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## Key role of alpha-crystallins in aging-related retinal disorders

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One of the major visual complications due to aging is cataract formation and is often associated to mutations and alterations affecting crystallin proteins. Because of this, the roles of crystallins in the lens during aging have been extensively studied, but recent observations have raised growing interest about their implication in normal and pathological aging of the retina. Function and regulation of  $\alpha$ -crystallins were analyzed using biochemical approaches on tissues from ko- $\alpha$ -crystallin animals under normal and pathological conditions. Ko- $\alpha$ -crystallin mice were also used to dissect the respective functions of  $\alpha$ A- and  $\alpha$ B-crystallins in the retina during normal and pathological aging. Retinal anatomy and function were analyzed by performing longitudinal studies using non-invasive methods. Additionally mass spectrometry was used to study the post-translational modifications affecting  $\alpha$ -crystallins in relation to their functional activity. We demonstrated that protein-protein interactions involving  $\alpha$ A- and  $\alpha$ B-crystallins are disrupted in pathological aging conditions. In addition we demonstrated that under these conditions, their solubility and sub-cellular properties were altered and that it is associated with specific changes of phosphorylation affecting their chaperone function. Interestingly while absence of  $\alpha$ A- or both  $\alpha$ A- and  $\alpha$ B-crystallin led to a larger increase in retinal cell death and perturbations of retinal functions during aging, absence of  $\alpha$ B-crystallin prevented any anatomical or functional defects. This work clearly demonstrates that pathological aging is associated with disruption of the protective function of  $\alpha$ -crystallins in the retina through alterations of protein-protein interaction associated with post-translational modifications and biochemical alterations. This study demonstrates how pathological aging can alter the action and regulation of intrinsic protective mechanisms in the retina.

### Biography

Patrice E. Fort earned his M.S. in Neuro sciences and Ph.D. 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. Promoted faculty in 2008, he characterized the role and regulation of crystallin proteins in the retina during diabetes. 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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