Limited self-renewal of stem cells in the brain

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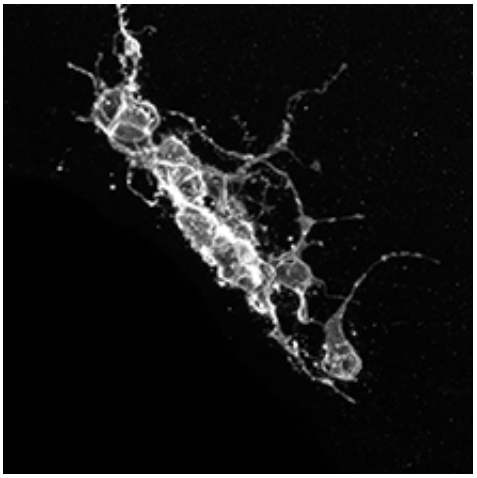

A subclone of transiently amplifying progenitors in the subependymal zone. Credit: J.Michel, ISF/Helmholtz Zentrum München

Stem cells in the brain can produce neurons and are consequently seen as a hope for treatment. A team of researchers from the Helmholtz Zentrum München and Ludwig-Maximilians-Universität München (LMU) has now discovered that the self-renewal rate of the stem cells is however limited, explaining why their number drops over the course of a lifetime. This work now sets the basis for further investigation of the signalling pathways that maintain the stem cells. The results have been published in the journal *Nature Neuroscience*.

The generation of neurons (neurogenesis) in humans is predominantly

limited to development; in the adult stage it takes place in only a few regions of the brain. These regions contain neural stem cells that generate neurons in a process with various intermediary stages.

Stem cell renewal is limited – total number drops

Until now it was thought that maintaining the stem cell pool was based on the self-renewal of individual stem cells. The team of scientists headed by Dr. Jovica Ninkovic and Professor Dr. Magdalena Götz were able to refute this: Both the self-renewal rate and the diversity of neurons formed from the stem cells are limited, and the number of stem cells decreases with age.

"Our findings explain why neurogenesis declines in later years, as there are fewer and fewer neural stem cells. At the same time, we gained new knowledge on basic mechanisms of neurogenesis that until now were not understood," says first author Dr. Filippo Calzolari.

Therapeutic approaches must focus on stem cells themselves

Approaches to new therapies for brain diseases, such as stroke or dementia, for example, particularly concentrate on replacing lost neurons by stimulating the generation of new cells from stem cells. "In light of the fact that the stem cell supply is limited, we must now also look for ways to promote the self-renewal rate of the stem cells themselves and maintain the supply for a longer time," emphasizes Götz, Director of the Institute for Stem Cell Research at the Helmholtz Zentrum München and Chair of the Institute of Physiological Genomics at LMU.

More information: Calzolari, F. et al. (2015). "Fast clonal expansion and limited neural stem cell self-renewal in the adult subependymal

zone." *Nature Neuroscience*. DOI: 10.1038/nn.3963