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Asters push embryonic nuclei to the brink

Researchers discover how nuclei in insect embryos travel to the cortex.

The nuclei in an early insect embryo need personal space. Telley et al. reveal that microtubule asters help these standoffish nuclei maintain their distance, maneuvering them into position in order for development to continue (1).

The early steps of insect development don't follow the familiar pattern of repeated cell divisions. Before the formation of distinct cell membranes, early insect embryos consist of a single, continuous mass of cytoplasm in which the nuclei divide again and again in synchrony (2). The reason for this organization could be efficiency, says first author Ivo Telley. By skipping the formation of cell membranes, the embryo might speed up division, producing thousands of nuclei in 60–90 min.

Like swimmers heading for the side of a pool, the nuclei move toward the cortex of the embryo. Any nuclei that don't make it to the cortex are destroyed. The ones that do arrive anchor themselves and divvy up the cytoplasm to form separate cells (3). Researchers aren't sure how the embryonic nuclei move apart; they travel too far to rely on diffusion. Studies indicate that the microtubule and actin cytoskeletons are involved, but the mechanism remains obscure. Researchers have suggested several explanations, including nuclei riding on streams of cytoplasm and microtubules in the central part of the spindle nudging nuclei toward the periphery (4, 5). However, testing these hypotheses is tricky because of the difficulty of tracking events deep in a yolk-packed embryo.

To improve visibility, Telley et al. created a cell-free system using droplets of cytoplasm from early *Drosophila* embryos. At ~80–100 µm in diameter, the droplets enabled the researchers to track nuclei movements with time-lapse fluorescence microscopy. Even with such small amounts of cytoplasm, nuclei continued to divide rapidly and in sync. The nuclei also spread out as they would in the embryo, even though the cortex was absent.

The researchers discovered that the nuclei arrange themselves so they are around 28 µm away from each other. To test whether this distance was a set limit, the team placed a dollop of cytoplasm containing a single nucleus into a small chamber measuring about 28 µm on each side. As nuclei accumulated in the chamber, their spindles bent and the microtubule asters around the centrosomes crumpled. That the nuclei couldn't adjust to the cramped conditions indicates that this separation distance is standard.

To determine what drives the nuclei to part company, Telley et al. added the drugs nocodazole and colcemid to destabilize microtubules. The low doses the researchers used collapsed the microtubules of the aster but had only a small effect on the ones in the central spindle. The nuclei separated more slowly and didn't move as far apart. Next, the researchers tested whether the central microtubules of the spindle had a role. Destroying these microtubules with a laser had no effect on separation distance. By contrast, zapping one centrosome, breaking down its associated aster, delayed separation. This suggests that asters provide much of the force to distance nuclei from one another.

But the asters need something to pull against. Telley et al. suspected that it was actin, which crowds around the spindle and the asters between metaphase and telophase. When the researchers stalled actin turnover with the compound latrunculin, nuclei didn't move as far away from each other.

"With this system, we've turned the embryo inside out," says Telley. The cell-free system suggests that asters, with a boost from the lengthening spindle during anaphase, space out nuclei in the embryo. The geometry of the egg means that as nuclei accumulate and attempt to separate from each other, more and more of them are forced toward the boundary of the embryo. And once a nucleus reaches the cortex, its space requirements shrink, enabling additional nuclei to pack in at the margin. Actin's contribution remains unclear, Telly notes. Actin might just serve as an anchor for the asters and molecular motors, but actin turnover could also provide a push.

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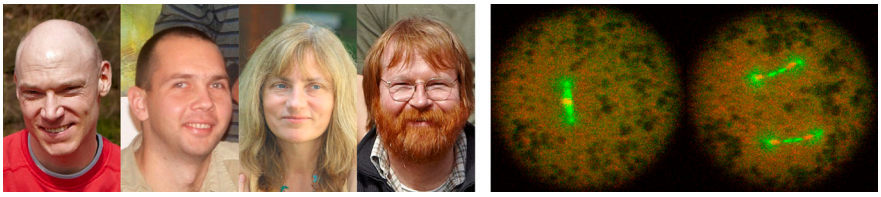
Focal Point



PHOTOS (LEFT TO RIGHT) COURTESY OF HUGO NEVES, YURI MOTORIN, SANJAY GHOSH, AND HUGO NEVES; CELL IMAGE COURTESY OF IVO TELLEY

(Left to right) Ivo Telley, Imre Gáspár, Anne Ephrussi, and Thomas Surrey used droplets of cytoplasm to determine how nuclei move to the cortex of an early insect embryo. The researchers found that microtubule asters ensure that the nuclei are separated from each other by a constant distance, driving most of the nuclei in the embryo toward the edge. The cell image shows the nuclei (red) and spindle (green) in an egg after one division (left) and after two divisions (right).

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