TRPM1 is required for the depolarizing light response in retinal ON-bipolar cells

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The ON-pathway of the visual system, which detects increases in light intensity, is established at the first retinal synapse between photoreceptors and ON-bipolar cells. Photoreceptors hyperpolarize in response to light and reduce the rate of glutamate release, which in turn causes the depolarization of ON-bipolar cells. This ON-bipolar cell response is mediated by the metabotropic glutamate receptor, mGluR6, which controls the activity of a depolarizing current. Despite intensive research over the past two decades, the molecular identity of the channel that generates this depolarizing current has remained elusive.

Here we present evidence indicating that TRPM1 is necessary for the depolarizing light response of ON-bipolar cells, and further that TRPM1 is a component of the channel that generates this light response. Gene expression profiling revealed that TRPM1 is highly enriched in ON-bipolar cells. In situ hybridization experiments confirmed that TRPM1 mRNA is found in cells of the retinal inner nuclear layer, and immunofluorescent confocal microscopy showed that TRPM1 is localized in the dendrites of ON-bipolar cells in both mouse and macaque retina. The electroretinogram (ERG) of TRPM1-deficient (TRPM1-/-) mice had a normal a-wave, but no b-wave, indicating a loss of bipolar cell response.

Finally, whole-cell patch-clamp recording from ON-bipolar cells in mouse retinal slices demonstrated that genetic deletion of TRPM1 abolished chemically-simulated light responses from rod bipolar cells and dramatically altered the responses of cone ON-bipolar cells.

Identification of TRPM1 as a mGluR6-coupled cation channel reveals a key step in vision, expands the role of the TRP channel family in sensory perception, and presents new insights into the evolution of vertebrate vision.