Neurons born in new places

Neurogenesis in the adult brain is generally considered to be restricted to the hippocampus and olfactory bulb—ancient parts of the brain that are found even in nonmammalian species. A few publications suggested that the neocortex—a well-developed region in primates that is implicated in higher thought—also supports neurogenesis. These reports have been met with skepticism, as other groups have been unable to replicate the findings. On page 415, Dayer et al. bolster the evidence for proliferating neurons in regions beyond the hippocampus and olfactory bulb.

The authors used a battery of neuronal markers to confirm that neurogenesis exists in the neocortex. Although difficult to find in the sparsely populated expanse of the cortex, replicating cells with markers of neuronal precursors were present in the adult rat neocortex. Their numbers suggest that these interneurons in the cortex turnover as rapidly as granule cells in the hippocampus, where up to 6% of the cells are replaced within a month.

The various markers that the authors used also revealed for the first time that the neocortical precursors produce GABAergic interneurons, which are small inhibitory neurons that regulate the larger pyramidal cells of the cortex. Because most neurons in the cortex are pyramidal cells, which are large and unmistakably neuronal, the new interneurons can be easily overlooked or mistaken for glial cells.

The precursors originate from within the cortex itself, rather than migrating from the subventricular zone (SVZ), which provides new neurons to the olfactory bulb. The authors did note, however, that some SVZ precursors also found their way to the striatum—a region associated with motor skill learning—where they formed interneurons.

Depression has been correlated with decreased hippocampal neurogenesis and a decrease in small cells in the neocortex that look like glia. The new findings hint that some of those missing cells may be newly born interneurons and suggest that neurogenesis in the cortex will be an important event to examine in disease states and old age.

Ring around the wound

Concentric rings of GTPase activity help to repair a wounded cell, as shown on page 429 by Benink and Bement.

A wounded cell, such as the frog oocyte system used by the authors, rapidly repairs its broken membrane by an onslaught of exocytosis. After sealing the hole, the cell must rebuild the actin cytoskeleton underneath the new membrane. This is partly accomplished by stretching the undamaged surrounding cytoskeleton inward over the wound, which requires actomyosin-based contraction.

The authors now see that this inward motion of actin is coordinated by ring-like patterns of the active form of two rho GTPase family members known to regulate actin dynamics. The appearance of these rings—an inner loop of RhoA-GTP circumscribed by a halo of Cdc42-GTP—preceded actin accumulation and occurred independently of actin assembly. Inward movement of the GTPases as the wound was repaired, however, depended on the F-actin array.

On the ring’s inside, RhoA turned on contraction by activating myosin-2 light chain phosphorylation. At the outer edges, Cdc42 promoted actin turnover, probably via WASP, and possibly also deactivated myosin-2. The resulting relaxation of the actin array on the outskirts may make actin’s inward motion easier. In fact, if the authors used constitutively active RhoA to prevent this relaxation, the actin array fractured as it tried to pull forward against high tension.

The upstream signals that set up these GTPase patterns are not known. Exocytosis may be the early spark, as extracellular calcium, whose entry triggers the exocytic patching of wounded membrane, was also needed to establish the GTPase rings. RhoA negatively regulated Cdc42 activity and so is at least partly responsible for the separation of the two rings. Microtubules were also needed for ring segregation, but how they are contributing is not yet clear.

Actomyosin-based contraction also controls cytokinesis and multicellular migration during wound healing in tissues. The authors expect that similar segregated patterns of active rho GTPases coordinate these processes as well.