Globally, stroke is the second leading cause of death, and the sixth most common cause of disability. Despite, the most advanced medical technologies, 60% of people who suffer a stroke either die or develop permanent disabilities - a loss of vision, speech or paralysis. The significant economic impact and social cost of caregiving for people living with disabilities makes its prevention and treatment crucial. Most people who suffer from vision loss after a stroke (about one-third of stroke survivors) do not fully recover their vision. It is therefore important to develop strategies to allow stroke victims to regain their sight. Injury can be severe and cause blindness by damaging the optic nerve, the link between the eye and brain. Central nervous system white matter stroke, and diseases such as ischemic optic neuropathy, causes permanent blindness due to retinal ganglion cell (RGC) axon damage and cell death. In the eye, RGCs are CNS neurons that transmit visual information from the retina via the optic nerve to the brain. My project will study how the regulation of genes in the eye can be controlled to help protect retinal cells from damage after a stroke. This proposal will reveal the role of myocyte enhancer factor 2 (MEF2) transcription factors and associated class IIa histone deactylases (HDACs 4/5/7/9) co-repressors in the regulation of RGC gene expression that is important for neuroprotection and potentially axon regeneration. Our results, showed that in RGCs, MEF2A and potentially MEF2D oppose RGC survival following axonal injury. Recent studies, support the premise of this project that inhibition of MEF2A transcriptional activity, either by loss or mutation or by enhancement of class IIa HDAC activity, would be protective in stroke. We will tested whether Mef2a/Mef2d gene deletion (either singly or together) is beneficial in ischemic optic neuropathy. An important strength of this application is the coupling of *in vitro* signal transduction research with *in vivo* functional studies, using primary neuronal cultures and a model for white matter ischemia. This project will be testing of new potential gene therapies that may prove beneficial to those who are at risk for losing their sight due to stroke. Importantly, although my research is directed towards the eye, the mechanism and potential therapies that will be studied are expected to be widely applicable to strokes in other parts of the brain. Using both in vitro and in vivo models, I anticipate that my research will elucidate novel basic neuronal mechanisms and provide novel therapeutics for the harmful sequelae of stroke.