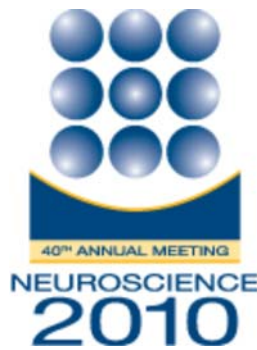


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Presentation Abstract

Program#/Poster#: 106.6/MMM13

Title: Temporally precise optical neural silencing in the nonhuman primate brain

Location: Halls B-H

Presentation Time: Saturday, Nov 13, 2010, 2:00 PM - 3:00 PM

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Abstract: The light-driven proton pump Archaeorhodopsin-3 (Arch) from *Halorubrum sodomense* has recently been demonstrated to be a high-performance 'optogenetic' neural silencer, capable of mediating nanoampere-scale currents in response to light (Chow et al, *Nature* 463:98-102, 2010). Arch thus enables temporally precise, safe, reversible and near-100% silencing of neurons in the awake rodent brain when virally expressed in the cortex and illuminated with green or yellow light. Here, we deepened our genomic and phylogenetic screen by performed a functional screen of all known full sequence clones of archaeorhodopsins, whose amino acid sequences are closely homologous to Arch, and which come from other organisms of the *Halorubrum* genus. We found that all of these closely-related molecules expressed well in neurons, exhibiting large hyperpolarizing photocurrents and similar action spectrum to Arch. One member of the family, ArchT, exhibited a near-double improvement in light sensitivity over that mediated by Arch, significantly increasing the brain volume silenceable. When lentivirally expressed in the cortex of the macaque brain, ArchT safely mediated silencing by 100.0% (median value experienced by n = 45 neurons that showed any degree of spike reduction with light; 532 nm laser; power ~200 mW/mm² at the fiber tip; electrode within 1 mm diameter sphere at fiber tip) of neocortical neuron spiking on the millisecond time scale. This demonstrates the technological viability of using outward proton pumps to perform neural activity silencing, e.g. for creating temporary lesions of defined pathways and cell types in the brain, thus enabling causal neural circuit investigations of perception,

cognition, emotion, and action. Furthermore, the translational potential here demonstrated, namely that of silencing neurons in a brain with similarities to the human brain, may support the prototyping of novel treatments for neurological and psychiatric disorders.

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