

 NEURAL STEM CELLS

Taking a 'peak' into neurogenesis

The existence of neurogenesis in the adult human brain raises the exciting possibility that by manipulating neural precursor cells (NPCs) it might be possible to repair neurological damage. The potential of this approach has been limited, partly, by the inability to detect these cells in live humans. Now, Maletić-Savatić and colleagues have identified a metabolic biomarker of NPCs that enables neurogenesis to be monitored by proton magnetic resonance spectroscopy ($^1\text{H-MRS}$) in the live human brain.

To identify unique features of NPCs, the authors compared the spectral profile of mouse NPCs with those of differentiated neurons, oligodendrocytes and astrocytes. They found a unique peak at the frequency of 1.28 parts per million (ppm) that was not found in the other cell types. Furthermore, the amplitude of the 1.28-ppm signal correlated with the number of NPCs that were analysed. The precise chemical identity of the 1.28-ppm signal remains to be determined, but there is evidence suggesting that it represents a mixture of lipids.

When the authors induced NPC differentiation *in vitro*, the 1.28-ppm signal decreased, whereas the levels of neuronal and astrocytic biomarkers increased. The strength of the 1.28-ppm signal also seemed to correlate with neurogenesis *in vivo*: the signal was stronger in samples taken

from mouse brain at embryonic day 12, when NPCs populate the brain, than in samples from postnatal day 30, when most cells have differentiated. The authors also found a difference between the signals from cells taken from the adult mouse hippocampus (a region that is known to retain the ability to generate new neurons) and cells from the cortex. Finally, the 1.28-ppm signal intensified in the adult rodent hippocampus following electroconvulsive shock (ECS), a treatment that is known to increase neurogenesis in this area. Together, these findings suggest that the 1.28-ppm signal is a faithful NPC biomarker.

The authors went on to investigate whether this biomarker could be used to monitor neurogenesis in live animals. Owing to the low signal-to-noise ratio associated with $^1\text{H-MRS}$ *in vivo*, Maletić-Savatić's team developed a more sensitive signal processing method based on signal-value decomposition. Using this method, they were able to detect significant differences in the biomarker between adult rat hippocampal and cortical spectra, and between NPC-implanted cortical hemispheres and saline-injected controls. Moreover, using $^1\text{H-MRS}$, the authors were able to monitor changes in NPC density in rat hippocampus following ECS.

In human subjects the 1.28-ppm biomarker was clearly detected in



the hippocampus, and the authors showed, for the first time, that there is an age-dependent decrease in neurogenesis in humans, which correlates with animal studies.

Researchers in the field are cautiously optimistic but, if validated, this non-invasive method for measuring NPCs has very promising implications for understanding the role of these cells in the development of neurological disease and for monitoring emerging therapies.

Monica Hoyos Flight

ORIGINAL RESEARCH PAPER

Manganas, L. N. *et al.* Magnetic resonance spectroscopy identifies neural progenitor cells in the live human brain. *Science* **318**, 980–985 (2007)