

Flow of cerebrospinal fluid regulates division

May 18 2018

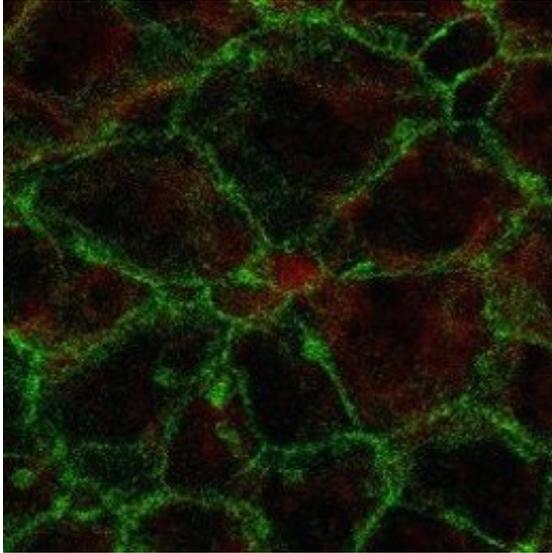


Image from a confocal microscope showing so-called pin-wheel structure of the lateral wall of the lateral ventricle: ENaC-positive adult neural stem cell (red) surrounded by ependymal cells. Credit: Helmholtz Zentrum München

Stem cells in the brain can divide and mature into neurons participating in various brain functions, including memory. In a paper scientists have discovered that the flow of cerebrospinal fluid is a key signal for neural stem cell renewal.

The ancient Greek aphorism *panta rhei* means "everything flows", a phrase used by philosophers to describe the constant flux and interplay between the past and renewal. A recent paper lends this relationship a whole new meaning: a team of researchers headed by Professor

Magdalena Götz and their collaborators from the LMU (Professor Benedikt Grothe, Chair of Neurobiology) and the Henrich-Heine University Düsseldorf have discovered that the flow of [cerebrospinal fluid](#) is a key signal for neural stem cell renewal.

"Neural [stem cells](#) in the brain can divide and mature into neurons and this process plays important roles in various regions of the brain – including olfactory sense and memory," explains Magdalena Götz, Head of LMU Department of Physiological Genomics and Director of the Institute for Stem Cell Research at Helmholtz Zentrum München.

"These [cells](#) are located in what is known as the neurogenic stem cell niche one of which is located at the walls of the lateral ventricles, where they are in contact with circulating cerebrospinal fluid."

The cerebrospinal fluid fills the brain and its roles are still ill understood. This work highlights the role of this fluid as a key signal – but this time not a chemical but a physical signal. Götz and her team, under the guidance of lead author Dr. David Petrik, discovered that [brain stem cells](#) are also influenced by the physical forces of the fluid flow.

Channel protein plays a key role

"The whole mechanism is controlled by the ENaC molecule," Petrik explains. This abbreviation stands for epithelial sodium (Na) channel and describes a channel protein on the cell surface through which [sodium ions](#) stream into the cell's interior. "We were able to show in an experimental model that brain stem cells are no longer able to divide in the absence of ENaC. Conversely, a stronger ENaC function promotes cell proliferation."

Further tests showed that the function of ENaC is augmented by shear forces exerted on the cells by the cerebrospinal fluid. The physical stimulation causes the [channel protein](#) to open for longer time and allow

sodium ions to flow into the cell, thus stimulating division.

"The results came as a big surprise, since ENaC had previously only been known for its functions in the kidneys and lungs," says study leader Götz. She and her team now want to better explore the fast signals mediated by ions in stem cells and clarify the extent to which the findings are also relevant to treatment. After all, pharmacological ENaC blockers are already used clinically to relieve certain types of hypertension. Now, it is known that they can also influence stem cells in the brain and thus brain function.

More information: David Petrik et al. Epithelial Sodium Channel Regulates Adult Neural Stem Cell Proliferation in a Flow-Dependent Manner, *Cell Stem Cell* (2018). [DOI: 10.1016/j.stem.2018.04.016](https://doi.org/10.1016/j.stem.2018.04.016)

Provided by Ludwig Maximilian University of Munich

Citation: Flow of cerebrospinal fluid regulates division (2018, May 18) retrieved 20 September 2024 from <https://phys.org/news/2018-05-cerebrospinal-fluid-division.html>

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