Astroglia reprogrammed to generate synapse-forming neurons

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The research team led by Professor Magdalena Goetz of Helmholtz Zentrum Muenchen and Ludwig-Maximilians-Universitaet Munich, Germany, reports a major step forward in discovering a therapy for neurodegenerative diseases such as Alzheimer's or stroke. The researchers were able to convert glial cells of the brain into two different functional classes of neurons. The findings are published on May 18 in the renowned journal *PLoS Biology*.

In this study Magdalena Götz and her team showed how astroglia can be directly converted into the two main classes of cortical neurons. This was made possible by the selective transduction of specific proteins - transcription factors - which regulate the transcription of DNA. While the transcription factor neurogenin-2 directs the generation of excitatory neurons, the same astroglial cells yield inhibitory neurons after transduction of the transcription factor Dlx2.

Neurons are the cells in the brain which transmit information, while the astroglia (star-shaped glial cells) serve as a supportive scaffold and are involved in metabolism. Moreover, they are closely related to radial glial cells, which during embryonic forebrain development function as precursors for most neurons. In fact, some glial cells even in the adult brain retain the capability of producing neurons - however these are only found in specific regions.

It is still not known exactly what differentiates normal astroglia from radial glial cells with neurogenic potential. However, the researchers led

by Magdalena Götz, director of the Institute of Stem Cell Research at Helmholtz Zentrum München and chair of Physiological Genomics at LMU, have already shown in previous studies that astroglia from the cerebral cortex of young mice, which are normally incapable of generating neurons, can be driven to convert into neurons by transducing special regulatory proteins.

"In this study we have succeeded in reprogramming the newly created neurons to the extent that they can now develop functioning synapses. These release - depending on the transcription factor used - either excitatory or inhibitory neurotransmitter substances," said Dr. Benedikt Berninger, lead author of the study. This process could not only be observed in young astroglia, but even in astroglia in the adult brain following tissue injury-induced reactivation. "Our findings nurture the hope that the barrier separating the astroglial and neuronal cells - closely related as they are - is not insurmountable," Dr. Berninger emphasized. Due to these encouraging results, the researchers intend to pursue this avenue further to gain new neurons from the glial cells present in the brain, in order to find therapies for neurodegenerative diseases such as Alzheimer's.

More information: Christophe Heinrich, Robert Blum, Sergio Gascón, Giacomo Masserdotti, Pratibha Tripathi, Rodrigo Sánchez, Steffen Tiedt, Timm Schroeder, Magdalena Götz, Benedikt Berninger. (2010): Directing Astroglia from the Cerebral Cortex into Subtype Specific Functional Neurons. PLoS Biol 8 (5): e1000373. (doi:10.1371/journal.pbio.1000373)

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