Bringing PIPs to root tips

Tiny hairs on Arabidopsis thaliana roots elongate via tip growth, in which new membrane is added specifically at the root hair tip. Vincent et al. (page 801) now show that a phosphatidylinositol transfer protein (PITP) related to yeast Sec14p is critical for this polarized growth, suggesting that PIP$_2$ may be the start of the polarity cascade in this system.

The authors show that Arabidopsis has a large family of these PITPs. One such PITP is AtSfh1p, which, along with its downstream product PIP$_2$, localized to the tip plasma membrane and on post-Golgi vesicles that accumulate at the hair tips.

AtSfh1p mutation disrupted several aspects of polarity normally found in wild-type hairs and culminated in the loss of tip-directed membrane secretion. These lost polarity cues include the tip localization of PIP$_2$, a tip-directed F-actin network, strong tip-localized calcium influx, and the microtubule polymerization that normally follows in the wake of high calcium.

In the authors’ model, AtSfh1p on post-Golgi vesicles produces PIP$_2$, which links the vesicles (possibly via interactions with motor proteins) to a tip-directed actin network that can be generated on demand. Once they reach the tip, the vesicles deposit PIP$_2$ in the plasma membrane and thereby reinforce tip-directed actin polymerization. Vesicles may also carry and deposit calcium channels, thus establishing the calcium signals at the tip. One insult to this system, such as the loss of AtSfh1p, would result in a domino effect that kills root hair polarity.

AtSfh1p and many other Arabidopsis PITPs also contain coiled-coil nod domains, which may target the PITPs to distinct subcellular locations. Nitrogen-fixing bacteria express nod domains during nodulation; they might use this trick to subvert AtSfh1p localization and thus polarized membrane secretion while they invade the plant cells.

Nerve damage surveillance

The regeneration of damaged nerves relies on a JNK-dependent MAPK pathway and the stress-responsive transcription factor it activates, c-Jun. In relatively small epithelial cells, JNK can simply diffuse to the nucleus to turn on c-Jun. But human neurons can be up to a meter long—too long for diffusion to suffice. On page 775, Cavalli et al. suggest that damage communication might be achieved quickly by hooking JNK to axonal vesicles.

JNK interacts with a scaffold protein called Sunday Driver (syd). Syd, in turn, has been proposed to link vesicles to the microtubule motor protein kinesin. With this knowledge in hand, the group now shows that JNK is a surveillance molecule ready to detect and report axonal injuries to the cell body.

JNK and syd were found in murine axons on vesicles that were traveling both out to axon tips (on kinesin motors) and back to the cell body (on dynein). Injuries activated JNK out in axons and enhanced its interaction with the dynein-associated complex dynactin. Axonal injuries are thus expected to bring active JNK to the cell body, where it can turn on c-Jun to start the repair process.

Other molecules in complex with JNK may keep the kinase in its activated form for the long trip, either by protecting JNK’s initial phosphorylation or by repeatedly phosphorylating it. As yet, though, it is unclear what other proteins reside in the vesicles. JNK and syd may be simply hitchhiking on vesicles that are transporting synaptic proteins. Alternatively, the vesicles may be dedicated damage repair packages. A cell culture model will be most helpful for the biochemistry that needs to be done next.

Neurons may be an extreme version of a problem that also exists in smaller cells. Although microtubules are not absolutely required for injury responses in epithelial cells, a motor-based transport mechanism may be used normally to improve repair efficiency.