Diabetic retinopathy

Retinal ganglion cell damage serves as a key indicator of various retinal degenerative diseases, including diabetic retinopathy (DR), glaucoma, retinal arterial and retinal vein occlusions, as well as inflammatory and traumatic optic neuropathies. Despite the growing body of data on the RGC proteomics associated with these conditions, there has been no dedicated study conducted to compare the molecular signaling pathways involved in the mechanism of neuronal cell death. Therefore, Starr et al. launched the study using two different insults leading to RGC death: glutamate excitotoxicity and optic nerve crush (ONC). C57BL/6 mice were used for the study and underwent NMDA- and ONC-induced damage. Twenty-four hours after ONC and 1 hour after NMDA injection, they collected RGCs using CD90.2 coupled magnetic beads, prepared protein extracts, and employed LC-MS for the global proteomic analysis of RGCs. Statistically significant changes in proteins were analyzed to identify changes to cellular signaling resulting from the treatment. They identified unique and common alterations in protein profiles in RGCs undergoing different types of cellular stresses. The study not only identified both unique and shared proteomic changes but also laid the groundwork for the future development of a therapeutic platform for testing gene candidates for DR and glaucoma [1].

Visual impairment in diabetes is a growing public health concern. Apart from the well-defined diabetic retinopathy, disturbed optic nerve function, which is dependent on the myelin sheath, has recently been recognized as an early feature of visual impairment in diabetes. However, the underlying cellular mechanisms remain unclear. Using a streptozotocin-induced diabetic mouse model, Wu et al. observed a myelin deficiency along with a disturbed composition of oligodendroglial lineage cells in the diabetic optic nerve. They found that new myelin deposition, a continuous process that lasts throughout adulthood, was diminished during pathogenesis. Genetically dampening newly generated myelin by conditionally deleting olig2 in oligodendrocyte precursor cells within this short time window extensively delayed the signal transmission of the adult optic nerve. In addition, clemastine, an antimuscarinic compound that enhances myelination, significantly restored oligodendroglia and promoted the functional recovery of the optic nerve in diabetic mice. The results point to the role of new myelin deposition in optic neuropathy under diabetic insult and provide a promising therapeutic target for restoring visual function [2]

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Starr CR, Mobley JA, Gorbatyuk MS. Comparative Proteomic Study of Retinal Ganglion Cells Undergoing Various Types of Cellular Stressors. Exp Eye Res. 2024 Aug 8:110032. doi: 10.1016/j.exer.2024.110032. Epub ahead of print. PMID: 39127235.
2)
Wu H, Chen X, Yu B, Zhang J, Gu X, Liu W, Mei F, Ye J, Xiao L. Deficient deposition of new myelin impairs adult optic nerve function in a murine model of diabetes. Glia. 2023 Jan 20. doi: 10.1002/glia.24341. Epub ahead of print. PMID: 36661098.