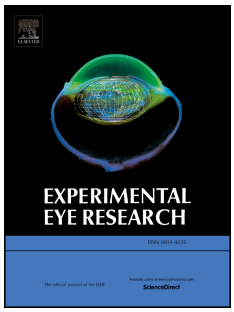
Accepted Manuscript



BetaB2-crystallin mutations associated with cataract and glaucoma leads to mitochondrial alterations in lens epithelial cells and retinal neurons

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PII: S0014-4835(17)30057-X

DOI: 10.1016/j.exer.2017.01.005

Reference: YEXER 7082

To appear in: *Experimental Eye Research*

Received Date: 31 May 2016

Revised Date: 19 January 2017

Accepted Date: 22 January 2017

Please cite this article as: Dulle, J.E., Rübsam, A., Garnai, S.J., Pawar, H.S., Fort, P.E., BetaB2-crystallin mutations associated with cataract and glaucoma leads to mitochondrial alterations in lens epithelial cells and retinal neurons, *Experimental Eye Research* (2017), doi: 10.1016/j.exer.2017.01.005.

BetaB2-crystallin mutations associated with cataract and glaucoma leads to mitochondrial alterations in lens epithelial cells and retinal neurons

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Abstract

Crystallin proteins are the most prominent protein of the lens and have been increasingly shown to play critical roles in other tissues, especially the retina. Members of all 3 sub-families of crystallins, alpha-, beta- and gamma-crystallins have been reported in the retina during diabetes, traumatic injury and other retinal diseases. While their specific role in the retina is still unclear and may vary, beta-crystallin proteins have been shown to play a critical role in ganglion cell survival following trauma. We recently reported the correlation between a gene conversion in the betaB2-crystallin gene and a phenotype of familial congenital cataract. Interestingly, in half of the patients, this phenotype was associated with glaucoma. Taken together, these data suggested that the mutations we recently reported could have an impact on the role of betaB2-crystallin in both lens epithelial cells and retinal neurons. Consistent with this hypothesis, we show in the current study that the gene conversion leading to an amino acid conversion lead to a loss of solubility and a change of subcellular localization of betaB2-crystallin in both cell types. While the overall observations were similar in both cell types, there were some important nuances between them, suggesting different roles and regulation of betaB2-crystallin in lens cells versus retinal neurons. The data reported in this study strongly support a significant role of betaB2-crystallin in both lenticular and retinal ocular tissues and warrant further analysis of its regulation and its impact not only in cataract formation but also in retinal neurodegenerative diseases.