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Researchers discover stem cells in the optic nerve that enable preservation of vision

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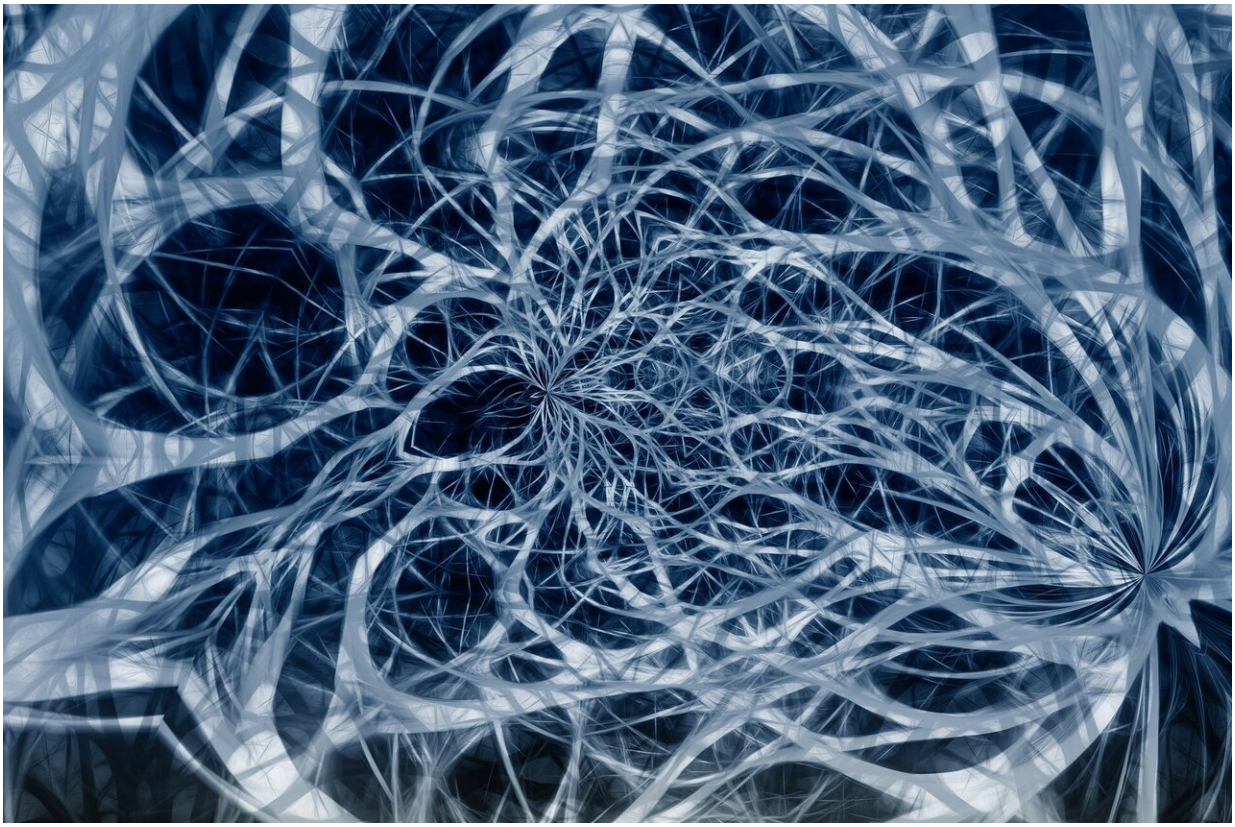

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Researchers at the University of Maryland School of Medicine (UMSOM) have for the first time identified stem cells in the region of the optic nerve, which transmits signals from the eye to the brain. The

finding, published this week in the journal *Proceedings of the National Academy of Sciences (PNAS),* presents a new theory on why the most common form of glaucoma may develop and provides potential new ways to treat a leading cause of blindness in American adults.

"We believe these cells, called neural progenitor cells, are present in the optic nerve tissue at birth and remain for decades, helping to nourish the nerve fibers that form the optic nerve," said study leader Steven Bernstein, MD, Ph.D., Professor and Vice Chair of the Department of Ophthalmology and Visual Sciences at the University of Maryland School of Medicine. "Without these cells, the fibers may lose their resistance to stress, and begin to deteriorate, causing damage to the optic nerve, which may ultimately lead to glaucoma."

The study was funded by the National Institutes of Health's National Eye Institute (NEI), and a number of distinguished researchers served as co-authors on the study.

More than 3 million Americans have glaucoma, which results from damage to the optic nerve, causing blindness in 120,000 U.S. patients. This nerve damage is usually related to increased pressure in the eye due to a buildup of fluid that does not drain properly. Blind spots can develop in a patient's visual field that gradually widen over time.

"This is the first time that neural progenitor cells have been discovered in the optic nerve. Without these cells, the nerve is unable to repair itself from damage caused by glaucoma or other conditions. This may lead to permanent vision loss and disability," said Dr. Bernstein. "The presence of neural stem/progenitor cells opens the door to new treatments to repair damage to the optic nerve, which is very exciting news."

To make the research discovery, Dr. Bernstein and his team examined a narrow band of tissue called the optic nerve lamina. Less than 1

millimeter wide, the lamina lies between the light-sensitive retina tissue at the back of the eye and the optic nerve. The long nerve cell fibers extend from the retina through the lamina, into the optic nerve. What the researchers discovered is that the lamina progenitor cells may be responsible for insulating the fibers immediately after they leave the eye, supporting the connections between nerve cells on the pathway to the brain.

The stem cells in the lamina niche bathes these neuron extensions with growth factors, as well as aiding in the formation of the insulating sheath. The researchers were able to confirm the presence of these stem cells by using antibodies and genetically modified animals that identified the specific protein markers on neuronal stem cells.

"It took 52 trials to successfully grow the lamina progenitor cells in a culture," said Dr. Bernstein, "so this was a challenging process." Dr. Bernstein and his collaborators needed to identify the correct mix of growth factors and other cell culture conditions that would be most conducive for the stem cells to grow and replicate. Eventually the research team found the stem cells could be coaxed into differentiating into several different types of neural cells. These include neurons and glial cells, which are known to be important for cell repair and cell replacement in different brain regions.

This discovery may prove to be game-changing for the treatment of eye diseases that affect the optic nerve. Dr. Bernstein and his research team plan to use genetically modified mice to see how the depletion of lamina progenitor cells contributes to diseases such as glaucoma and prevents repair.

Future research is needed to explore the neural progenitors repair mechanisms. "If we can identify the critical growth factors that these cells secrete, they may be potentially useful as a cocktail to slow the

progression of glaucoma and other age-related vision disorders." Dr. Bernstein added.

"This exciting discovery could usher in a sea change in the field of age-related diseases that cause vision loss," said E. Albert Reece, MD, Ph.D., MBA, Executive Vice President for Medical Affairs, UM Baltimore, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. "New treatment options are desperately needed for the millions of patients whose vision is severely impacted by glaucoma, and I think this research will provide new hope for them."

More information: S. L. Bernstein et al, The optic nerve lamina region is a neural progenitor cell niche, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2001858117

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