Viability of Transplanted De Novo Retinal Ganglion Cells in Human Donor Eyes Maintained Under Elevated Intraocular Pressure

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Purpose: Glaucoma is a group of optic neuropathies characterized by visual field loss, classically due to increased intraocular pressure (IOP) and retinal ganglion cell (RGC) degeneration. Current treatment options reduce IOP, but RGC degeneration persists. De novo RGCs can be differentiated from reprogrammed human corneal fibroblasts and transplanted into the retina to potentially restore vision in patients with late-stage disease when most RGCs are irreversibly damaged. We investigate the survival of these human induced pluripotent stem cell (IPSC) derived RGCs after culturing them in human donor eyes under conditions of elevated and normal IOP using the ocular translaminar autonomous system (TAS) chamber.

Methods: Human iPSCs were generated by reprogramming human donor corneal fibroblasts using Sendai viral vectors with Yamanaka factors. These iPSCs were then differentiated into retinal organoids from which RGCs were obtained. The RGCs were transduced with AAV2-GFP and transplanted into donor human eyes obtained from control individuals. They were pressurized for approximately 5 days, with the left eye maintained at normal IOP and right eye at elevated IOP. Viability was measured by expression levels of pro-survival pathways via qRT-PCR, immunohistochemistry staining, and electroretinography for retinal function (ERG).

Results: We successfully transplanted human RGCs into human donor eyes and visualized them after GFP transduction. We maintained a pressure differential between the two eyes for approximately 5 days using the TAS model. Differential expression of survival, inflammatory and apoptotic genes was identified between normal and high IOP. We identified retinal function changes under normal and high IOP after RGC transplantation.

Conclusions: Human iPSC derived RGCs provide a potential strategy to overcome vision loss in patients with diseases that damage RGCs such as glaucoma, Parkinson’s, Alzheimer's, multiple sclerosis, and traumatic optic neuropathy. Future investigation would involve integration of transplanted RGCs and directing their axons towards visual centers in the brain.