Mitochondrial Heat Shock Protein 70: New Target for Optic Neuritis Therapy

Grazyna Adamus

Ocular Immunology Laboratory, Casey Eye Institute, Oregon Health and Science University, Portland, Oregon, United States; adamusg@ohsu.edu

Optic neuritis is an inflammatory disorder of the optic nerve and often the first presenting symptom of multiple sclerosis (MS). Typically, it results in loss of a significant number of retinal ganglion cells (RGC) axons and thinning of retinal nerve fiber layer. Multiple sclerosis is chronic mediated by inflammatory and autoimmune mechanisms, leading to loss of neurons and axonal damage and in consequence permanent disability. The disease involves focal demyelinated plaques within the central nervous system (CNS), with varying levels of inflammation, gliosis, and neurodegeneration. Most available treatments are focused on the inflammatory component of the disease; however, those treatments fail in preventing neurodegeneration that cause irreversible loss of function. In recent years, a failure of mitochondrial function has been shown to contribute to the pathogenesis of neurodegeneration in MS. Dysfunctional mitochondria are crucial contributors to damage and loss of both axons and neurons. In particular, the mitochondrial protein HSP70 that ameliorates mitochondrial dysfunction led to irreversible visual loss and atrophy of the optic nerve in EAE (experimental autoimmune encephalomyelitis; model of MS), suggesting that this protein may be useful therapeutic target in optic neuritis and MS. In this issue, Talla et al. sought to determine whether overexpressing mitochondrial HSP70 in retinal RGCs in EAE mice trigger neuroprotection in the visual system. When researchers targeted neurons in the optic nerve by using a gene therapy approach, an overexpression of the intracellular mtHSP70 in RGCs and their axons not only preserved of EAE mice vision, but also prevented neuronal apoptosis and axonal death. These finding suggests that new therapeutic approach using gene therapy with mitochondrial HSP70 may also benefit patients with optic neuritis and MS.

References