# Neuroprotective effects of transcription factor Brn3b in an ocular hypertension rat model of glaucoma

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PURPOSE: Glaucoma is an optic neuropathy commonly associated with elevated intraocular pressure (IOP) , leading to optic nerve head (ONH) cupping, axon loss and apoptosis of retinal ganglion cells (RGCs) which could ultimately result in blindness. Brn3b is a class-4 POU domain transcription factor that plays a key role in RGC development, axon outgrowth and pathfinding. Previous studies suggest that a decrease in Brn3b levels occurs in animal models of glaucoma. The goal of this study was to determine if adeno-associated virus (AAV) -directed overexpression of the Brn3b protein could have neuroprotective effects following elevated IOP-mediated neurodegeneration.

METHODS: IOP was elevated in one eye of Brown Norway rats (Rattus norvegicus) , following which the IOP-elevated eyes were intravitreally injected with AAV constructs encoding either the GFP (rAAV-CMV-GFP and rAAV-hsyn-GFP) or Brn3b (rAAV-CMV-Brn3b and rAAV-hsyn-Brn3b) . Retina sections through the ONH were stained for synaptic plasticity markers and neuroprotection was assessed by RGC counts and visual acuity tests.

RESULTS: AAV-mediated expression of the Brn3b protein in IOP-elevated rat eyes promoted an upregulation of growth associated protein-43 (GAP-43) , actin binding LIM protein (abLIM) and acetylated α-tubulin (ac-Tuba) , both posterior to the ONH and in RGCs. The RGC survival as well as axon

integrity score were significantly improved in IOP-elevated rAAV-hsyn-Brn3b injected rats compared to those of the IOP-elevated rAAV-hsyn-GFP injected rats. Additionally, intravitreal rAAV-hsyn-Brn3b administration significantly restored the visual optomotor response in IOP-elevated rat eyes.

CONCLUSION:AAV-mediated Brn3b protein expression may be a suitable approach for promoting neuroprotection in animal models of glaucoma.

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