Core transcription programs controlling injury-induced neurodegeneration of retinal ganglion cells

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Regulatory programs governing neuronal death and axon regeneration in neurodegenerative diseases remain poorly understood. In adult mice, optic nerve crush (ONC) injury by severing retinal ganglion cell (RGC) axons results in massive RGC death and regenerative failure. We performed an in vivo CRISPR-Cas9-based genome-wide screen of 1,893 transcription factors (TFs) to seek repressors of RGC survival and axon regeneration following ONC. In parallel, we profiled the epigenetic and transcriptional landscapes of injured RGCs by ATAC-seq and RNA-seq to identify injury-responsive TFs and their targets.

These analyses converged on four TFs as critical survival regulators, of which ATF3/CHOP preferentially regulate pathways activated by cytokines and innate immunity and ATF4/C/EBP? regulate pathways engaged by intr

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