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Helping the embryo find closure

Loss of protein from neighbors tells migrating cells they are in the vanguard.

Hikers and migrating embryonic cells need to know their location so they can eventually reach their destination. Laplante and Nilson (1) reveal that some epidermal cells in the *Drosophila* embryo find out where they are from their neighbors.

Although it looks almost ready to hatch, a late-stage *Drosophila* embryo still has a gaping hole in its back. The opening seals through the process of dorsal closure (2), in which the embryo resembles a duffel bag being zipped up. Two sheets of epidermal cells slide toward each other along an extraembryonic layer called the amnioserosa. As they approach one another, cells at the leading edges of the sheets stick together and close the gap. During dorsal closure, cells change shape, move, and revamp their cytoskeleton. For example, in cells at the leading edges of the epidermal sheets, known as the dorsal-most epidermal (DME) cells, actin and non-muscle myosin weave a contractile cable that researchers think provides some of the force that pushes the sheets forward (3).

Scientists have seized on dorsal closure as a model for embryonic epithelial rearrangements and for wound healing, but some aspects of the process remain mysterious. One open question is how DME cells know that they are at the front of an epithelial sheet. Researchers also don't understand what spurs the cells to polarize in the dorsal–ventral plane—a situation known as planar polarity—with the actomyosin cable at the cells' leading, dorsal edge. Laplante and Nilson's chief candidate for both functions was the membrane-spanning protein Echinoid (Ed). Ed molecules protruding from neighboring cells interlock, suggesting that the protein allows cells to interact. Laplante and Nilson had previously discovered (4) that Ed vanishes from amnioserosa cells during dorsal closure, possibly providing a spatial signal for DME cell identity and planar polarity.

"[Echinoid] provides spatial information that lets cells know they are at the leading edge."

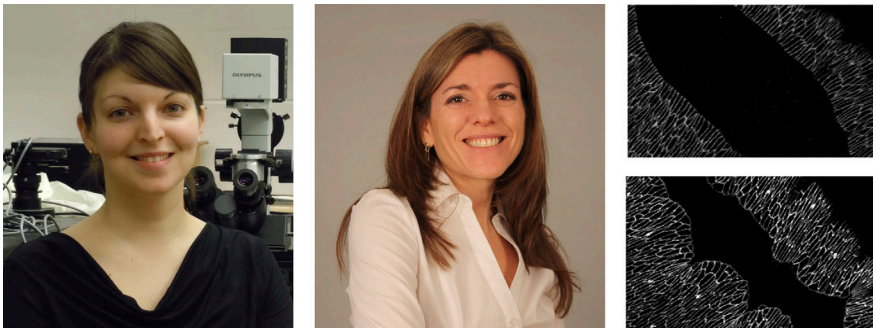
The researchers tested Ed's role using engineered embryos whose amnioserosa maintains production of the protein throughout dorsal closure. In these embryos, DME cells, which touch the amnioserosa, no longer formed an actomyosin cable at their leading edge. Next, the team ensured that Ed production continued only in bands around the embryo, meaning that some DME cells contacted amnioserosa that made Ed, whereas other DME cells contacted normal tissue. DME cells touching amnioserosa that had correctly shut off Ed built the cable and migrated normally. But DME cells that contacted Ed-making amnioserosa sprawled and migrated too far. Thus, instead of pushing the cells forward, the cable might hold them back to ensure that the leading edge stays in line.

Laplante and Nilson found that in normal embryos DME cells respond to the loss of Ed from the amnioserosa by removing Ed from their leading edge. The researchers think that Ed serves as a GPS for DME cells. "It provides spatial information that lets cells know they are at the leading edge—they are the ones whose neighbors lack Ed," says senior author Laura Nilson. The key cue comes when the amnioserosa eliminates Ed, breaking the molecular handshake with the epidermis.

The next step involves RhoGEF2, which turns on the GTPase Rho1 to spur construction of the actomyosin cable. After relocating Ed, normal DME cells stockpile RhoGEF2 at their leading edge. However, DME cells contacting Ed-making amnioserosa don't accumulate the molecule. Relocation of Ed also spurs cells to shift the polarity-inducing protein Bazooka away from the leading edge, and its absence might allow the cable to form.

Removal of Ed from the leading edge of DME cells helps establish the cytoskeleton's planar polarity by promoting formation of the actomyosin cable. The next step, the researchers say, is nailing down Ed's effects on the cytoskeleton to determine why the cable forms only on one side of the cell.

Focal Point



Caroline Laplante (left) and Laura Nilson (right) determined how loss of the protein Echinoid (Ed) helps cells at the leading edge of a migrating epidermal sheet find their position. The image at the top right shows dorsal closure in a normal embryo in which the amnioserosa stops making Ed. But in the embryo at the bottom right, the amnioserosa continues to make part of Ed during dorsal closure, and the cells at the leading edge fail to elongate in the correct direction.

PHOTOS COURTESY OF IRENE REYNOLDS TEBBS (LEFT) AND JOHN COMISKEY (CENTER)

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