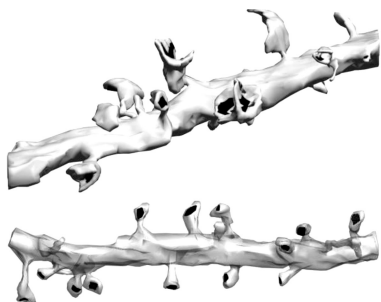


In This Issue



More PSD-95 means bigger spines (top), and multiple axon connections.

Multiple axons and actions with PSD-95

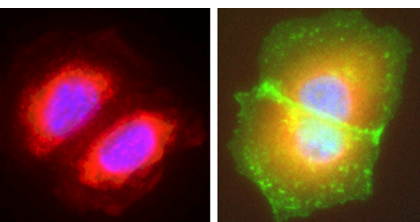
Nitric oxide gets neurons together. And it seems to do it backward. Work by [Nikonenko et al.](#) suggests that a protein called PSD-95 prompts nitric oxide release from postsynaptic dendritic spines, prompting nearby presynaptic axons to lock on, and develop new synapses.

It is becoming increasingly clear that synaptogenesis is not solely axon driven. PSD-95 is a major component of postsynaptic densities—a conglomeration of scaffolding proteins, neurotransmitter receptors, and signaling proteins that are thought to shape dendritic spines—and reduced levels of PSD-95 impair synapse development. How PSD-95 works, however, was unknown.

Nikonenko et al. overexpressed PSD-95 in cultured hippocampal neurons and found that the cells' dendritic spines grew two to three times their normal size and were often contacted by multiple axons—a rare occurrence in the adult brain. By mutating different parts of PSD-95, the team discovered that the region responsible for prompting multi-axon connections was also required for binding nitrogen oxide synthase. The team cut to the chase, bathed neurons in nitric oxide, and showed this was sufficient to promote the extra axon connections. Since bathing cells in nitric oxide and overexpressing proteins do not reflect normal physiological conditions, the team also inhibited nitric oxide synthase in wild-type neurons and confirmed that synapse density was reduced.

Overexpressing PSD-95 increased the amount of nitric oxide synthase at postsynaptic densities, suggesting PSD-95 recruits the synthase to its required locale. Interestingly, PSD-95 that lacked its synthase interaction domain still induced super-sized dendritic spines, suggesting PSD-95 wears more than one hat at the synapse construction site. **RW**

Nikonenko, I., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200805132.



Without α -E-catenin (green), dynactin (red) and its associated organelles remain on the microtubule highways (left).

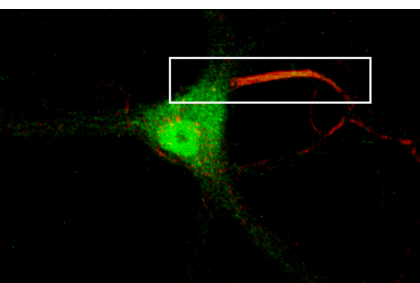
Junction protein goes on the road

If microtubules are the highways of the cell, then actin filaments are the local roads. [Lien et al.](#) suggest that α -E-catenin might sit at the junction between the two and help organelles transit from one to the other—a curious discovery for a protein commonly known to operate at an entirely different type of junction.

α -E-catenin is a major component of adherens junctions, binding via β -catenin to transmembrane protein E-cadherin to hold neighboring cells together. However, α -E-catenin is also suspected to control cell proliferation. Lien et al. set out to discover how the protein performs this alternate function, by searching for new α -E-catenin interaction partners. Much to the authors' surprise they identified dynamin—a crucial piece of microtubule motor machinery, and not an immediately obvious candidate in proliferation control.

The microtubule motors traffic organelles around the cell, and in cells that lacked α -E-catenin this trafficking was faster. This might be caused by a reduced connection between microtubules and actin; α -E-catenin is a known actin binder, and similarly increased organelle speeds are seen in cells with disrupted actin filaments. Indeed, when the team replaced endogenous α -E-catenin with a version of the protein that could not bind actin (but that still bound dynamin), organelle speeds matched that of cells that lacked α -E-catenin entirely. Thus, α -E-catenin might slow organelles' passage along microtubules by continually tempting them to take the scenic actin route. **RW**

Lien, W.-H., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200805041.



CK2 (green) localizes with ankyrin G (red) at the axon initial segment.

CK2: channel controller

In neurons, the kinase CK2 ensures that sodium channels are positioned for maximum potential, report [Bréchet et al.](#)

Action potentials shoot down axons thanks to a wave of membrane depolarization that triggers specialized membrane regions at the start of the axon—the axon initial segment (AIS)—and at regular intervals along the axon corresponding to gaps in the myelin sheath—the nodes of Ranvier. These specialized regions are characterized by a local clustering of sodium channels.

The clustering requires binding of the sodium channels to a cytoskeletal protein called ankyrin G, also spatially restricted to the AIS and nodes of Ranvier. However, ankyrin G has a homologous protein called ankyrin B that localizes to different parts of the neuron. Given that sodium channels