Research Roundup

Sticky polarity

Cell polarity researchers believe that communication between the neighboring cells is essential. “The process is not merely one of cells taking positional values but actively comparing positional values,” says Simon. “In that way, cadherins make sense,” because cell contact is probably needed for the comparison to take place. Furthermore, Simon thinks that differences in cadherin levels between the two cells could provide the information the cells need to sense direction.

Yang and Simon began their investigation with a chance observation of eye polarity defects in a mutant defective for Fat, a cadherin superfamily member. Another cadherin superfamily member, Dachsous, also affects polarity, and is found in a gradient that tapers off close to the eye equator. An opposing gradient is formed by another transmembrane protein called Four-jointed.

The researchers induced patches of mutant cells, and looked for cases where one member of the presumptive R3/R4 pair was mutant and one not. This told them that the gradient molecules were working to induce differences first in Fat function and then in Frizzled signaling. Frizzled is a Wnt receptor, but a ligand that might determine PCP has not been found. Simon now believes that differences in Fat function in neighboring cells might be the crucial switch.

Simon hopes to translate his new genetic clues into a biochemical understanding. He is attempting to reproduce the signaling pathway in cultured cells, and to determine which of the new PCP candidates interact with each other in vitro.

Reference: Yang, C.-H., et al. 2002. Cell. 108:675–688.

A BAFfling actin function

New results from Oliver Rando, Jerry Crabtree, and colleagues (Stanford University, Stanford, CA) suggest an unusual function for nuclear actin. Rather than restricting itself to the cytoskeleton, actin may help anchor a chromatin-remodeling complex in the nucleus.

Crabtree’s study of antigen-stimulated lymphocyte activation has previously shown that phosphatidylinositol 4,5-bisphosphate (PIP$_2$) signaling helps retain a greater proportion of a mammalian chromatin remodeling complex called BAF in the nucleus. Rando and Crabtree have now determined that BAF binds PIP$_2$ directly, but only if the complex retains two particular subunits: actin and the actin-related protein BAF53.

PIP$_2$ does not trigger exchange of BAF’s actin subunit, but PIP$_2$ plus BAF does increase the extent of in vitro actin polymerization. In vitro, BAF binds PIP$_2$ vesicles and the ends and junctions of actin filaments.

Crabtree found that actin contacted two separate domains of the Brg1 subunit of BAF, but only one of these contacts was regulated by PIP$_2$. He suggests that PIP$_2$ may free up a domain of actin so that it can interact with other actin subunits, thus anchoring the complex in the nucleus.

The interaction is unlikely to involve long actin polymers. These have not been seen in the nucleus, despite extensive searches. Instead, Crabtree suggests that BAF might interact with a short actin polymer, immediately capped off, that then binds to a membranous structure. “It’s a speculative model,” he says, “but it’s consistent with all the data we have at the moment.”

Crabtree is not the only one interested in inositol derivatives. Carl Wu (NIH, Bethesda, MD) and Erin O’Shea (University of California, San Francisco, CA) have recently found in vitro and in vivo evidence for regulation of chromatin remodeling by certain water-soluble inositol polyphosphates. The connection with Crabtree’s work remains unclear, however, as the inositol polyphosphates directly regulate remodeling activity, rather than affecting nuclear tethering or a nuclear matrix.

Reference: Rando, O.J., et al. 2002. Proc. Natl. Acad. Sci. USA. 99: 2824–2829.