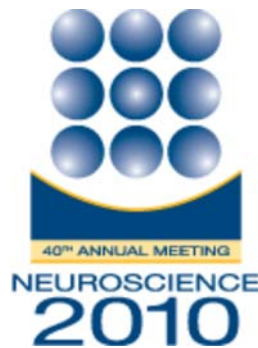


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Presentation Abstract

Program#/Poster#: 106.1/MMM8

Title: Novel classes of optogenetic reagent derived from screening genomic and ecological diversity

Location: Halls B-H

Presentation Time: Saturday, Nov 13, 2010, 1:00 PM - 2:00 PM

Authors: ***N. KLAPOETKE**¹, A. CHUONG², B. CHOW², T. MORIMOTO², X. HAN², E. BOYDEN²;
¹Cambridge, MA; ²MIT, Cambridge, MA

Abstract: Over the last few years, we and others have revealed novel classes of opsin (e.g., light-gated cation channels, light-driven chloride pumps, light-driven proton pumps) that each have unique spectral, ionic, and kinetic features, thus resulting in unique neuroengineering capabilities such as neural activation via a light-driven cation channel (e.g., ChR2), neural silencing via self-limiting light-driven outward proton pumping (e.g., with Arch), or multicolor silencing of two different neuron populations that express different hyperpolarizing pumps (e.g., with Mac and Halo). These 'optogenetic' technologies are in widespread use in neuroscience, and are freely available (e.g., see <http://syntheticneurobiology.org/protocols>). We are currently seeking to expand the kind of experimental capability that is possible, by developing reagents with fundamentally new capabilities. Accordingly, we are both broadly exploring the space of opsins in genomic/ecological space, and also strategically directing our search towards opsins that are homologous to opsins of known value. We are pursuing this search across breadth and depth by using a number of novel and powerful genomic strategies, and here present some results from this screen expansion. As a first example, we present a family of light-driven chloride pumps whose action spectra are significantly red-shifted when compared to the *N. pharaonis* halorhodopsin (Halo/NpHR). The current mediated by the product of one natural gene in this family, for example, is 50% more than that mediated by the *N. pharaonis* halorhodopsin at 633 nm illumination, thus supporting long-distance neural silencing with a minimum of brain tissue absorption. As a second example, we describe a class of opsins which, when

strategically mutated and then expressed in neurons, present a linear current-voltage relationship similar to that exhibited by various ion channels and receptors. Notably, the reversal potential of this current-voltage relationship can be set to specific values between -80 mV and 0 mV, by the power and color of the incident light. As a third example, we are continuing to explore new and powerful classes of blue-light drivable neural silencers, to complement the excellent yellow-red silencers that we and others have generated. We continue to explore novel classes of opsin in order to innovate unique and new strategies for controlling cellular functions in the brain.

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neural silencing

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