Geneticists develop novel gene therapy for glaucoma

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Scientists at Trinity College Dublin today announced a significant development toward a new therapeutic treatment of glaucoma.

Approximately 80 million people globally are affected by glaucoma, with a projected increase to more than 110 million by 2040. While topical eye drops are critical in preventing disease progression, up to 10% of patients become treatment resistant, putting them at risk for permanent vision loss.

The main clinical risk factor for glaucoma is elevated intraocular pressure; dangerous increases in pressure in the globe of the eye can lead to serious damage to the optic nerve head, which transmits light signals to the brain to allow us to see. This elevated pressure is caused by a build-up of unwanted proteins causing a blockage in drainage channels that, over time, can cause fluid to accumulate and pressure to increase.

The team at the Smurfit Institute of Genetics, in collaboration with the biotechnology company Exhaura Ltd., have shown that a gene therapy–based approach can decrease intraocular pressure in pre-clinical models of glaucoma. Their research is published this week in the journal *Science Advances*.

A single injection of a viral vector—essentially a virus the scientists have hijacked with the purpose of using it to deliver specific instructions to cells in the body—can increase the flow of aqueous fluid from the front of the eye and thereby decrease pressure in the eye. The key instructions are for cells to produce an enzyme matrix (metalloproteinase-3, or MMP-3) that helps kick this process into gear.

"This exciting project allowed us to bridge the gap between academia and industry and work very closely with a gene therapy company to develop a cutting edge therapy that we believe holds immense promise for patients in the future," said Professor Matthew Campbell, Professor in Genetics at Trinity.

Importantly, the work used multiple models of disease as well as making

use of donor human eyes to screen the therapeutic efficacy of the gene therapy approach. This makes the impressive results all the more promising.

From rare to common diseases

Gene therapies have seen a dramatic advance in recent years, with multiple drugs now approved by both the FDA and EMA. However, to date, all of the approved gene therapies are for the treatment of rare or ultra-rare conditions. As our understanding of the underlying mechanism of common diseases is now becoming more evolved, the concept of using gene therapy for common diseases is now possible.

Dr. Jeffrey O'Callaghan, Postdoctoral research fellow at Trinity and first author of the study, added, "Our novel approach to treating glaucoma using gene therapy is the culmination of over seven years of research. We are now hopeful that this therapy will pave the way to the development of treatments for other forms of blinding eye diseases."

A multidisciplinary team of geneticists, ophthalmologists and translational biologists undertook the study. The close collaboration with Exhaura Ltd also allowed the team to direct all experimental outputs towards the translation of the findings to a regulatory focused clinical program.

More information: Jeffrey O'Callaghan et al, Matrix metalloproteinase-3 (MMP-3) mediated gene therapy for glaucoma, *Science Advances* (2023). DOI: 10.1126/sciadv.adf6537. www.science.org/doi/10.1126/sciadv.adf6537

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