Channels rush in

Channels lurking in vesicles just beneath the cell surface can leap into action by inserting into the plasma membrane, say Vassilios Bezzerides, David Clapham (Harvard Medical School, Boston, MA), and colleagues. The resulting increase in Ca$^{2+}$ current slows down and perhaps changes the outgrowth direction of advancing neurites.

The Boston group saw TRPC5 Ca$^{2+}$ channels transferring into the plasma membrane, as measured by total internal reflection microscopy, electrophysiology, and surface biotinylation, in response to several growth factors. “Instead of controlling just gating, you are controlling availability,” says Clapham.

Recruitment and activation of TRPC5 Ca$^{2+}$ currents were dependent on activated Rac and production of PIP$_3$. In combination with previous work, this suggests the following scenario: activated growth factor receptors turn on P13K-mediated production of PIP$_3$, which recruits an exchange factor for Rac; and active Rac binds a kinase that produces PIP$_3$. The binding target for PIP$_3$ may be synaptotagmin, which colocalizes with TRPC5 in vesicles.

The recruitment is transient, thus helping the cell to avoid flooding its narrow neurites with too much calcium. The calcium admitted by TRPC5 may be synaptotagmin, which colocalizes with TRPC5 in vesicles.

The split rings of fission yeast septin and even the septin patches seen in mammalian cells may perform a similar function.

Dobbelnaere suspects that the division proteins may be endocytosed and then delivered via vesicles to the site between the septin rings. The alternative is that membrane-associated proteins slip through the septin rings when the rings are flexible and then are trapped when the rings regain their solidity.

Reference: Dobbelnaere, J., and Y. Barral. 2004. Science. 305:393–396.

License to glue

Replication of DNA and cohesion of the resultant sister chromatids are two activities that must be coordinated. Now, Peter Gillespie and Tatsuya Hirano (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY) have found that the same “licensing” process that gets DNA ready for replication is also necessary to allow loading of the cohesion complex responsible for sister chromatid cohesion.

Gillespie and Hirano used the sequence of yeast cohesion-loading proteins to identify human and frog versions. They confirmed biochemically in frog extracts what had been inferred genetically in yeast: that Scc2 (in frogs via two isoforms) is required for the loading of cohesin onto DNA.

Association of Scc2 with chromatin was inhibited by two treatments that block DNA replication licensing: addition of geminin, a small protein that binds to the prereplication complex protein Cdt1, and depletion of an origin recognition complex subunit. The cyclin-dependent kinase inhibitor p21$\text{CIP1}$, which inhibits DNA replication initiation, had no such inhibitory effect.

Cohesin may get onto specialized sites such as the centromere and damaged DNA via other mechanisms, but at least in frogs the licensing machinery would make a sensible chaperone to ensure that the glue arrived before duplication. Gillespie and Hirano also suggested that mitotic Cdc2 activity displaced Scc2. Soon afterwards, most of the cohesin is displaced by Polo and Aurora B, two kinases downstream of Cdc2, thus allowing the sister chromatids to be prepared for the onset of anaphase and another cell cycle.

Reference: Gillespie, P.J., and T. Hirano. 2004. Curr. Biol. doi:10.1016/S0960982204005603.