Tugging and pulling in asymmetric cell divisions

In asymmetric divisions, the cell alters the normal process that centers the spindle in the mother cell, but how it regulates the timing of spindle movement is unclear. Now, on page 245, Labbé et al. describe a tethering system that resists premature movement of the mitotic spindle during asymmetric cell divisions in C. elegans embryogenesis.

It was known that when researchers cut spindle microtubules with a laser, both centrosomes moved toward their respective cell poles, but the posterior one moved more quickly. To find out what establishes these uneven pulling forces and when the asymmetry first arises, Labbé and his colleagues used a laser to sever microtubules at different times throughout the first cell cycle. If they destroyed the anterior centrosome in prophase, the posterior centrosome moved posteriorly. But after destruction of the posterior centrosome the anterior one stayed centered, suggesting that there is a force pulling toward the tail of the embryo and something resisting it—but not actively pulling—on the anterior end.

When the team ablated microtubules near the anterior centrosome but on the cortical side, they found that the whole spindle moved toward the posterior pole. They hypothesize that the cut releases a tether that anchors the anterior centrosome to the anterior cortex and resists the posterior pulling forces. By metaphase, the tether releases and the spindle moves to the posterior of the embryo in preparation for the asymmetric division.

Because microtubules are known to be more stable at the anterior cortex compared with the posterior, the researchers speculate that such asymmetry might contribute to the tether. They are exploring this hypothesis by monitoring changes in microtubule dynamics at the cell cortex throughout the cell cycle.

Slipping through the middle

In the 1960s scientists saw evidence in electron micrographs that leukocytes migrate through the middle of endothelial cells in vivo. But when others couldn’t replicate the findings in vitro and instead saw the immune cells slip between the endothelial cells, the field largely abandoned the idea of transcellular movement. Finally, on page 377, Carman and Springer show in vitro evidence that leukocytes can pass through the middle of cells as they leave the blood vessels and move into the tissue.

The team found that once a leukocyte attaches to the surface of an endothelial cell, microvilli protrude from the vascular cell surface, partially surrounding the immune cell. Adhesion proteins in the microvilli appear to realign the integrin molecules in the leukocytes, providing them with directional information. Meanwhile, a pore in the membrane of the endothelial cell forms and the leukocyte squeezes through.

So why did Carman and Springer see transmigration where others have not? Unlike previous studies, which relied on junctional vascular markers, the Harvard team also used antibodies against ICAM-1, an adhesion protein that lines the whole intravascular surface of the endothelial cells. With high resolution imaging, they could distinguish endothelial surface from junctional events even if the surface events occurred near a junction. Lower resolution images just couldn’t distinguish exactly where the changes were happening. Other groups now hint that they see similar results.

Carman speculates that transcellular migration and passage between cells are probably used in different tissues and under different inflammatory conditions. But just what molecules regulate how an immune cell chooses its route remains unclear.

Meanwhile, on page 223, Weis et al. provide insight into how tumor cells move from the blood into surrounding tissue. Tumor cells in the blood secrete VEGF, an angiogenesis factor that compromises the integrity of the endothelial barrier. When the team injected tumor cells into mice deficient for either Src or Yes signaling kinases, few cancer cells passed through the endothelial barrier, relative to wild-type controls. VEGF appears to work through the kinases to disrupt VE-cadherin-β-catenin complexes, which maintain junctions between endothelial cells.