γ-Synuclein Antibodies Have Neuroprotective Potential on Neuroretinal Cells via Proteins of the Mitochondrial Apoptosis Pathway

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The family of synuclein proteins (α, β and γ) are related to neurodegenerative disease e.g. Parkinson disease and Morbus Alzheimer. Additionally, a connection between γ-synuclein and glaucoma, a neurodegenerative disease characterized by a progressive loss of retinal ganglion cells, which finally leads to blindness, exists. The reason for the development of glaucoma is still unknown. Recent studies evaluating the participation of immunological components, demonstrate complex changed antibody reactivities in glaucoma patients in comparison to healthy people, showing not only up-regulations (e.g. alpha-fodrin antibody) but also down-regulations (e.g. γ-synuclein antibody) of antibodies in glaucoma patients. Up-regulated antibodies could be auto-aggressive, but the role of down-regulated antibodies is still unclear. Previous studies show a significant influence of the serum and the antibodies of glaucoma patients on protein expression profiles of neuroretinal cells.

The aim of this study was to investigate the effect of γ-synuclein antibody on the viability and reactive oxygen species levels of a neuroretinal cell line (RGC-5) as well as their interaction with cellular proteins. We found a protective effect of γ-synuclein antibody resulting in an increased viability (up to 15%) and decreased reactive oxygen species levels (up to -12%) of glutamate and oxidative stressed RGC-5. These can be traced back to anti-apoptotic altered protein expressions in the mitochondrial apoptosis pathway indicated by mass spectrometry and validated by microarray analysis such as active caspase 3, bcl-2 associated-x-protein, S100A4, voltage-dependent anion channel, extracellular-signal-regulated-kinase (down-regulated) and baculoviral IAP repeat-containing protein 6, phosphorylated extracellular-signal-regulated-kinase (up-regulated) . These changed protein expression are triggered by the γ-synuclein antibody internalization of RGC-5 we could see in immunohistochemical stainings.

These findings let us assume a novel physiological function of γ-synuclein antibodies and give insights in the role of autoantibodies in glaucoma. We hypothesize that the down-regulation of autoantibodies found in glaucoma patients lead to a loss of protective autoimmunity.

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