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Manipulating ER chaperones and the UPR for neuroprotection in retinal diseases

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ER chaperones are a group of proteins in the ER that assist in *de novo* protein folding/refolding and the timely removal of irreversibly misfolded and aggregated proteins to maintain the cellular proteome homeostasis. They are critical components and major downstream targets of the highly conserved unfolded protein response (UPR) that harnessing transcriptional and translational regulatory systems to reduce/eliminate ER stress. Major chaperones and folding enzymes in the ER include: Chaperones of the heat shock protein family such as GRP78 and its co-chaperone partners (e.g., p58^{IPK}); Chaperone lectins such as calnexin and calreticulin and thioredoxins of the protein disulfide isomerase (PDI) family. Recent work demonstrates that manipulating the UPR or enhancing ER chaperone activities can protect retinal neurons in a wide range of acute or chronic injury models. Over expression of GRP78 or p58^{IPK} attenuates ER stress and protects retinal ganglion cells (RGCs) against apoptosis and cell death. Mice lacking p58^{IPK} are more sensitive to ER stress and RGC loss related to glutamate toxicity or aging. The presentation will discuss the intriguing neuroprotective potential of ER chaperones and UPR manipulation in retinal neurons and RPE cells and highlight their probable implication in the prevention and treatment of retinal degeneration.

Biography

Sarah X Zhang is currently a tenured Associate Professor of Ophthalmology, Biochemistry and Neuroscience at School of Medicine and Biomedical Sciences, State University of New York. She is a Faculty Member at the SUNY Eye Institute and Graduate School at SUNY Buffalo. She is a well-established Clinician Scientist and Vision Researcher and has published over 75 peer-reviewed journal articles, reviews and book chapters. Her laboratory studies disease mechanisms and ER stress signaling in diabetic retinopathy, age-related macular degeneration and glaucomatous retinopathy. She has served on editorial boards for 7 professional journals and on NIH and international grant review panels.

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