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Inkjet Printing Retinal cells vs. Gene Therapy in the treatment of Glaucoma

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Abstract

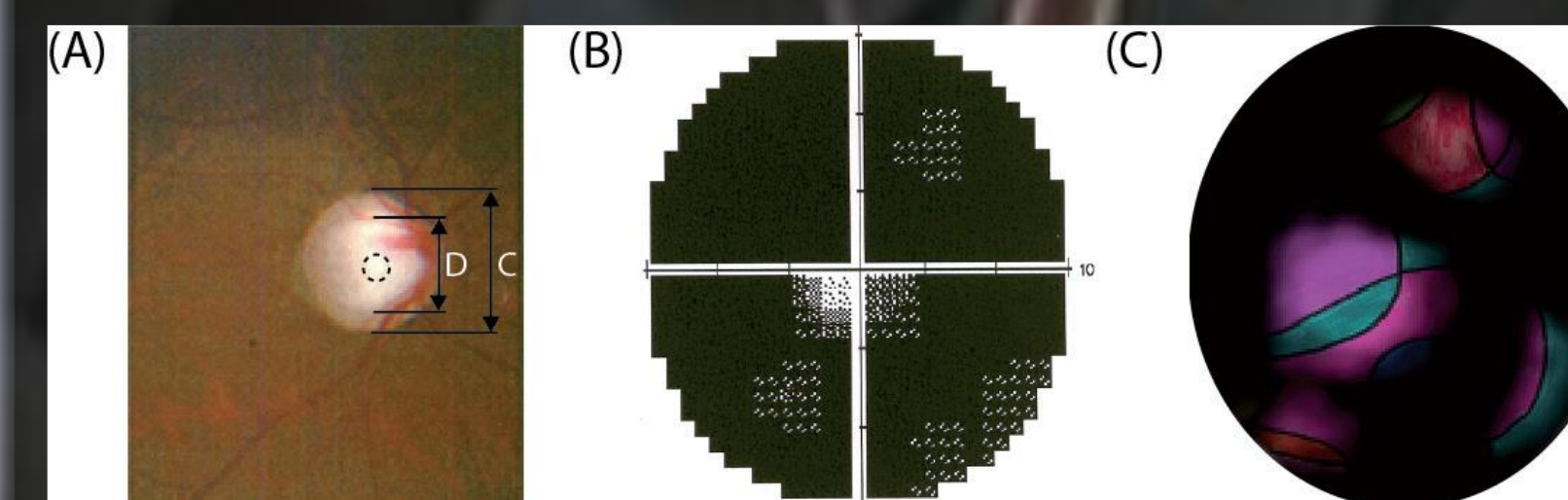
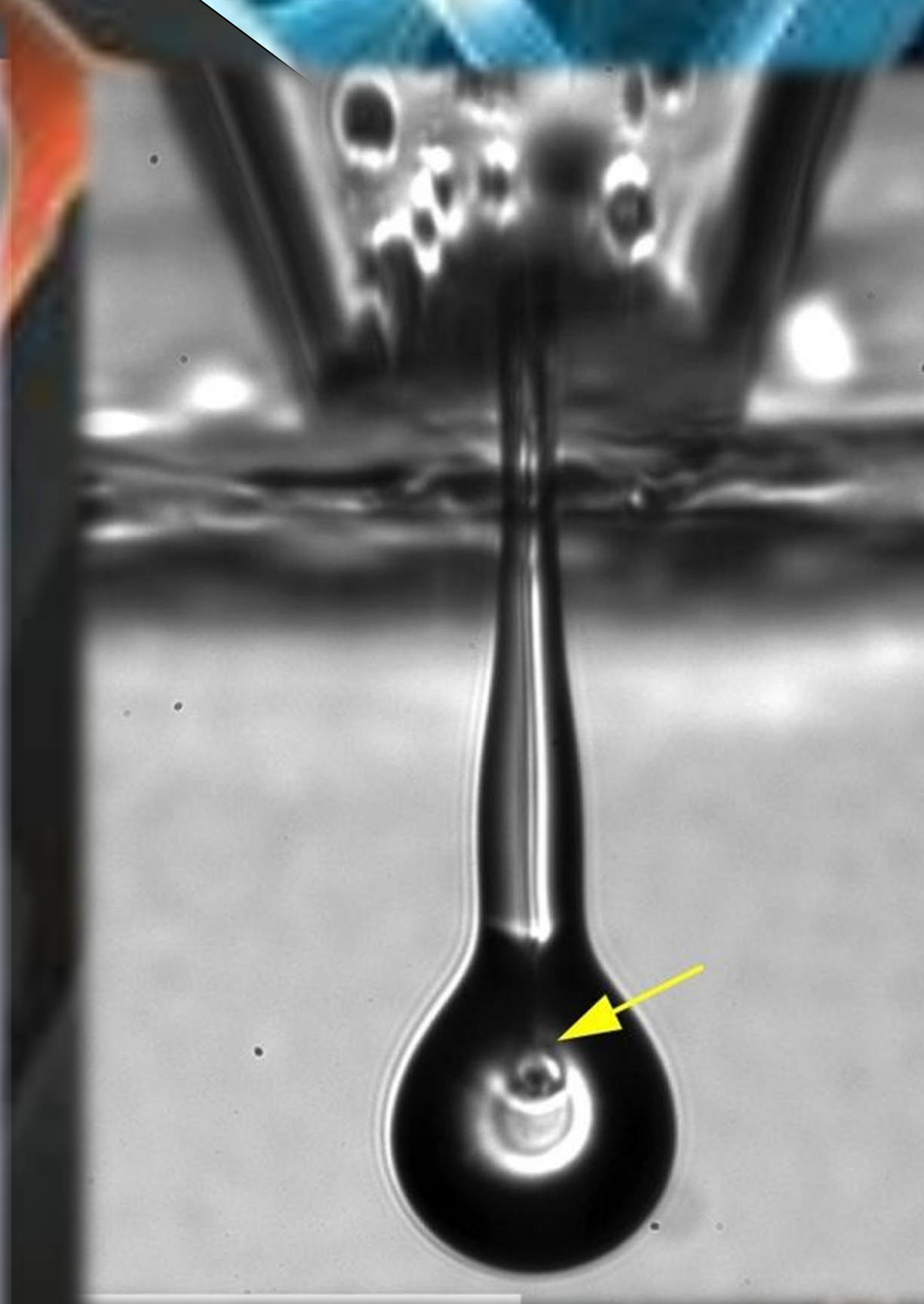
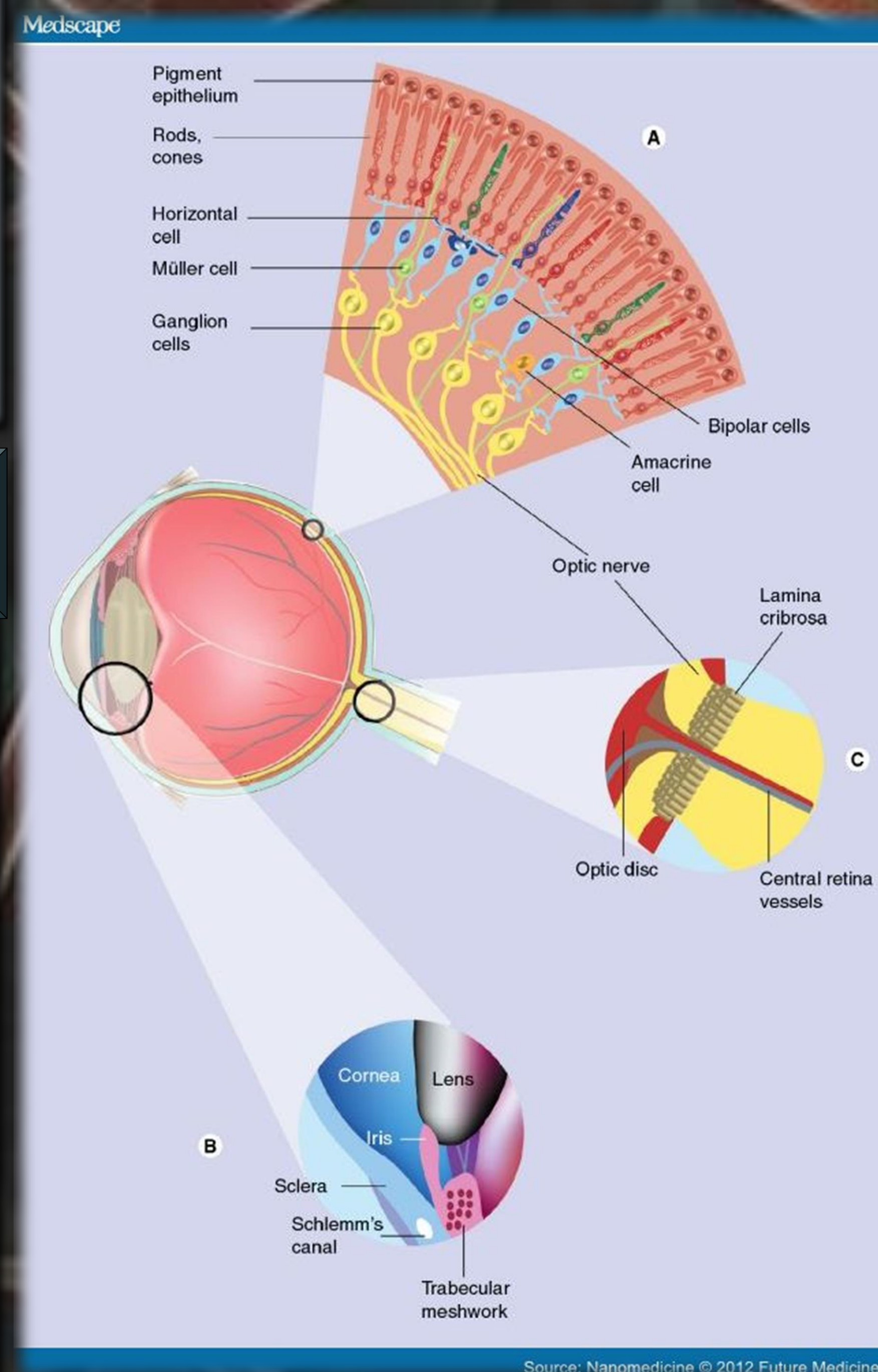
The neurodegenerative disease glaucoma is one of the leading causes of blindness and accounts for over ten million visits to physicians for treatment. Unfortunately, there is yet to be a concrete accepted approach to alleviating the effects of glaucoma. This dissertation examines recent studies and reports on the specifics of viral vectors, non-viral vectors, piezoelectric inkjet printing, heat inkjet printing, and glaucoma. A few of the studies involve the progression of an experiment while others combine and discuss the results of multiple experiments. Using these articles I compared the effectiveness of gene therapy to the use of inkjet printing to create retinal cells. By replacing, adding, or deleting a specific sequence in the human body, the gene expression of the eye can be altered. There are two different types of injections for gene therapy, viral vectors and non-viral vectors. Both methods typically target the trabecular meshwork and neuroretina to regulate the aqueous humor outflow and lower the intraocular pressure. In the case of glaucoma, the treatment solely provides neuroprotection instead of curing the disease, thus patients must undergo repeated injections in order to keep the disease from deteriorating. Inkjet printing of retinal cells have shown to produce three dimensional tissue grafts that may replace defective tissues. The printed cells have been tested for survivability and regeneration properties, since it has been suggested that the printing process can cause defects. Both heat inkjet printing and piezoelectric printing have been used to create neural cells. By evaluating the advantages and disadvantages of gene therapy as well as printing, I can evaluate whether or not inkjet printing can overtake gene therapy to become a conventional treatment for glaucoma in the near future. There have not been many clinical trials done on either of these methods for glaucoma, thus it is difficult to obtain a certain answer to the question at hand. At this point advancements in the area of three-dimensional printing neural sheets may provide a more promising cure. However, more research must be done on how each of these treatments affect glaucoma in humans.

