The challenge of regenerative therapies for the optic nerve in glaucoma

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This review arose from a discussion of regenerative therapies to treat optic nerve degeneration in glaucoma at the 2015 Lasker/IRRF Initiative on Astrocytes and Glaucomatous Neurodegeneration. In addition to the authors, participants included Jonathan Crowston, Andrew Huberman, Elaine Johnson, Richard Lu, Hemai Phatnami, Rebecca Sappington, and Don Zack. Glaucoma is a neurodegenerative disease of the optic nerve, and is the leading cause of irreversible blindness worldwide. The disease progresses as sensitivity to intraocular pressure (IOP) is conveyed through the optic nerve head to distal retinal ganglion cell (RGC) projections. Because the nerve and retina are components of the central nervous system (CNS) , their intrinsic regenerative capacity is limited. However, recent research in regenerative therapies has resulted in multiple breakthroughs that may unlock the optic nerve's regenerative potential. Increasing levels of Schwann-cell derived trophic factors and reducing potent cell-intrinsic suppressors of regeneration have resulted in axonal regeneration even beyond the optic chiasm. Despite this success, many challenges remain. RGC axons must be able to form new connections with their appropriate targets in central brain regions and these connections must be retinotopically correct. Furthermore, for new axons penetrating the optic projection, oligodendrocyte glia must provide myelination. Additionally, reactive gliosis and inflammation that increase the regenerative capacity must be outweigh pro-apoptotic processes to create an environment within which maximal regeneration can occur.

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