Early Gene Expression Changes in the Retinal Ganglion Cell Layer of a Rat Glaucoma Model

Guo Y, Johnson EC, Cepurna WO, Dyck J, Doser T, Morrison JC.

Ophthalmology, Oregon Health & Sciences University, Portland, United States.

PURPOSE: To identify patterns of early gene expression changes in the retinal ganglion cell layer (GCL) of a chronic rodent model of glaucoma.

METHODS: Chronic elevation of intraocular pressure (IOP) was produced in rats by episcleral vein injection of hypertonic saline (N = 30) . GCLs isolated by laser capture microdissection were grouped by grading of the nerve injury (25% for advanced injury) . Gene expression was determined by cDNA microarray of independent GCL RNA samples. Quantitative PCR (qPCR) was used to further examine expression of selected genes.

RESULTS: By array analysis, 533 GCL genes (225 up, 308 down) were significantly regulated in early injury. Compared to only one major upregulated gene class of metabolism regulation, more were downregulated including mitochondria, ribosome, proteasome, energy pathways, protein synthesis, protein folding, and synaptic transmission. qPCR confirmed an early upregulation of Atf3. With advanced injury, 1790 GCL genes were significantly regulated (997 up, 793 down) . Altered gene categories included upregulated protein synthesis, immune response, cell apoptosis, and downregulated dendrite morphogenesis and axon extension. Of all the early changed genes 50% were not present in advanced injury. These uniquely affected genes were mainly associated with upregulated transcription regulation and downregulated protein synthesis.

CONCLUSIONS: Early GCL gene responses to pressure-induced injury are characterized by an upregulation of Atf3 and extensive downregulation in genes associated with cellular metabolism and neuronal functions. Most likely, these changes represent those specific to RGCs and are thus potentially important for enhancing RGC survival in glaucoma.

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