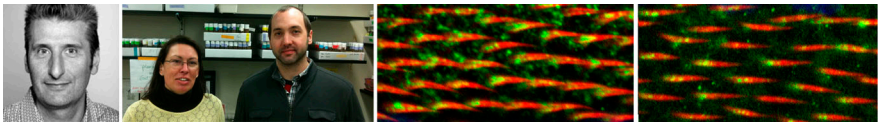
Text by Mitch Leslie
mitchleslie@comcast.net

Fly wing cells choose sides

Kinase guides membrane trafficking to specify where wing hairs emerge.

Focal Point



PHOTOS AND IMAGES COURTESY OF MAREK MLODZIK

(Left to right) Marek Mlodzik, Ursula Weber, William Gault, and Patricio Olguin (not pictured) investigated how a fly wing cell decides where to grow a hair. They found that the gene CK1-γ/*gilgamesh* pinpoints the hair's location by controlling delivery of Rab11-carrying recycling endosomes to the plasma membrane. Early in hair growth (second from right), Rab11 (green) concentrates at the base of individual hairs (red). Later in the process (right), Rab11 enters the hairs themselves.

Each cell in a fruit fly's wing has to be able to tell its outer and inner edges apart so that it can grow a hair in the right place. Gault et al. (1) show that a protein previously implicated in learning and cell migration helps restrict where the hair will sprout by controlling membrane trafficking.

A fly's wing sports a stubble of actin hairs, or trichomes, that help make the surface more aerodynamic. Each wing cell extends a single hair from its outer, or distal, edge, and researchers want to know why trichomes grow only in this position. The Frizzled/planar cell polarity (Fz/PCP) pathway appears to limit where trichomes can appear—meddling with the pathway results in hairy cells (2, 3). But how the pathway dictates hair location remains unclear, because its proteins are not restricted to the distal tip of wing cells (4). Gault et al. wondered if the Fz/PCP pathway has a helper.

To find out, the researchers searched for fly chromosome deletions that worsened defects caused by faulty Fz/PCP signaling. That analysis led the team to a gene called casein kinase 1γ (CK1-γ)—known as *gilgamesh* in *Drosophila*—which previous studies had connected to processes from sperm differentiation to the ability to remember smells. In flies with a defective version of CK1-γ, multiple hairs often grew from each wing cell, Gault et al. found.

> **"There are multiple mechanisms to restrict the location of this actin hair."**

The researchers noticed that the apical surfaces of mutant cells were enlarged, suggesting overactive transport to this section of the plasma membrane. Gault et al. therefore tested whether CK1-γ helps control trafficking to the cell surface. The team found that early in hair growth, the GTPase Rab11—which is necessary to route recycling endosomes to the plasma membrane—tends to cluster at the base of a nascent hair, eventually moving into the hair itself. But in cells with faulty CK1-γ, Rab11 was scattered. In contrast, early endosomes were in their normal positions in CK1-γ–deficient cells, indicating that the protein doesn't influence their movements.

Next, the researchers probed the roles of two Rab11 partners that help deliver recycling endosomes. The protein Nuclear-fallout links endosomes to the microtubules that they ride to the membrane. But flies with reduced levels of Nuclear-fallout grew deformed or stumpy hairs from their wing cells. Another Rab11 collaborator is Sec15, which anchors recycling endosomes to the plasma membrane. Flies lacking Sec15 also showed misshapen or short trichomes, and the researchers demonstrated that CK1-γ helps direct Sec15 to its location near the plasma membrane.

Gault et al. also dissected CK1-γ's interaction with the Fz/PCP pathway. Wing cells lacking *mwh*, a component of the pathway and a key regulator of hair formation, carry extra trichomes, but they were hairier still if CK1-γ was also missing. That suggests that CK1-γ and the Fz/PCP pathway work in parallel to shape wing cell polarity and limit where hairs grow. "There are multiple mechanisms to restrict the location of this actin hair," says senior author Marek Mlodzik. The researchers think that the Fz/PCP pathway circumscribes a zone where a hair can sprout, whereas CK1-γ determines the exact site.

The study expands CK1-γ's job description, suggesting that it defines the location of trichome growth by directing recycling endosomes to a specific section of the apical membrane. Thus, the kinase serves as a regulator of localized membrane traffic. Several details of the mechanism remain unclear, Mlodzik notes. The researchers found that CK1-γ gathers at the base of developing hairs, but they aren't sure how it affects the movement of recycling endosomes. It might help tether the endosomes to the plasma membrane, acting in combination with Sec15. But it could also help the endosomes connect to microtubules, working with Nuclear-fallout. What those recycling endosomes haul is also unclear. The researchers suspect that they carry cargo that spurs actin fibers to grow, such as the Arp2/3 nucleation complex.

1. Gault, W.J., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201107137.
2. Wong, L.L., and P.N. Adler. 1993. *J. Cell Biol.* 123:209–221.
3. Strutt, D., and S.J. Warrington. 2008. *Development.* 135:3103–3111.
4. Adler, P.N. 2002. *Dev. Cell.* 2:525–535.