Keeping wing cells in line

Cell polarity in fly wing cells is set with extraordinary precision. Out of the distal end of each cell grows an actin-rich protrusion known as a wing hair. Although the wing contains over 30,000 epidermal cells, it produces this distal-specific hair pattern without error. Dali Ma, Jeffrey Axelrod (Stanford University, Stanford, CA), and colleagues report that this precision is achieved through cooperation between two pathways. They find that wide-ranging gradients and locally acting signaling molecules work together to ensure high fidelity throughout the wing.

The local signaling is based on an intercellular feedback loop that has been shown to put Frizzled (Fz) on one side of the cell and keep it from the adjacent side of the neighboring cell. Fz localization is thus propagated from one wing cell to the next. Axelrod’s group now shows that the initial polarity of this local pathway is set by global regulators that have thus far been characterized in the eye.

As in the eye, opposing gradients of the cadherin Dachsous (Ds) and a transmembrane protein Four-jointed (Fj) were found in the wing. In both cases, the Ds and Fj gradients activate another cadherin, called Fat (Ft), on the distal sides of the cells where there is more Fj and less Ds. They show that Ds/Ft polarity is necessary for Fz localization, and thus sets the local polarity system. Disruption of the global signal, by mutation of Ds and Ft, produced clones of cells with hairs pointing in a locally organized direction (due to the action of Fz), but the direction was uncoupled from the overall wing axis.

The authors propose that the global pathway, which sets overall direction, is a subtle signal that is prone to cell-to-cell variation. They suggest that deviations are removed through the local Fz pathway, which propagates among neighboring cells to correct errors. Vertebrate systems also exhibit similar precision in polarity—in hair cells in the human ear, for example. Mutations causing deafness syndromes have been mapped to cadherins, suggesting that similar high fidelity mechanisms may be at work.

Reference: Ma, D., et al. 2003. Nature. 421:543–547.

A minus-end motor sees the plus side

New results from Brina Sheeman, David Pellman (Harvard Medical School, Boston, MA), and colleagues indicate that dynein, a minus end–directed microtubule motor, hops a ride to the membrane on plus ends. The results are inconsistent with current models of dynein activation and localization.

As a minus end–directed motor, dynein walks along astral microtubules toward the spindle pole, and thus could reel in the spindle during anaphase. The favored model for this movement predicts that dynein first binds to the bud cortex, where it captures passing microtubules. From there it could pull the spindle toward the bud. However, at least in budding yeast, significant amounts of dynein have not been found at the cortex. Nonetheless, according to Pellman, “the model is so intuitively appealing that the supposition is that [dynein] must be there even though we cannot see it.” But his results now suggest that this is not the case.

The group looked at endogenous levels of dynein in budding yeast. Even a triple-GFP tagged version of dynein was not found at the cortex, but rather on microtubule plus ends. This localization depended on the yeast homologues of CLIP-170 and LIS1, proteins implicated in dynein function in mammalian systems. Dynein was also seen on the spindle poles, its expected end-point after its motility is activated. Disturbing dynein activity, by mutating either its ATPase domain or by inactivating the dynactin complex, caused the motor to accumulate at plus ends rather than moving to the spindle poles.

Based on the localization results, Pellman suggests that “the microtubule brings its own tethering and motor device out to the membrane.” He proposes that dynein is inactive on plus ends until it is activated by local recruitment to membrane domains, as has been shown for at least one class of kinesins. Local transfer to the membrane (and thus activation) could be done by Num1p, a pleckstrin homology–containing protein, as dynein again accumulated at plus ends in the absence of Num1p.

Reference: Sheeman, B., et al. 2003. Curr. Biol. 10.1016/S0096-0982(03)00137.