

Researchers discover mechanism that promotes neurogenesis in zebrafish, potential for activation in humans

August 31 2023



Credit: [National Institute of Child Health and Human Development](#)

Evolution is usually equated with advancement, but the most useful biological innovations aren't always found in the "highest" organisms.

Zebrafish, for example, can continually generate new neurons in their brains, which protects these vertebrates from the ravages of neurological

disease and injury. Adult humans, on the other hand, can only make a meager number of new neurons, mostly in the hippocampus (the brain's memory center), and diseases like Alzheimer's suppress this production even further.

Fortunately, zebrafish are giving up their secrets.

Columbia University researchers have discovered a mechanism that promotes neurogenesis in the zebrafish brain and has the potential to be activated in people. The work is published in the journal *npj Regenerative Medicine*.

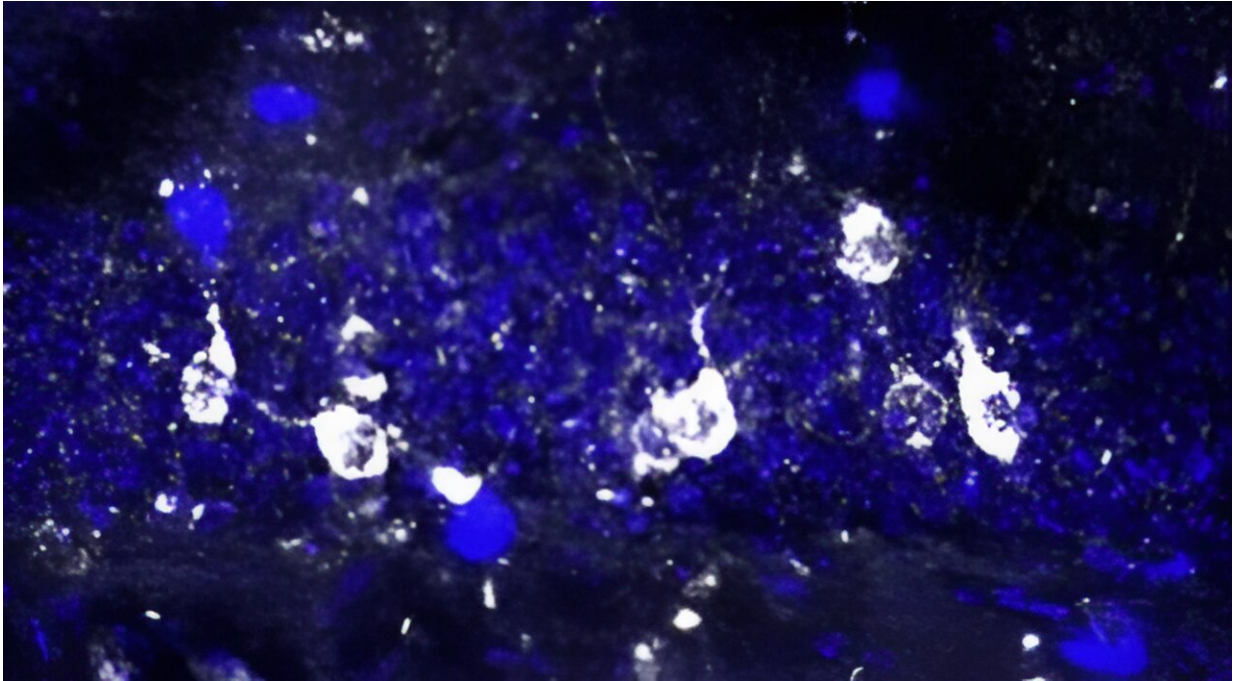
"It's possible that by activating neurogenesis in people with Alzheimer's disease, we could slow the disease's progression," says study leader Caghan Kizil, Ph.D., associate professor of neurological sciences (in neurology and in the Taub Institute).

Growth factor helps zebrafish regenerate their brains

Kizil and his colleagues previously found a molecule in zebrafish brains called nerve [growth factor](#) receptor (NGFR) that nudges [stem cells](#) to make [new neurons](#).

NGFR increases neuron production even in zebrafish whose brains show signs of Alzheimer's disease, which impedes neurogenesis.

In the new study, the researchers wanted to determine if the [zebrafish](#) trick could also work in mammals with Alzheimer's disease.



New neurons. Activating a gene called NGFR in the brains of Alzheimer's model mice increased the production of new neurons (white cells), which may slow the progression of the disease. Credit: Caghan Kizil laboratory, Columbia University Irving Medical Center

Mouse brains do not normally express NGFR, but when the researchers activated it in mouse models of Alzheimer's, they found that NGFR stimulated long-term neurogenesis by converting the disease-related physiology of the brain's astrocytes to a healthy and neurogenic state. Remarkably, NGRF activation also reduced the accumulation of amyloid and [tau proteins](#), two of the hallmarks of Alzheimer's disease.

Analysis of human brain cells, including those from deceased Alzheimer's patients, showed that NGFR is expressed in the brain during early human development but not later in life.

How to activate the zebrafish trick in people

Turning on NGFR in relevant cell types could be a therapy option yet it would require gene therapy approaches. Instead, Kizil and his colleagues deciphered how NGFR works to promote neurogenesis to find other synergistic targets that could be modified. They identified two potential drug targets that act downstream to NGFR.

The first target, lipocalin-2, is a protein that is elevated in mouse and human brain cells and must be blocked for neurogenesis to proceed. "Our findings suggest that if we simply block lipocalin-2's receptor—Slc22a17—we might be able to increase neurogenesis," says Kizil.

The researchers also identified a second protein called phosphofructokinase that also hampers [neurogenesis](#) and is highly expressed in human [brain](#) cells. And because phosphofructokinase works independently from lipocalin-2, it might be more effective to go after both targets simultaneously, Kizil says.

In vivo studies and behavioral tests in preclinical Alzheimer's models are needed to determine if more neurons and less Alzheimer's pathology would lead to cognitive improvement.

More information: Tohid Siddiqui et al, Nerve growth factor receptor (Ngfr) induces neurogenic plasticity by suppressing reactive astroglial Lcn2/Slc22a17 signaling in Alzheimer's disease, *npj Regenerative Medicine* (2023). [DOI: 10.1038/s41536-023-00311-5](https://doi.org/10.1038/s41536-023-00311-5)

Provided by Columbia University Irving Medical Center

Citation: Researchers discover mechanism that promotes neurogenesis in zebrafish, potential for activation in humans (2023, August 31) retrieved 2 May 2024 from <https://medicalxpress.com/news/2023-08-mechanism-neurogenesis-zebrafish-potential-humans.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.