster in cells in 3D cultures. However, the flexibility of the material no longer affected how long MTs remained intact, suggesting that ECM stiffness modifies only MT growth rate in 3D cultures. The next question to answer, the researchers say, is how the cell translates differences in ECM characteristics into changes in MT dynamics.

Myers, K.A., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201006009.

N-WASP allows axons to cover up



Two axons from a mouse lacking N-WASP, one (top) with very short myelin segments (green), and one (bottom) that shows almost no myelin.

A protein that helps build the actin cytoskeleton enables Schwann cells to fashion the myelin insulation that speeds nerve conduction, Novak et al. reveal.

In the peripheral nervous system, a Schwann cell wraps its membrane around individual axons again and again, eventually producing a myelin coating. Researchers think that myelination requires renovation of the actin cytoskeleton, but they haven't worked out the mechanism. One possible link between actin and myelination is the neural Wiskott-Aldrich syndrome protein (N-WASP). N-WASP spurs actin polymerization by turning on the Arp2/3 complex.

To test whether N-WASP promotes myelination, Novak et al. engineered mice whose Schwann cells lacked the protein. The animals showed signs of peripheral nerve damage, including poor coordination and balance. Novak et al. also found that nerve impulses traveled much slower than normal in the rodents.

When the researchers scrutinized the sciatic nerves from the mice, they observed that most axons had no myelin at all, whereas a few axons showed thin, short myelin segments. Thus, Schwann cells in the engineered animals could enclose the axons, but they couldn't produce myelin sheaths. That finding indicates that N-WASP allows a Schwann cell to coil its membrane around an axon. The researchers now want to decipher the signals that control N-WASP activity during this process.

Novak, N., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201010013.

Downloaded from http://rupress.org/jcb/article-pdf/192/2/204/1565513/jcb_1922iti.pdf by guest on 17 April 2024