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Zebrafish aid effort to regenerate damaged retinas

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The tiny zebrafish may hold the secret to regenerating damaged retinas in humans, Vanderbilt University researchers reported last week in the journal *Cell Reports*.

Currently there are few effective treatments for retinal degenerative diseases such as age-related macular degeneration (AMD), the most common cause of blindness in millions of Americans over age 55. The prognosis is equally dim for another 100,000 Americans with retinitis pigmentosa. Many of them are legally blind by age 40.

Mammals cannot spontaneously regenerate retinal neurons that are lost or damaged by disease. But in bony fish like the 1-inch-long zebrafish, which is widely used as a "model organism" in biological and medical research studies, retinal damage triggers a spontaneous regenerative response that restores both retinal structure and function.

Since the cells and structure of the retina are highly conserved among vertebrates, from fish to humans, understanding how zebrafish regenerate damaged retinas could lead to new ways to enhance retinal regeneration in people.

One key factor explored by James Patton, Ph.D., and colleagues in the Department of Biological Sciences at Vanderbilt University is a microRNA, miR-216a, which regulates the expression of Dot1l, an enzyme involved in regulating gene expression.

Suppressing miR-216a, they showed, initiates the differentiation and proliferation of Müller glia (MG), the source of regenerated neurons in the zebrafish retina, in part by releasing inhibition of Dot1l. A next step is to test whether suppressing miR-216a can induce MG reprogramming and proliferation in mammals.

"Müller glia constitute an adult stem cell in the zebrafish retina and our goal is to identify pathways and genes that could be activated to induce similar behavior in the human retina," said Patton, Stevenson Professor of Biological Sciences and director of the Interdisciplinary Graduate Program at Vanderbilt.

More information: Nergis Kara et al. The miR-216a-Dot1l Regulatory Axis Is Necessary and Sufficient for Müller Glia Reprogramming during Retina Regeneration, *Cell Reports* (2019). DOI: 10.1016/j.celrep.2019.07.061

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