

THE PHOTORECEPTOR RHODOPSIN IN NIGHT VISION ENHANCEMENT, NIGHT BLINDNESS, AND RETINAL DEGENERATION

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Rhodopsin is the prototypical member of the largest family of cell surface receptors, the G protein-coupled receptors (GPCRs) and functions as the primary dim light photoreceptor in vision. The sensitivity and spectral range of rhodopsin depend on the habitat of the organism, such as balancing day and night vision, or optimizing dim-light vision at night and in the depths of the oceans. The visual systems of some deep-sea fish have evolved to “see” with chlorophyll,” where a derivative, chlorin e6 (Ce6), enhances the activation response of rhodopsin to red light. Other natural compounds such as anthocyanins from berries are also believed to affect night vision in humans. Through ^{19}F NMR, fluorescence spectroscopy and biochemical experiments, we show that both, Ce6 and anthocyanins, bind directly to rhodopsin, with μM affinity, and modulate a key functional region, the cytoplasmic domain. Previously known small-molecule ligands of rhodopsin are retinal isomers, conferring light sensitivity, as well as metal ions, in particular zinc (Zn^{2+}). Zn^{2+} deficiency can cause retinal dysfunctions including abnormal dark adaptation, night blindness and retinal neurodegeneration. It binds directly to rhodopsin and alters its bleaching rates. These are also changed in the presence of Ce6. We therefore derived and tested by biophysical means the hypothesis that the two compounds may have additive effects. We find that when both Ce6 and Zn^{2+} are present together, a pronounced increase in their effect on rhodopsin stability is observed as compared to either compound alone. Rhodopsin instability and tendency to misfold has been identified as a factor contributing to retinal degeneration and night blindness. Taken together, our findings may have implications in finding novel pharmacological agents for night vision enhancement, treatment of night blindness and/or retinal degeneration.