The TRPM1 Channel plays a functional role in the ON-Bipolar Cell Light Response. [1]Steve M Nelson, [1]Jianmei Zhang, [1]Neal Burke, [3]S-X Zheng, [1]Lane Squires, [3]Catherine W Morgans, [4]Robert M Duviosin, [1]R. Lane Brown. [1]Washington State University, VCAPP, Pullman, WA; [3]Casey Eye Institute, OHSU, Portland, Oregon; [4]Department of Physiology and Pharmacology, OHSU.

The reduction in glutamate release from a light activated photoreceptor results in the opening of a selective cation channel that is negatively coupled to the metabotropic glutamate receptor, mGluR6 in ON-bipolar cells (Nakajima et al., JBC, 1993). The G-protein downstream of mGluR6 in the signaling cascade has been identified as Go (Vardi et al., JCN, 1998) however, the identity of the cation channel has remained elusive. Quite recently, the absence of functional TRPM1 in the Appaloosa horse retina was shown to result in congenital stationary night blindness (CSNB) with a corresponding absence of ON-bipolar cell depolarization (Bellone et al., Genetics, 2008). Our goal was to determine the localization of TRPM1 protein in the mouse retina and to determine if it plays a functional role in the ON-bipolar cell response to light. Gene profiling arrays performed by our lab suggested that TRPM1 and several additional TRP channels were highly enriched within the bipolar cell population. In order to verify this finding, *in situ* hybridization and immunocytochemistry were performed on retinal sections. Our findings indicate that TRPM1 is expressed in the distal inner nuclear layer (INL) a region corresponding to the ON-bipolar cell population and that the TRPM1 protein localized in dendrites of these cells in the mouse and macaque retina. ERG recordings similarly revealed a lack of rod bipolar depolarization and were consistent with the findings in the Appaloosa horse. In addition, simulated light responses using the mGluR6 antagonist, CPPG, were generated in the whole-cell configuration on retinal slice preparations from TRPM1 knockout and Wild-type mice. These recordings suggest that rod bipolar cells of TRPM1 knockout mice do not depolarize in response to a simulated light response however, there is a transient response remaining in cone ON-bipolar cells. The most parsimonious explanation for our findings is that TRPM1 is a major player in the ON-bipolar cell pathway. Future directions will include a pharmacological analysis of TRPM1 channel activation in transfected HEK cells and an evaluation of other TRP channels as candidates for mediating rod bipolar cell depolarization in response to light. NIH MH76094 (RLB), EY014700 (CWM), EY09534 (RD).