In This Issue

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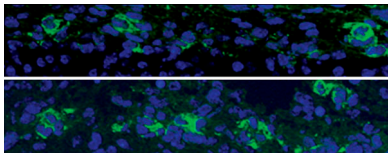
Brain building



Early-born neurons (green) are more abundant in the Vangl2-lacking mouse embryo brain (bottom) due to premature progenitor differentiation.

How your brain grows might come down to how your cells divide. Lake and Sokol report that mouse protein Vangl2 controls the asymmetrical cell division and developmental fate of progenitor neurons.

Vangl2 (aka Strabismus in flies) is a component of the PCP (planar cell polarity) pathway that is active in a variety of tissues and organisms. Mice that lack Vangl2 have a number of neurological defects including incomplete neural tube closure and reduced brain size.

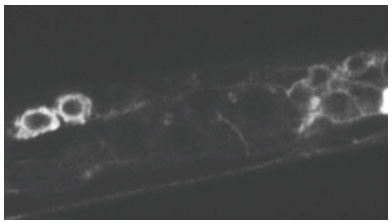
Lake and Sokol wondered how Vangl2 might influence brain development. In the cerebral cortex, neurons are born from a pool of progenitor cells, and the time of their birth determines their fate. The research duo found that Vangl2-lacking mouse embryos had large numbers of early-born neurons and few remaining progenitor cells. This hinted that Vangl2-lacking neurons were differentiating prematurely—a suspicion confirmed in vitro.

The progenitor pool is maintained by asymmetrical division—one daughter cell becomes a neuron, the other self-renews. This fate asymmetry is thought to depend on the orientation of cell division, and the authors observed an increase in the number of symmetrically dividing progenitors in the brains of Vangl2-lacking mouse embryos. Also, Vangl2-lacking cells in culture showed symmetrical distribution of a spindle-orienting factor that in normal cells distributes asymmetrically.

Such similarities between Vangl2-lacking cells in vitro and in vivo will facilitate ongoing studies of the PCP pathway in neurogenesis.

Lake, B.B., and S.Y. Sokol. 2009. *J. Cell Biol.* doi:10.1083/jcb.200807073.

Speedy versus sluggish cells



Ou and Vale measured speed and distance of fluorescent cells (white) in the worm.

Some cells live a fast-paced life, traveling far and wide. Others are more sedentary and stay closer to home. Ou and Vale now report molecular differences that underlie these lifestyle choices.

Cell migration studies in living multicellular organisms are not easy. Ou and Vale used spinning disc confocal microscopy—a technique that allows fine focusing and rapid image capture—to follow the paths of individual fluorescent cells in the bodies of worms. Images were captured from up to 10 worms at once over a period of hours, and the microscope automatically moved to specific focal points for each cell in each worm. Because the worms (and cells) were alive and moving, however, Ou had to readjust the focal points every 15 minutes or so.

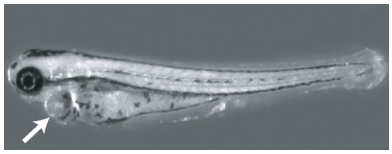
The cells of interest were neuroblasts, which are known to vary in their migration distances. The authors now report that these cells also vary in their speed, and faster cells ultimately go farther.

Compared with their sluggish sisters, fast cells boosted their levels of a cytoskeletal regulator, lowered their levels of an extracellular matrix attachment factor, or did both. Essentially, they revved the engine and/or took off the brakes.

The team now plans to use its microscopy setup to investigate how neuroblasts move in multiple cell migration mutants.

Ou, G., and R.D. Vale. 2009. *J. Cell Biol.* doi:10.1083/jcb.200812077.

What do kidneys and embryonic fish skin have in common?



Fish lacking *miR-8* microRNAs are unable to cope with osmotic pressure and can develop edemas (arrow).

Both have to cope with fluctuations in osmotic pressure and acidity. Flynt et al. now show how a microRNA (miRNA) molecule acts as a crucial part of the osmoregulatory machinery.

miRNAs are small noncoding RNAs that bind to gene transcripts, preventing their translation into proteins. There are potentially thousands of miRNAs encoded in the genomes of higher eukaryotes, and predicting their target transcripts is tricky, as binding occurs via imperfect sequence matches.

Researchers like Flynt and colleagues are taking a one-at-a-time approach to identify miRNA targets and functions, starting with the most highly conserved miRNAs. Among these are the *miR-8* family, which has several conserved members in vertebrates. In fish, the team observed, *miR-8* family members were abundant in cells called ionocytes. These cells are dotted throughout the skin and participate in osmoregulation.

Without *miR-8*, ionocytes looked normal, but couldn't cope with pH changes or osmotic stress—in the latter case the fish developed edemas due to water retention. *miR-8*, it turns out, was targeting an mRNA that encodes a protein called *nherf1* (Na^+/H^+ exchange regulatory factor 1). Originally identified in renal brush border membrane extracts, Nherf1 acts as an adaptor between the plasma membrane and cytoskeleton. In ionocytes lacking *miR-8* family members, membrane trafficking of ion channels and other proteins was disrupted.

miR-8 is predicted to target *nherf1* in mammals too. The team now plans to see whether intercalated cells of the kidney—the functional equivalents to ionocytes—use the same osmotic regulation pathway.

Flynt, A.S., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200807026.