The Impact of Neuritin 1 on Retinal Ganglion Cell Survival in Human Donor Glaucomatous Eyes using the Translaminar Autonomous System

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Purpose: Glaucoma is a progressive optic neuropathy characterized by degeneration of retinal ganglion cells (RGCs), thinning of the retinal nerve layer, and atrophy of the optic nerve. Disease progression is characterized by increased intraocular pressure (IOP) and visual field loss. The only efficacious therapy for treating glaucoma is modification of IOP through pharmacological or surgical intervention. Although these interventions slow disease progression, they do not prevent RGC death entirely. Decreased axonal transport of essential neurotrophic factors contributes to RGC death. Neurotrophic factor supplementation has shown to improve RGC survival and sustain retinal function. We have previously demonstrated that secreted human Neuritin-1 (hNRN1) exhibits neuroprotection, regeneration, and preservation of RGC function in non-glaucomatous human eyes perfused in the ex-vivo Translaminar Autonomous System (TAS). We will investigate the effects of hNRN1 in glaucomatous human donor eyes within the TAS to evaluate if hNRN1 can protect RGC loss in diseased retinas.

Methods: Three pairs of glaucomatous human donor eyes were obtained from eye banks in accordance with the Declaration of Helsinki. Posterior cups were perfused using the TAS for 6-7 days under high and normal pressures with and without hNRN1. We then assessed RGC survival by measuring apoptosis, inflammation, and retinal markers using qRT-PCR and immunostaining. Retinal activity was measured using the OcuScience® Ex Vivo electroretinogram.

Results: Posterior eye cups were successfully maintained in the TAS under normal and high-pressure conditions for 6-7 days. Human NRN1 treated eyes showed differential expression of various inflammatory and apoptotic markers. Decreased extra cellular matrix deposition (Collagen, Fibronectin, Laminin) and improved retinal activity was seen within the treated glaucomatous eyes.

Conclusions: The TAS model can mimic pressure induced pathogenesis in human glaucoma. Data from this study shows that hNRN1 may serve as a potential therapeutic target by promoting RGC survival in glaucoma patients.