Role of crystallin proteins in retinal neurodegeneration and neuroinflammation

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Alpha-crystallins have been extensively studied for their role in the lens and more specifically cataract formation, which is often associated to mutations and alterations affecting crystallin proteins. More recently, observations have raised growing interest about their implication in retinal function under normal and pathological conditions. We are particularly interested in the role that α-crystallins can play in retinal neurodegeneration and associated neuroinflammation. The function and regulation of α-crystallins in retinal neurodegenerative diseases were analyzed using a combination of experimental approaches ranging from in-vivo analyses of transgenic mice, to validation and specific analyses in post-mortem human tissues, including by cell specific analyses of crystallin mutants. While Ko-α-crystallin mice were used to dissect the respective functions of αA- and αB-crystallins in the retina over time, human tissues were used to identify specific changes affecting crystallins in disease conditions, and cell culture models were used to assess the impact of those changes on cellular function and survival. We demonstrated a separate function and regulation of αA- and αB-crystallins in retina under normal and pathological conditions. We also characterized the cellular specificity of expression of αA- and αB-crystallins in these conditions. We further identified specific alterations affecting alpha-crystallins under chronic disease conditions that have a dramatic impact on retinal cell function and ultimately survival. This work clearly demonstrates the important role played by alpha-crystallins in the regulation of retinal cell function and survival under chronic conditions associated with neuroinflammation and neurodegeneration. It also points to the specificity of each crystallin and their respective differences in regards to their cellular expression, regulation and implications.

Biography
Patrice E Fort has earned his MS in Neurosciences and PhD in Cellular and Molecular Aspects of Biology from the University of Strasbourg, France before joining in 2005 the Penn State Retina Research Group to study the diabetes associated mechanisms that lead to vision loss. He has characterized the role and regulation of crystallin proteins in the retina during diabetes in 2008. He was then recruited in 2011 as an Assistant Professor in the Department of Ophthalmology of the University of Michigan where he continues to study the regulation of intrinsic protective mechanisms in the retina under normal and pathological conditions.

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