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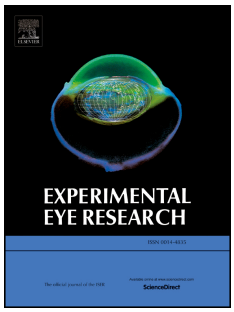

BNIP3L/NIX is required for elimination of mitochondria, endoplasmic reticulum and Golgi apparatus during eye lens organelle-free zone formation

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BNIP3L/NIX is required for elimination of mitochondria, endoplasmic reticulum and Golgi apparatus during eye lens organelle-free zone formation

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ABSTRACT: The formation and life-long growth of the ocular lens depends on the continuous differentiation of lens epithelial cells into lens fiber cells. To achieve their mature structure and transparent function, newly formed lens fiber cells undergo a series of cellular remodeling events including the complete elimination of cellular organelles to form the lens organelle-free zone (OFZ). To date, the mechanisms and requirements for organelle elimination by lens fiber cells remain to be fully elucidated. In previous studies, we detected the presence of mitochondria contained within autophagolysosomes throughout human and chick lenses suggesting that proteins targeting mitochondria for degradation by mitophagy could be required for the elimination of mitochondria during OFZ formation. Consistently, high-throughput RNA sequencing of microdissected embryonic chick lenses revealed that expression of a protein that targets mitochondria for elimination during erythrocyte formation, called BCL2 interacting protein 3-like protein (BNIP3L/NIX), peaks in the region of lens where organelle elimination occurs. To examine the potential role for BNIP3L in the elimination of mitochondria during lens fiber cell remodeling, we analyzed the expression pattern of BNIP3L in newborn mouse lenses, the effect of its deletion on organelle elimination and its co-localization with lens organelles. We demonstrate that the expression pattern of BNIP3L in the mouse lens is consistent with it playing an important role in the elimination of mitochondria during lens fiber cell organelle elimination. Importantly, we demonstrate that deletion of BNIP3L results in retention of mitochondria during lens fiber cell remodeling, and, surprisingly, that deletion of BNIP3L also results in the retention of endoplasmic reticulum and Golgi apparatus but not nuclei. Finally, we show that BNIP3L localizes to the endoplasmic reticulum and Golgi apparatus of wild-type newborn mouse lenses and is contained within mitochondria, endoplasmic reticulum and Golgi apparatus isolated from adult mouse liver. These data identify BNIP3L as a novel requirement for the elimination of mitochondria, endoplasmic reticulum and Golgi apparatus during lens fiber cell remodeling and they suggest a novel function for BNIP3L in the regulation of endoplasmic reticulum and Golgi apparatus populations in the lens and non-lens tissues.