UNIVERSITY OF LOUISVILLE

COLLEGE OF ARTS & SCIENCES

Department of Chemistry

Brown and Williamson Series
January 27, 2023
@4:00 pm
CBLL16

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What night blind mice tell us about synapse assembly in the retina-and gene therapy

ABSTRACT:

Complete congenital stationary night blindness (cCSNB) is a heterogeneous disorder characterized by poor dim light vision, myopia, and nystagmus that is caused by mutations in genes critical for signal transmission between photoreceptors and depolarizing bipolar cells (DBCs). One such gene, *LRIT3,* is required for assembly of the post-synaptic signaling complex (signalplex) at the dendritic tips of DBCs, although the number of signalplex components impacted is greater in cone DBCs than in rod bipolar cells. We used LRIT3 knockout mice to determine if gene therapy using rAAV was feasible for this form of CSNB. We constructed rAAV vectors that used to promoters to express LRT3 in either rods or cones. rAAV was introduced in 2 month old mice by sub-retinal injection. Two months after treatment electroretinograms to test for function, and immunohistochemistry to test for signalplex components was done.

The results showed that the ERG b-wave could be partially restored in both rods and cones. All components in the signalplex, mGluR6, GPR179 and TRPM1 were expressed and localized normally.

These data show gene therapy using rAAV to restore expression of LRIT3 in photoreceptors of mutant mice partially restores function. This presents the possibility that night vision in patients with cCSNB caused by mutations in LRIT3 could be restored by a similar strategy.

EDUCATION:

Ph.D., 1984, Biochemistry, University of Queensland, Queensland, Australia