Molecular time signalling controls stem cells during brain's development

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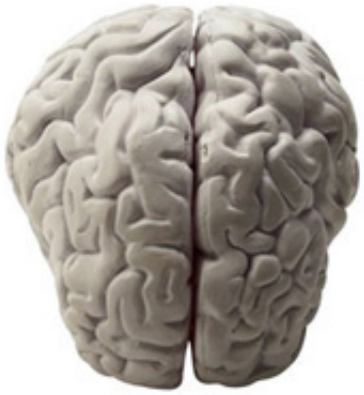

Researchers at Karolinska Institutet in Sweden have succeeded in explaining how stem cells in the brain change to allow one type of stem cell to produce different cell types at different stages. In a study being published in the journal *Neuron*, researchers show that the signal molecule TGF-beta acts as a time signal that regulates the nerve stem cells' potential at different stages of the brain's development - knowledge that may be significant for future pharmaceutical development.

The human brain consists of thousands of different types of nerve cells that are all formed out of what in simple terms can be described as immature stem cells. It has long been known that the neural stem cells change as the human brain develops and ages. One type of stem cell can produce multiple types of nerve cells at different stages of the brain's development. In this process, ageing stem cells also gradually become more limited in their development potential and lose the ability to develop the maturated cell types that form during the early stages.

How neural stem cell identity and potential is regulated over time has been poorly understood. But in the study being published, researchers at the Department of Cell and Molecular Biology at Karolinska Institutet present a molecular time mechanism that can help explain neuronal stem cell regulation and therefore also the occurrence of cellular diversity in the brain.

"TGF-beta functions as an important time signal that controls when a stem cell should stop producing one type of nerve cell and instead start producing another, while also gradually limiting the stem cell's future development capacity," says Johan Ericson, Professor of Developmental Biology, who led the study.

In their work, the researchers also show how TGF-beta can be used in stem cell cultures to mass-produce nerve cells which in turn produce the signalling substance serotonin. Today the brain's serotonin system is already a known target for the treatment of depression, and according to researchers it should be possible to use time signals in pharmaceutical development based on stem cells.

"This is the first known signalling molecule that regulates the potential of neuronal stem cells", says Johan Ericson. "With a better understanding of how potential is regulated, it could be possible to broaden the development spectrum of ageing stem cells, allowing them to regain their capacity to produce cell types from earlier development stages, which in the long-term perspective could be relevant to future treatment methods for neurodegenerative disease".

More information: "Tgf? signaling regulates temporal neurogenesis and potency of neural stem cells in the CNS", José M. Dias, Zhanna Alekseenko, Joanna M. Applequist and Johan Ericson, *Neuron* online 13 November 2014.