Poster Presentation

High-performance halorhodopsin variants for improved genetically-targetable optical neural silencing

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Recently developed optogenetic tools to modulate transmembrane potential - such as the blue light activated cation channel, channelrhodopsin-2 (ChR2), and yellow light-activated chloride pump, N. pharaonis halorhodopsin (Halo/NpHR) - offer many advantages over physical electrodes for brain circuit mapping, neural prostheses, and therapeutic applications. For example, they can be genetically-targeted to specific cell types, conduct specific ions, and enable large populations of cells to be stimulated or silenced in a spatio-temporally complex manner. We here present a novel set of halorhodopsin variants and homologs with improved currents and kinetics. The first molecule, sp-Halo, demonstrates a three-fold improvement in photocurrents by employing a N-terminal signal sequence ("ss," from a MHC class I antigen) and the prolactin ER-location sequence ("prl"). The second molecule, "Arch" is a green-light activated, outwardly rectifying proton pump from H. sodomense (canonically known as AR-3) that also shows a three-fold increase in photocurrent versus Halo, as well as demonstrating improved chromophore regeneration kinetics over Halo by not requiring a blue-light pulse to recover from long-lived inactive states after prolonged exposure. Effective *in vivo* neural silencing by Arch in an awake-mouse is demonstrated.

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