

Neural stem cells lend the brain a surprising capacity for self-repair

The brain contains stem cells with a surprising capacity for repair, researchers report in the December 15 issue of the journal *Cell*, published by Cell Press. The novel insight into the brain's natural ability to heal might ultimately have clinical implications for the treatment of brain damage, according to the researchers.

The researchers found that mice whose brains were severely damaged by loss of the genes "Numb" and "Numblake" in one region just after birth showed substantial mending within weeks. They attributed that repair to neural stem cell "escapees" that had somehow retained or restored the genes' activity and, with it, their regenerative potential.

"At two weeks, the knockout animals' brains had developed a big hole," said Yuh-Nung Jan, a Howard Hughes Medical Institute investigator at the University of California, San Francisco. "We thought that the mice would not live long, but by four weeks, the hole was largely repaired and the animals survived.

"It was a big surprise. It was not known that the brain has this kind of ability to repair itself."

Jan and his colleagues first discovered Numb in the fruit fly *Drosophila* more than 10 years ago. The gene was found by them and others to play a role in determining the fate of neuroblasts, cells that develop into neurons or other support cells in the insects' brains. Later, researchers found two functionally related mammalian proteins, dubbed Numb and Numblake, to be critical in the development of neurons in embryonic mice.

To investigate the genes' role after birth, Jan's team developed mice in which Numb and Numblake could be turned off only in a portion of the brain termed the subventricular zone (SVZ) when they administered a particular drug. The SVZ is known to be a site, or niche, that contains neural stem cells after birth.

In newborn mice, loss of the genes left the SVZ "greatly disturbed," Jan said.

Their results indicated that Numb and Numblake have two important functions, namely a role in the survival of neuroblasts and an unexpected role in maintaining the cellular wall that lines the ventricular region of the brain in which the SVZ resides. Without the normal complement of genes, that wall "disintegrated," he said, leaving holes in the brain.

Surprisingly, they reported, the ventricular damage was eventually repaired. SVZ reconstitution and remodeling of the ventricular wall was driven by progenitor cells that escaped Numb deletion, they found.

"Although the exact mechanisms are still being worked upon, these observations raise the possibility that postnatal neurogenesis can one day be used to repair brain damage," the researchers concluded.

"Our results here show that self-repair and local remodeling can indeed happen along the brain's lateral ventricular wall, and further insights into this process should shed light on whether SVZ neural stem cells participate in stroke/trauma-induced brain remodeling and postnatal/adult brain tumor formation. Furthermore, understanding how the SVZ cells participate in local repair should help bring us closer to the goal of using neural stem cells as therapeutic agents in neurodegenerative diseases."

Source: Cell Press

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