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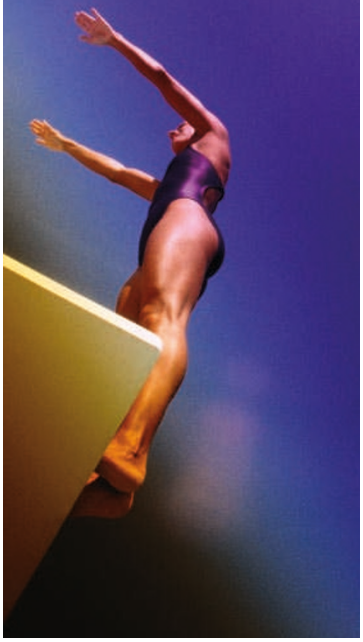
NEUROGENESIS

# In the zone



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> a population of radial-glia-like cells ... may distinguish cortical growth in primates from that in other species.

An expansion of cerebral cortex size during human evolution is thought to underlie our unique cognitive abilities; however, little is known about the developmental mechanisms that mediated the dramatic growth of the human cortex. Kriegstein and colleagues have now characterized a population of radial-glia-like cells in the developing human brain that may distinguish cortical growth in primates from that in other species.

The cells that populate the mammalian cortex arise from progenitors in the ventricular zone (VZ) and subventricular zone (SVZ). The outer part of the SVZ (OSVZ) is unusually large in primates. Kriegstein and colleagues sought to characterize the progenitor cells in this region and determine their contribution to cortical size.

The authors found that 40% of the proliferating cells in the OSVZ of the fetal human cortex share characteristics with radial glia, which are the neural progenitors in the VZ. Like radial glia, these cells express progenitor cell markers, including paired box protein PAX6 and transcription factor SOX2, and have a long basal process that often reaches the pial surface. However, unlike radial glia, the OSVZ progenitors do not have an apical process or make contact with the ventricular surface. The authors termed the cells OSVZ radial-glia-like cells (ORGs) to distinguish them from their VZ counterparts.

To determine the proliferative capacity of ORGs, the authors carried out real-time imaging of these cells. The ORGs underwent asymmetrical cell divisions, producing one daughter cell that retained ORG characteristics and another that adopted a bipolar or multipolar morphology. Both daughter cells were shown to divide again, suggesting that they form distinct progenitor cell populations in the OSVZ.

Immunostaining revealed that the daughter cells that retained ORG morphology remained undifferentiated, whereas the other daughter cells sometimes expressed eomesodermin homologue (also known as TBR2) or achaete-scute homologue 1 — transcription factors that are indicative of neuronal commitment.

Next, the authors examined the mechanisms that maintain ORG identity, finding evidence to support a role for Notch signalling in this process. Most ORGs expressed the Notch effector HES1, and treatment of brain slices with a Notch inhibitor caused SOX2-positive cells in the OSVZ to undergo premature neuronal differentiation.

These findings suggest that the proliferation of OSVZ progenitors may underlie cortical expansion in humans. Indeed, the authors found that the OSVZ surpasses the VZ and inner SVZ as the major source of new cortical cells between gestational weeks 13 and 17 in humans. Further characterization of ORGs and their progeny should shed more light on the origins and functional contribution of these cells to the human cortex.

*Katherine Whalley*

**ORIGINAL RESEARCH PAPER** Hansen, D. V., Lui, J. H., Parker, P. R. L. & Kriegstein, A. R. Neurogenic radial glia in the outer subventricular zone of human neocortex. *Nature* 14 February 2010 (doi:10.1038/nature08845)
**FURTHER READING** Kriegstein, A., Noctor, S. & Martinez-Cerdano, V. Patterns of neural stem and progenitor cell division may underlie evolutionary cortical expansion. *Nature Rev. Neurosci.* **7**, 883–890 (2006) | Rakic, P. Evolution of the neocortex: a perspective from developmental biology. *Nature Rev. Neurosci.* **10**, 724–735 (2009)