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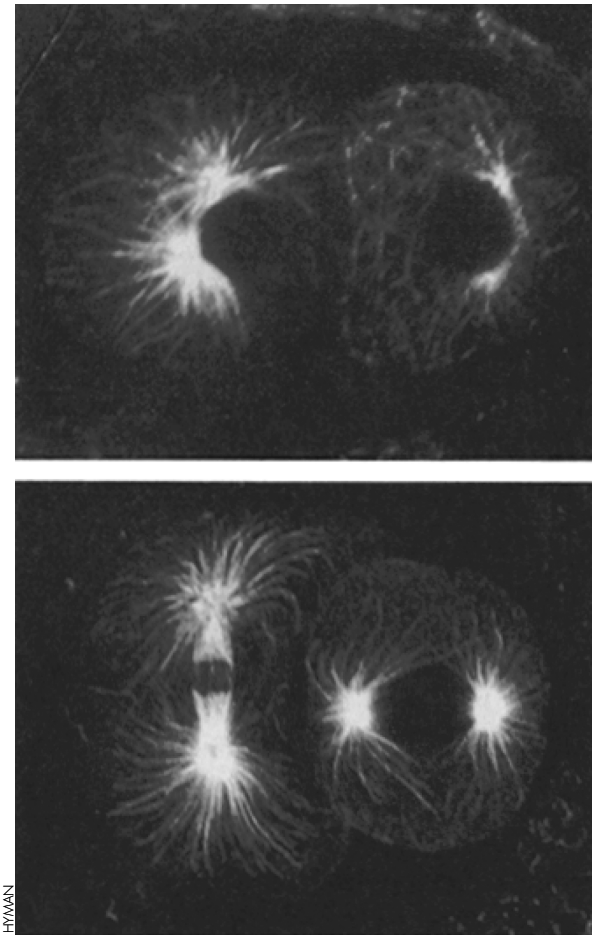
Centrosome choreography

Tony Hyman investigates how centrosome movements are choreographed, and how they determine the division axis.

Depending on the position of the mitotic spindle, a dividing cell can split evenly or unevenly, lengthwise or down the middle. As a graduate student at the MRC Laboratory of Molecular Biology in Cambridge, England, Anthony Hyman showed how the centrosomes' travels set up the division axis in *Caenorhabditis elegans* (Hyman and White, 1987).

Hyman was rummaging through the literature when he stumbled across the question of how the cell division axis gets set up. Everyone assumed that the centrosomes determined the positions of the spindle poles, but nobody knew how. His test system was the fertilized worm egg, and the AB and P_1 cells that result from its first cleavage. These cells behave differently from each other. Divisions in the AB lineage are symmetric, and each occurs at a 90-degree angle relative to its predecessor. Consistent with this change in direction, Hyman (now at the Max Planck Institute of Molecular Cell Biology in Dresden, Germany) found that in AB cells the newly duplicated centrosomes migrated to opposite sides of the nucleus before mitosis. This effectively spun the axis of the cell around.

In the P_1 lineage, by contrast, divisions are asymmetric but the cells always part along the same axis. The same migration of duplicated centrosomes occurred in P_1 cells, but then the nucleus rotated 90 degrees, dragging the centrosomes with it. Nobody had observed this rotation before, but Hyman wasn't surprised. "At that stage, you are too young and naive to be surprised," he says. Immunofluorescence revealed nets of microtubules stretching from the centrosomes to the cell cortex, suggesting that these fibers helped position the structures and turn the nucleus.



HYMAN

The spindle of the P_1 cell (right) rotates in a 2-cell worm embryo.

Hyman tackled this issue in a follow-up study, using a laser to slice the microtubules between either of the centrosomes and the cell's anterior cortex (Hyman, 1989). In normal cells, the centrosomes are equally likely to turn toward the cell's anterior. But in lasered cells, the unzapped centrosome always rotated in that direction. Hyman concluded that one spot on the anterior cortex was hooking the centrosome's microtubules and reeling in the centrosome, thereby turning the nucleus.

Other workers, however, postulate a different mechanism based on recent discoveries about the protein LET-99, which girdles the egg (Tsou et al., 2002, 2003). According to this hypothesis, microtubules from around the cortex are tugging on the nucleus, but LET-99 weakens the pulling force from some parts of the cell, and the resulting imbalance causes the nucleus to turn. What exerts the force on the nucleus and centrosomes remains uncertain. The proposed pulling site on the cortex holds an abundance of dynein (Waddle et al., 1994), which suggests that this molecular motor might provide the power.

Recent work suggests that centrosome movements are linked to another intracellular migration: the spindle's shift toward the posterior end of the cell during anaphase, which sets up an unequal division. Heterotrimeric G proteins help get the spindle moving toward the cell's rear end in *C. elegans*, *Drosophila* (Schafer et al., 2001), and vertebrates (Du and Macara, 2004), and one G protein component also controls centrosome rotation (Gotta and Ahringer, 2001). JCB

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