SNAP-25, but not SNAP-23, is Essential for Photoreceptor Development, Survival, and Function in Mice

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Introduction: Vision requires the effective communication of light information by photoreceptors onto their second-order cells. Photopigments in the outer segments of photoreceptors transform photons of light into an electric signal. This signal is then passed on from photoreceptors through the release of the neurotransmitter glutamate. SNARE-mediated vesicular transport is thought to play roles in photoreceptor glutamate exocytosis and photopigment delivery. However, the functions of Synaptosomal-associated protein (SNAP) isoforms in photoreceptors are unknown.

Methods: We revisit the expression of SNAP-23 and SNAP-25 using a combination of in situ hybridization and immunohistology. Following, we generate photoreceptor-specific knockout mice to investigate the roles of SNAP-23 and SNAP-25. We look at retinal morphology, light response, and visual acuity in these conditional knockout mice. Using immunohistology and electron micrographs, we examine photoreceptor morphology and ultrastructure.

Results: Although we found that SNAP-23 shows weak mRNA expression in photoreceptors, SNAP-23 removal did not affect retinal morphology or vision. SNAP-25 mRNA was developmentally regulated and underwent mRNA trafficking to photoreceptor inner segments at postnatal day 9 (P9). SNAP-25 knockout photoreceptors developed normally until P9 but degenerated by P14 resulting in severe retinal thinning. Photoreceptor loss in SNAP-25 knockout mice was associated with abolished electroretinograms and vision loss. We found mistrafficked photopigments, enlarged synaptic vesicles, and abnormal synaptic ribbons which potentially underlie the observed photoreceptor degeneration.

Conclusion: Our results conclude that SNAP-25, but not SNAP-23, mediates photopigment delivery and synaptic functioning required for photoreceptor development, survival, and function. Using this study, we uncover that the other target plasma membrane SNARE protein required for vesicle fusion in photoreceptors is SNAP-25.