Researchers develop potential glaucoma treatment strategy to guide stem cells to the retina

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Petr Baranov, MD, PhD, (right) has a conversation with a colleague at his lab at the Schepens Eye Research Institute of Mass Eye and Ear in Boston. Credit: Mass Eye and Ear

Glaucoma is one of the leading causes of blindness worldwide, and vision loss, due to the loss of retinal ganglion cells (RGCs), cannot currently be reversed with any treatment. Some studies have looked at replacing RGCs through cell transplants, but this process is still in the research and development stage and fraught with limitations that highlight a need for a more precise manner of effectively repopulating these cells in the retina. Now, a multidisciplinary team led by researchers at the Schepens Eye Research Institute of Mass Eye and Ear has identified a promising new strategy for glaucoma cell replacement therapy.

In their new study, researchers changed the microenvironment in the eye in a way that enabled them to take stem cells from blood and turn them into retinal ganglion cells that were capable of migrating and surviving into the eye's retina. They conducted their study on the adult mouse retina, but the work's implications could one day be applied to human retina, according to the researchers who published their findings November 6th in Proceedings of the National Academy of Sciences (PNAS).

One limitation that prevents the success of current stem cell transplantation strategies in retina studies is that the majority of donor cells remain at the site of injection and do not migrate where they are most needed. To identify an improved solution, the researchers created RGCs out of stem cells, then tested the ability of various signaling molecules known as chemokines to guide these new neurons to their correct positions within the retina. The research team utilized a "big data" approach and examined hundreds of such molecules and receptors to find 12 unique to RGCs. They found stromal derived factor 1 was the best performing molecule for both migration and transplantation.

"This method of using chemokines to guide donor cell movement and integration represents a promising approach to restoring vision in

glaucoma patients," said senior author Petr Baranov, MD, Ph.D., of Mass Eye and Ear, who is also an assistant professor of Ophthalmology at Harvard Medical School. "It was an exciting journey to work with a team of talented scientists with unique expertise to develop novel techniques in this study to modify the local environment to guide cell behavior—techniques that potentially be applied to treat other neurodegenerative conditions."

The study was co-led by members of Baranov's lab at Mass Eye and Ear including bioengineer and lead study author Jonathan R Soucy, Ph.D., and lead bioinformatician Emil Kriukov, MD.

In addition to Baranov, Soucy and Kriukov, co-authors of the study include Levi Todd, Monichan Phay, Volha V. Malechka, John Dayron Rivera and Thomas A Reh.

The University of Washington discloses a patent incorporating the endogenous reprogramming technology described in this report with inventors LT and TAR.

More information: Jonathan R. Soucy et al, Controlling donor and newborn neuron migration and maturation in the eye through microenvironment engineering, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2302089120

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