NEURONAL MIGRATION

Marching of the neurons

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In the adult brain, neuroblasts that are born in the subventricular zone (SVZ) have to travel a long way to their final destination in the olfactory bulb. How do they orient over such a distance and through complex territories? Writing in *Science*, Sawamoto and colleagues show that these newborn neurons are guided by signalling molecules streaming in specific directions with the flow of cerebrospinal fluid (CSF) in the brain ventricles.

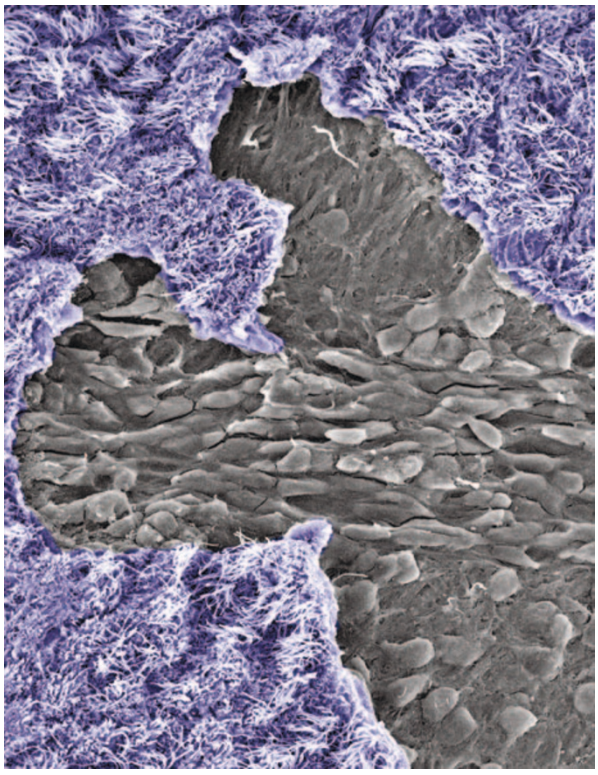
It has been proposed that the flow of CSF might be crucial for neural function, but researchers do not know how the direction of CSF movement in the ventricles is established, or its associated functional consequences. Sawamoto *et al.* found that the flow of CSF correlated with the planar polarity of the ependymal cells that line the ventricles. When Indian ink was deposited onto the exposed surfaces of dissected walls of lateral ventricles, the pattern of ink flow, which was generated by the beating ependymal cilia, paralleled that of CSF flow observed *in vivo*. So, ependymal ciliary beating and the planar polarity of ependymal cells are important for establishing CSF flow in the brain.

The researchers then traced migrating neuroblasts at different locations in the SVZ and determined the direction of migration by inferring the average orientation of the leading processes. Interestingly, the orientation of neuroblast migration correlates with the direction of CSF flow rather than with the relative position of the olfactory bulb. In $Tg737^{orpk}$ mutant mice, which have severe defects in ciliary motility, the flow of CSF is aberrant and only ~9.3% of the neuroblasts generated in the SVZ reach the olfactory bulb.

CSF is mainly secreted by the choroid plexus, which is located in caudal regions of the lateral ventricles. The choroid plexus is also a source of chemorepulsive factors, including members of the SLIT family. The researchers found that SLIT was distributed in a gradient along the dorsal SVZ, with the highest concentration in the caudal region, which declined rostrally. This gradient corresponds to the direction of CSF flow and neuronal migration. These results suggest that the flow of CSF generates the chemorepulsive gradient in the SVZ, which might help guide neuroblasts along the treacherous journey towards the olfactory bulb.

It has been reported that nodal cilia are important for the determination of left–right symmetry. Therefore, it might be a general theme that polarized ciliated cells provide important vectorial information for body-plan development.

Jane Qiu



Scanning electron microscopy image of the ventricular wall with part of the ependymal surface (blue) peeled off to show the chains of migrating cells oriented similarly to the bending of ependymal cilia. Image courtesy of A. Alvarez-Buylla, University of California at San Francisco, USA.

ORIGINAL RESEARCH PAPER Sawamoto, K. *et al.* New neurons follow the flow of cerebrospinal fluid in the adult brain. *Science* 12 January 2006 (doi:10.1126/science.1119133)
FURTHER READING Okada, Y. *et al.* Mechanism of nodal flow: a conserved symmetry breaking event in left–right axis determination. *Cell* **121**, 633–644 (2005)
WEB SITE
Alvarez-Buylla's laboratory: http://neurosurgery.medschool.ucsf.edu/faculty_staff/department_faculty/alvarez_buylla.html