Reprogramming 'support cells' into neurons could repair injured adult brains

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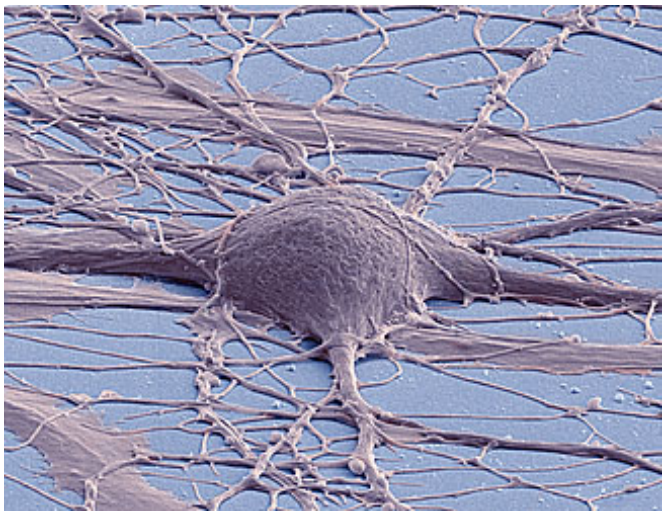

This is a scanning electron micrograph (false color) of a human induced pluripotent stem cell-derived neuron. Credit: Thomas Deerinck, UC San Diego

The portion of the adult brain responsible for complex thought, known as the cerebral cortex, lacks the ability to replace neurons that die as a result of Alzheimer's disease, stroke, and other devastating diseases. A study in the International Society for Stem Cell Research's journal *Stem Cell Reports*, published by Cell Press on November 20 shows that a Sox2 protein, alone or in combination with another protein, Ascl1, can cause nonneuronal cells, called NG2 glia, to turn into neurons in the injured cerebral cortex of adult mice. The findings reveal that NG2 glia represent a promising target for neuronal cell replacement strategies to treat traumatic brain injury.

"Our study is the first to demonstrates unambiguously the conversion of a specific subtype of glia, the so-called NG2 glia, into induced neurons in living animals," says senior study author Benedikt Berninger of Johannes Gutenberg University Mainz. "The findings pave the way for future studies aimed at harnessing the potential of these cells for brain repair."

The cerebral cortex plays a key role in memory, attention, perception, language, and consciousness. Unlike other regions in the adult brain, the cerebral cortex is not capable of generating new neurons after traumatic injury. Berninger and others have previously shown that Sox2, Ascl1, and other transcription factors—proteins that bind to specific DNA sequences to control the activity of genes—can induce the nonneuronal "support cells" known as glia to turn into neurons. It has been difficult, however, to convert glia into neurons after brain injuries such as stroke in the adult cerebral cortex of living animals.

To test potential brain repair strategies, Berninger and Magdalena Götz of Ludwig-Maximilians University Munich delivered transcription factors into the cerebral cortex of adult mice three days after traumatic injury. Surprisingly, they found that Sox2 alone or in combination with Ascl1 was sufficient to trigger the emergence of neurons, contrary to the widely accepted view that Sox2 prevents stem cells from turning into more mature cells such as neurons. Notably, the majority of cells that converted into neurons were NG2 glia. These glial cells have received relatively little attention in the past, even though they represent a promising cellular source for brain repair strategies because of their abundance and life-long capacity for proliferation.

Taken together, these findings support the notion that cellular reprogramming may become a way of replacing degenerated neurons in the adult brain. "Our study sets the stage for further research to identify which additional cues could induce these neurons to fully mature and incorporate into functional circuits, thereby allowing this approach to potentially be used in the clinic," Berninger says.

More information: *Stem Cell Reports*, Heinrich et al.: "Sox2-mediated conversion of NG2 glia into induced neurons in the injured adult cerebral cortex" www.cell.com/stem-cell-reports … 2213-6711(14)00329-4

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