

Identification of the molecular pathological basis for L540P-IRBP linked to retinal dystrophy

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Background: IRBP plays a pivotal role in supporting visual function and survival of photoreceptors. L540P mutation in IRBP may cause retinal dystrophy; yet its pathogenic mechanism was unknown. This study aimed to identify a disease mechanism for the mutation.

Purpose: The L540P mutation of interphotoreceptor retinoid-binding protein (IRBP) is found in patients with retinal dystrophy; yet, its pathogenicity and underlying disease mechanisms remain unknown. The purpose of this study was to determine the effect of the mutation on IRBP secretion and to identify factors that regulate secretion of L540P-IRBP.

Methods: Wild-type & mutant IRBPs were expressed in HEK293T cells under varying concentrations of fetal bovine serum (FBS) at 30°C & 37°C. Secreted- and intracellular-IRBP were detected by immunoblot analysis.

Results: Wild-type but not mutant IRBP was secreted into the media at 37°C. FBS concentrations did not influence secretion of L540P-IRBP at 37°C. However, low temperature significantly rescued secretion of the mutant IRBP.

Conclusion: Our findings suggest that 1) L540P mutation abolishes secretion of IRBP, resulting in a lack of functional IRBP in the subretinal matrix, 2) extracellular conditions influence secretion of L540P-IRBP.