Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/hirnstammzellen-lebenslaenglich-unter-interferon-kontrolle

Brain stem cells are contolled by interferon during the entire lifetime

Interferons represent the first line of defence against viral infections and are at the same time an important cause of the age-related loss of function of brain stem cells. Scientists from the German Cancer Research Center (DKFZ) and the University of Heidelberg have now shown in mice that interferon regulates the activity and self-renewal of brain stem cells throughout life: In young brains, it increases, but in the less active ageing brain, it reduces the production of nerve progenitor cells. In older age, a blockade of interferon signals could possibly slow down this process and counteract the age-related decline in brain function.

Interferons are cell messengers that stimulate and modulate the immune system during a viral infection. It has also been known for some years that interferon signals are also a cause of the functional capacity of neuronal stem cells, which declines with age. The stem cells, which are responsible for the formation of new nerve cells in the brain, then lose the ability to produce a sufficient number of progenitor cells.

A team led by Ana Martin-Villalba, DKFZ, and Anna Marciniak-Czochra, University of Heidelberg, has now jointly investigated the molecular background of stem cell control by interferon - using a combination of single cell analyses in mice and mathematical modelling.

Contrary to the prevailing expert opinion, the Heidelberg researchers found that interferon signals influence the activity of brain stem cells not only in old age, but throughout the entire lifespan, even in young animals. Brain stem cells react to interferon, but precursor cells no longer do after a certain developmental stage. Only the differentiated neurons respond to the messenger substance again.

The interferons act on a central control molecule of protein synthesis. This has the effect of suppressing Sox2, an essential transcription factor that maintains the self-renewal capacity of stem cells.

"The biphasic interferon control of brain stem cell activation apparently helps to adapt the production of progenitor cells to the respective demand," Martin-Villalba explains. In the young brain, interferon increases the number of progenitor cells, whereas in the less active ageing brain, it reduces them.

The researchers see in interferon as a possible target structure for therapies that could promote the self-renewal capacity of the brain stem cells and thus counteract the age-related decline in brain function. "From an older age, interferon blockade by drugs could benefit the brain," the researchers surmise. Whether this could also be an option for ageing people, however, must first be tested in clinical trials.

The virus defence in the brain would not be affected by such drugs, since brain stem cells can perform this function completely independently of the presence of interferon. They trigger the cell-internal interferon signals without the need for interferon to bind to its receptor. This trick has so far only been known in brain stem cells, which use it to protect themselves against infections. Whether other adult stem cells in the body also master this molecular shortcut has not yet been researched.

Publication:
Damian Carvajal Ibañez, Maxim Skabkin, Jooa Hooli, Santiago Cerrizuela, Manuel Göpferich, Adrien Jolly, Katrin Volk, Marc Zumwinkel, Matilde Bertolini, Gianluca Figlia, Thomas Höfer, Guenter Kramer, Simon Anders, Aurelio A.Teleman, Anna Marciniak-Czochra, Ana Martin-Villalba: Interferon regulates neural stem cell function at all ages by orchestrating mTOR and cell cycle. EMBO Mol. Med 2023, DOI https://doi.org/10.15252/emmm.202216434.

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Further information

- German Cancer Research Center (DKFZ), Heidelberg
- University of Heidelberg