NgCAM takes a scenic route to the axon

To establish and maintain their asymmetrical structure, neurons must sort different proteins to their somatodendritic and axonal membranes. Previous work has supported three different models to explain selective transport to axons: direct transport to the axon; selective fusion of vesicles with the axon; and transport to the somatodendritic membrane followed by transcytosis. A detailed analysis by Wisco et al. (page 1317) now identifies evidence that the adhesion molecule NgCAM can take two of these three paths.

Some recent evidence suggests that vesicles containing NgCAM are blocked from fusing with the somatodendritic membrane in the first place. But in a kinetic analysis, Wisco et al. show that in fact NgCAM does transiently appear on the somatodendritic membrane, but is then endocytosed and sent to the axonal membrane by a transcytotic pathway.

The NgCAM protein encodes all of the signals necessary to direct it to the transcytotic pathway. A mutant NgCAM protein lacking the transcytosis signal is instead sent directly to the axonal membrane from the trans-Golgi network, suggesting that two distinct pathways are available to NgCAM, but transcytosis normally supersedes direct targeting. The authors now hope to determine whether this circuitous route is unique to NgCAM or common to many axonal proteins.

A long version of Short stop

The Drosophila Short stop (Shot/Kakapo) gene encodes several protein isoforms, some of which may link integrins to microtubules. In analyzing the Shot locus, Röper and Brown (page 1305) found something odd: a previously unnoticed exon encoding a series of plakin repeats. The only known function of plakin repeats though is to interact with cytoplasmic intermediate filaments, which flies lack.

Based on a biochemical analysis, the plakin repeats are incorporated into a gigantic isoform of Shot that is the third-largest protein discovered in flies. This isoform includes an actin-binding domain, the plakin repeats, a microtubule-binding domain, and spectrin repeats, and is found in adherens junctions, a localization that seems to be determined by a portion of the plakin domain. Reducing the quantity of the largest Shot isoform in early embryos weakens epithelial intercellular contacts, so it is essential for maintaining epithelial integrity.

The authors propose that the giant Shot isoform helps link the adherens junction to an associated belt of actin filaments and microtubules. This novel intermediate filament-independent activity of plakin repeats may be a conserved function of the domain, or it could be a distinct adaptation in insects, where a lack of intermediate filaments left the plakin domain free to evolve a new function.

Pop goes the acrosome

Although most cell biologists think of molecular motors as chemically driven machines, some of the fastest and most dramatic movements in nature may actually be powered by stored mechanical energy. On page 1183, Shin et al. present a detailed characterization of the forces driving acrosome extension in the sperm of the horseshoe crab Limulus polyphemus, and show that this process relies on mechanical energy stored in a molecular spring. Springs also underlie other phenomena such as bacteriophage infection.

To penetrate the jelly coat of an egg, Limulus sperm extends a bundle of actin filaments from a coiled position in the sperm head into a sturdy 60-mM-long rod called the acrosomal process. The reaction takes only five seconds. The authors calculated the amount of mechanical energy theoretically required to drive the movement from the energy stored in the structure and expended during extension. Neither ATP hydrolysis nor calcium binding provides enough energy during the reaction, but the potential mechanical energy in the coiled actin bundle is more than sufficient to drive acrosome extension. The data suggest that calcium binding triggers, but does not power, a progressive mechanical uncoiling reaction, extending the acrosomal process like a Jack-in-the-box toy.