Neuroregenerative Effects of Human Neuritin 1 on Glaucomatous Human Retinal Ganglion Cells

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Purpose: Glaucoma is a group of optic neuropathies characterized by progressive loss of retinal ganglion cells (RGC) and corresponding visual field deficits. Current treatments can only slow the progression of glaucoma, but RGC death is not preventable and irreversible. Thus, neurotrophic factor therapy may be a suitable therapeutic approach. Human Neuritin 1 (NRN1) has demonstrated neurodegenerative and neuroprotective properties, and our group has previously established that NRN1 is downregulated in glaucomatous RGCs. We will investigate the therapeutic potential of NRN1 on human RGCs using a human stem cell-derived RGC model.

Methods: Corneal fibroblasts from glaucomatous and non-glaucomatous post-humous donor tissue were reprogrammed into induced pluripotent stem cells (iPSCs) using the CytoTuneTM-iPSC 2.0 Sendai reprogramming kit. These iPSCs were characterized via PCR (C-MYC, KLF4, SOX2, NANOG) and immunofluorescence staining (TRA-1-60, SOX2) and karyotyped. The iPSCs were differentiated into three-dimensional retinal organoids (ROs) from which RGCs were dissociated. PCR (*RBPMS, THY1)* and immunofluorescence staining (RBPMS, BRN3A, DAPI) were used to characterize RGCs. The RGC apoptosis and neurite outgrowth were measured with and without NRN1 treatment using markers such as CASP3 and NEFL respectively.

Results: NRN1 treatment enhanced neurite outgrowth and reduced RGC apoptosis in NRN1 treated RGCs compared to untreated cells.

Conclusions: These findings confirm that NRN1 enhances neurite outgrowth and RGC survival in human glaucomatous cells, further demonstrating its potential as a candidate for glaucoma therapy.