Compartmentalization and Ca2+ Buffering Are Essential for Prevention of Light-Induced Retinal Degeneration

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Abstract:

Fly photoreceptors are polarized cells, each of which has an extended interface between its cell body and the light-signaling compartment, the rhabdomere. Upon intense illumination, rhabdomeric calcium concentration reaches millimolar levels that would be toxic if Ca2+ diffusion between the rhabdomere and cell body was not robustly attenuated. Yet, it is not clear how such effective attenuation is obtained. Here we show that Ca2+ homeostasis in the photoreceptor cell relies on the protein calphotin. This unique protein functions as an immobile Ca2+ buffer localized along the base of the rhabdomere, separating the signaling compartment from the cell body. Generation and analyses of transgenic Drosophila strains, in which calphotin-expression levels were reduced in a graded manner, showed that moderately reduced calphotin expression impaired Ca2+ homeostasis while calphotin elimination resulted in severe light-dependent photoreceptor degeneration. Electron microscopy, electrophysiology, and optical methods revealed that the degeneration was rescued by prevention of Ca2+ overload via overexpression of CalX, the Na+?Ca2+ exchanger. In addition, Ca2+-imaging experiments showed that reduced calphotin levels resulted in abnormally fast kinetics of Ca2+ elevation in photoreceptor cells. Together, the data suggest that calphotin functions as a Ca2+ buffer; a possibility that we directly demonstrate by expressing calphotin in a heterologous expression system. We propose that calphotin-mediated compartmentalization and Ca2+ buffering constitute an effective strategy to protect cells from Ca2+ overload and light-induced degeneration.

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