Title: Calcium-permeable AMPA receptors and TARPs in retinal amacrine cells

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Background: Calcium-permeable AMPA receptors (CP-AMPARs) are an important class of glutamate receptor, implicated in several neurological disease states. Retinal amacrine cells provide an attractive system for physiological investigation of their regulation and role in synaptic transmission. Amacrine cells are a diverse class of interneuron that mediate inhibitory activity the inner retina. We have discovered that A17 amacrine cells receive excitatory input from rod bipolar cells (RBCs) via CP-AMPARs and use the calcium influx through these receptors to trigger the release of GABA back onto the RBCs. Subsequent work has identified a signaling complex within the A17 cell that regulates the strength of feedback inhibition. It remains unknown how AMPARs are integrated with this complex, and what role modulatory proteins such as TARPs (transmembrane AMPAR regulatory proteins) might play at these synapses. To address this issue, the project will combine experiments on retina with recombinant and molecular approaches to examine the pharmacological and functional properties of receptors composed of the various AMPAR subunits and TARPs present in amacrine cells. The unique functional properties of certain retinal CP-AMPARs, and their resistance to specific toxins make them of particular interest in health and disease.

Methods: High-resolution patch-clamp methods in retinal interneurons and heterologous systems; multiphoton imaging approaches and electrical and physiological (light) stimulation of the retinal circuitry in acute retinal slices and in a ‘whole-mount’ preparation; molecular biology of AMPAR subunits and associated proteins; pharmacological approaches to investigation of AMPAR function and synaptic transmission.

References:


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