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PAR proteins cross the boundary

Polarity proteins don't stay on their own side of the membrane.

Like Berlin during the Cold War, the membrane of a single-celled *C. elegans* embryo is divided. But unlike Berlin, no barrier separates the two sections, Goehring et al. conclude (1) after discovering that PAR proteins can travel freely between the anterior and posterior domains of the membrane. The researchers tested several explanations for what preserves the difference between these domains and found all of them wanting.

When it comes to cell division, the *C. elegans* embryo is no egalitarian. The first division spawns one large cell, which gives rise to some of the animal's neurons and muscle, and one small cell, whose descendants include the germline (2). Before this asymmetric division, the embryo's membrane becomes polarized along the anterior–posterior axis, and the cytoplasm follows suit (3). The PAR proteins help to polarize the membrane, splitting into two gangs, each of which claims its own turf. PAR-3, PAR-6, and PKC settle in the anterior membrane; PAR-1, LGL, and PAR-2 favor the opposite side. These molecules even defend their territories. If PAR-2 is defective, for instance, the opposing PAR proteins expand throughout the embryo (4). Despite the stability of these domains, researchers don't understand how they stay distinct.

Goehring et al. gauged the movement of one anterior and one posterior membrane protein in a series of photobleaching experiments. The researchers found that the proteins slowly transfer between the membrane and the cytoplasm. But the proteins also diffuse around the membrane. "Their dominant behavior on the membrane is this aimless wandering," says first author Nathan Goehring. The team estimated how far a typical protein could travel in a single ramble. PAR-2, a posterior protein, could move more than 6 µm, whereas the anterior protein PAR-6 could manage more than 10 µm, quite a journey considering that the egg is only about 50 µm long.

Focal Point

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(Left to right) Nathan Goehring, Stephan Grill, Carsten Hoege, and Anthony Hyman investigated what preserves anterior–posterior polarity in the single-celled *C. elegans* embryo. The team found that the polarity-defining PAR proteins can move freely between the anterior and posterior portions of the membrane. Their work also suggests that the actomyosin skeleton beneath the cell membrane doesn't help maintain polarity. As these before (far right, left panel) and after (right panel) images show, the embryo remains polarized after treatment with cytochalasin D, which disrupts the actomyosin cytoskeleton.

Surprisingly, the proteins even wander outside of their own territory. Goehring et al. discovered that anterior PAR proteins continually diffuse into the posterior membrane, and vice versa. That result rules out one possible explanation for preservation of the membrane's polarity—a barrier separating the two sections—but it also raises a question. "If the proteins are free to diffuse throughout the membrane, how are two distinct polarity domains maintained?" asks Goehring.

> "If the proteins are free to diffuse... how are two distinct polarity domains maintained?"

The researchers also discounted three other possible mechanisms. They found no evidence that a transport molecule, such as kinesin, gathers up errant PAR proteins and lugs them back to the proper side. Nor does a mutual repulsion between the two groups of PAR proteins, similar to the effect that causes oil and water to separate, appear to maintain distinct membrane domains. Some studies have suggested that the actomyosin cytoskeleton helps keep the two sections of the membrane separate. Although the actomyosin cytoskeleton is involved in setting up polarity, the team's findings indicate that it doesn't maintain protein segregation.

PAR proteins help establish polarity in most animals, so researchers are keen to know what keeps the proteins on their own turf. Goehring et al. don't yet have an answer, but the behavior of individual PAR proteins clearly is important, and competition between them may be a key factor. One possibility is that the proteins might be more attracted to their own side, and clusters of resident proteins might dislodge any wayward protein that entered the wrong side, allowing it to return to its own territory. Regardless of the mechanism involved, a crucial question to answer is how interactions between individual proteins define the polarity domains, specifying their sizes and the position of the boundary between them.

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