Introduction

Glaucoma is a neuropathy caused by the failure of the eye to regulate the balance between the amount of internal fluid produced and drained. The apoptosis of retinal ganglion cells (RGC) has been found to cause obstruction in the trabecular meshwork that drains the aqueous humor. This results in dangerously high levels of intraocular pressure (IOP) which will damage the optic nerve and cause vision loss. Currently, the top approach to treating glaucoma is medication used to lower the intraocular pressure. This method provides only temporary relief, since the intraocular fluid will build back up again within a short time span. Patients receive side-effects, such as ocular surface disease, from the medication and often do not comply with daily dosages. Thus, it is crucial to work towards a treatment with long-lasting outcomes, less side-effects, and more patient compliance. Researchers have used gene therapy to target the genes myocilin, optineurin, and WDR 36 in order to establish neuroprotection and to lower intraocular pressure. Inkjet printing and scaffolding of retinal ganglion cells, on the other hand, can be used to implant healthy RGCs into a patient.

Results/Discussion

Gene therapy can be used to target specific parts within the eye, particularly the trabecular meshwork and neuroretina, using either viral or antiviral vectors. Targeting the trabecular meshwork would help regulate aqueous humor outflow and lower IOP. The trabecular meshwork's morphology can be altered by the transduction of coenzyme3, but the transduction also leads to the disruption of increased outflow in the anterior segments. The growth factor TGF- β has been a target for gene therapy, as it affects cell migration and proliferation, consequently slowing the progression of glaucoma. Alternatively, targeting astrocytes, microglia and Muller cells could promote the survival of RGCs especially in the early stages of glaucoma. Gene therapy's fallbacks lie in its intracellular and extracellular barriers to successful vector delivery. Piezoelectric or heat inkjet printing of retinal ganglion cells aims to replace the dead RGCs in the eye. The advantage of printing cells is that these RGCs can be printed in any pattern, ideally in one that mirrors the RGCs in the retina. These patterns subsequently can be made into a scaffold to implant into the eye. The main inquiry about this process is regarding the viability of the printed cells. Experiments using certain mediums and bio-papers have found that the electrophysiological and tensile properties of the printed cells remain intact, thus, capable to be implanted.



Conclusion

It is crucial to identify the strengths and weaknesses of advancing treatments for glaucoma before they are implemented on patients.

- Gene therapy can lower intraocular pressure and provide neuroprotection for long periods.
- While gene therapy can insert vectors to stop the apoptosis of retinal ganglion cells, it lacks the concrete ability to regenerate the cells that went through apoptosis.
- Printed RGCs can be made into scaffolds and are viable to be implanted into the tissue of the retina, acting as substitutes.
- The printing of RGCs is a first step, the next step of implanting printed neural tissues must be experimented and evaluated.
- It is difficult to conclude which is the better absolute treatment without further research done on the printing of cells, but the potential outcomes of printed RGCs indicate a more promising cure.

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