inSight

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Glaucoma Awareness Month

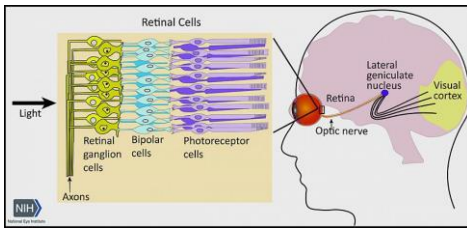
January is Glaucoma Awareness Month. We know that we need to raise awareness about glaucoma detection among the public. According to the National Eye Institute (NEI), of the 2.7 million Americans who have glaucoma, 50 percent don't know it.

Fortunately, we have many new treatment options available to us, MIGS in regards to surgery and lately Netarsudil in regards to medical therapy. We deploy selective laser trabeculoplasty, but still need to perform trabeculectomies, place drainage tubes and perform cyclo-destructive procedures to control the intraocular pressure.

Here is some current research that may give us hope in some day improving the care we give to our glaucoma patients:

Using gene editing, scientists at Northwestern University and the University of Wisconsin - Madison have developed new models of glaucoma in mice that resembled primary congenital glaucoma. By injecting a new, long-lasting and non-toxic protein treatment (Hepta-ANGPT1) into mice, the scientists were able to replace the function of genes that, when mutated, cause glaucoma. With this injectable treatment, the scientists also successfully prevented glaucoma from ever forming in this model. This same therapy, when injected into the eyes of healthy adult mice, reduced pressure in the eyes, supporting it as a possible new class of therapy for the most common cause of glaucoma in adults

Cellular crosstalk regulates the aqueous humor outflow pathway and provides new targets for glaucoma therapies: NATURE COMMUNICATIONS | (2021) 12:6072 | https://doi.org/10.1038/s41467-021-26346-0 | www.nature.com/naturecommunications



We know that Glaucoma results from irreversible neurodegeneration of the retinal ganglion cells. Available therapies slow vision loss by lowering elevated eye pressure, however some glaucoma progresses to blindness despite normal eye pressure. Neuroprotective therapies would be a leap forward, meeting the needs of patients who lack treatment options. Researchers at Mount Sinai School of Medicine and Yale showed that activating the CaMKII pathway helps protect retinal ganglion cells from a variety of injuries and in multiple glaucoma models.

The CaMKII (calcium/calmodulin-dependent protein kinase II) pathway regulates key cellular processes and functions throughout the body, including retinal ganglion cells in the eye. Using an antibody marker of CaMKII activity, the team discovered that CaMKII pathway signaling was compromised whenever retinal ganglion cells were exposed to toxins or trauma from a crush injury to the optic nerve, suggesting a correlation between CaMKII activity and retinal ganglion cell survival.

Searching for ways to intervene, they found that activating the CaMKII pathway with gene therapy proved protective to the retinal ganglion cells. Administering the gene therapy to mice just prior to the toxic insult (which initiates rapid damage to the cells), and just after optic nerve crush (which causes slower damage), increased CaMKII activity and robustly protected retinal ganglion cells.

Among gene therapy-treated mice, 77% of retinal ganglion cells survived 12 months after the toxic insult compared with 8% in control mice. Six months following optic nerve crush, 77% of retinal ganglion cells had survived versus 7% in controls.

Similarly, boosting CaMKII activity via gene therapy proved protective of retinal ganglion cells in glaucoma models based on elevated eye pressure or genetic deficiencies. Increasing retinal ganglion cell survival rates translated into greater likelihood of preserved visual function, according to cell activity measured by electroretinogram and patterns of activity in the visual cortex.

Three vision-based behavioral tests also confirmed sustained visual function among the treated mice. In a visual water task, the mice were trained to swim toward a submerged platform on the basis of visual stimuli on a computer monitor. Depth perception was confirmed by a visual cliff test based on the mouse's innate tendency to step to the shallow side of a cliff. Lastly, a looming test determined that treated mice were more apt to respond defensively (by hiding, freezing or tail rattling) when shown an overhead stimulus designed to simulate a threat, compared with untreated mice.

Preservation of vision after CaMKII-mediated protection of retinal ganglion cells
Cell 2021 Aug 5;184(16):4299-4314.e12. doi: 10.1016/j.cell.2021.06.031. Epub 2021 Jul 22

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