

Centrosomes remember which way is up

Microtubule-based memory helps orient dividing brain stem cells.

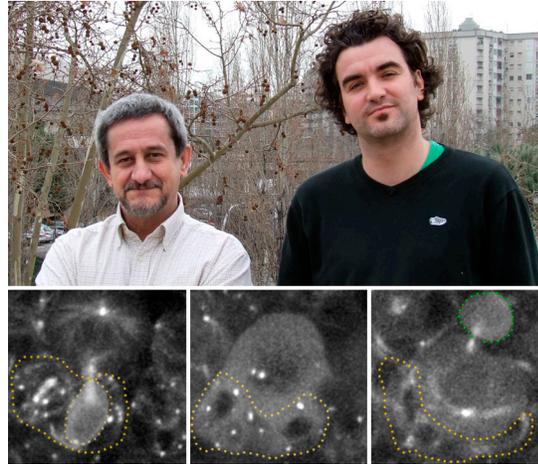
The centrosome is more than a hub for microtubules and an anchor for the mitotic spindle. The structure also helps stem cells recall their orientation so they can divide along the right axis, as Jens Januschke and Cayetano Gonzalez show (1).

Neuroblasts are stem cells in the brains of larval *Drosophila*. Each round of division yields another neuroblast and a much smaller ganglion mother cell (GMC) that differentiates into a neuron or a glial cell, a nervous system helper. Although a neuroblast can split more than 100 times, the orientation of the divisions remains constant. The fresh GMC almost always sprouts from the basal end of the neuroblast (2).

So how does a neuroblast remember where its top should be? Perhaps through molecular differences that accumulate at its opposite poles. During mitosis, for example, the Pins and Par protein complexes are stationed at the so-called apical crescent of the cell, whereas other proteins settle at the opposite end. But these asymmetries disappear after each division, ruling them out as permanent polarity pointers.

An alternative suggestion is that the centrosome orients the neuroblast. Researchers previously noted (3, 4) that just after mitosis, the centrosome sidles up to the previous—and future—apical crescent of the cell, attaching to the cortex with microtubules. These scientists proposed that the aster, the starburst of microtubules around the centrosome, retains and transmits neuroblast polarity.

Januschke and Gonzalez tested that proposal by dosing *Drosophila* neuroblasts with the drug colcemid, which spurs microtubules to collapse. “The cells can’t remember where to put the crescent,” says Januschke. The apical crescent arose anywhere within



FOCAL POINT

Cayetano Gonzalez (left) and Jens Januschke show that brain stem cells called neuroblasts rely on the centrosome to store their orientation for division. A neuroblast normally divides so that the daughter cells emerge basally (yellow outline in left panel). But after the researchers depolymerized the neuroblast’s microtubules with colcemid (middle panel), a daughter cell (green outline in right panel) could emerge from other locations around the neuroblast.

290 degrees of its previous location, the researchers found. By contrast, in untreated cells the apical crescent formed within a narrow 38-degree window.

The researchers saw similar apical wandering in cells that lack centrosomes due to a mutation in the *dsas-4* gene.

To determine how polarity shifts affect cell division, Januschke and Gonzalez added colcemid and then inactivated it with UV light at different times in the cell cycle. If the team waited until the cell had already begun mitosis to neutralize colcemid, the GMC split off almost anywhere around the circumference of the neuroblast. The cell’s axis had already drifted to a new alignment before the microtubules reassembled. But if the researchers removed colcemid during interphase, thus allowing the cell to lock in polarity before mitosis, the GMC emerged close to the previous axis.

From these results, the researchers conclude that the centrosome re-

members a neuroblast’s orientation, somehow relaying that information through microtubules. How microtubules indicate where to establish the next apical

crescent is unclear, says Januschke. By following repeated divisions of cells in which microtubules had been disrupted and then restored, the researchers discovered that this memory is short, lasting only for the duration of one mitotic division.

Microtubules probably don’t work alone. In the colcemid experiments, the position of the axis showed a slight bias toward the original orientation, hinting that factors other than microtubules also help set the alignment. The researchers haven’t pinned down the identity of these factors. “I’d love to know that,” says Januschke.

The findings also reveal that, at least in the case of fly neuroblasts, cells go it alone when establishing polarity. Neuroblasts first polarize during embryonic development, when they peel away from another cell layer. Division after division, neuroblasts maintain their axis orientation, independent of the polarity of their neighbors. “The orientation of the stem cells doesn’t depend on the external environment,” says Januschke. “It’s generated in a cell-autonomous manner.”

1. Januschke, J., and C. Gonzalez. 2010. *J. Cell Biol.* doi:10.1083/jcb.200905024.
2. Ito, K., and Y. Hotta. 1992. *Dev. Biol.* 149:134–148.
3. Rusan, N.M., and M. Peifer. 2007. *J. Cell Biol.* 177:13–20.
4. Rebollo, E., et al. 2007. *Dev. Cell.* 12:467–474.

“The orientation of the stem cells doesn’t depend on the external environment. It’s generated in a cell-autonomous manner.”