May 20th, 12:30 PM

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Purpose: Mutations in the *CEP290* gene are a frequent cause of childhood blindness disorder, Leber congenital amaurosis (LCA). Not much is known about the mode of action of CEP290 in the retina. We previously showed that CEP290 interacts with RKIP and that RKIP protein is abnormally accumulated in *rd16* (retinal degeneration 16) mouse, a model of *Cep290*- associated retinal degeneration. The purpose of this study is to evaluate the role of RKIP accumulation in mediating photoreceptor degeneration in the *rd16* mouse.

Methods: *rd16/rd16*:*Rkip ko/Rkip ko* double homozygous knock out mice were generated by breeding *rd16* and *Rkip ko* mice (both on C57BL6/J background). Photoreceptor structure and function were evaluated by Histology, Transmission electron microscopy (TEM), Immunofluorescence microscopy and Electroretinography (ERG).

Results: We detected improved photoreceptor structure in the double homozygous mutant mice compared to *rd16* at postnatal day 18 (P18). In addition, Rhodopsin and M-opsin staining in Rd16 Rkip$^{-/-}$ mouse showed increased outer segment localization in the double mutant mice. Finally, ERG analysis showed 40% scotopic response recovery in Rd16 Rkip$^{-/-}$ from Rd16 mouse.

Conclusions: We propose that accumulation of RKIP due to mutation in CEP290, although not the only pathway is a critical step in the pathogenesis of associated severe retinal degeneration. Altering RKIP levels may potentially be used in combination with other modalities as an approach for treating such disorders.