



## Presentation Abstract

Program#/Poster#: 305.07/XX81

Presentation Title: Red-shifted optogenetic neural silencers: Improvements, and *in vivo* use for inactivation of large brain volumes

Location: Hall A-C

Presentation time: Sunday, Nov 13, 2011, 3:00 PM - 4:00 PM

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Abstract: The ability to rapidly, safely and effectively silence the electrical activity of individual neurons or neuron populations in the brain is invaluable in the analysis of how specific neurons, pathways, and subcircuits contribute to brain computations. A major barrier to *in vivo* silencing is the light power attenuation created by tissue and hemoglobin optical absorption. Computational modeling of light scattering and absorption in brain tissue using realistic parameters (e.g., including blood at *in vivo* densities) suggests that 660 nm light could be used to inactivate tissue at distances of 7-10 millimeters (i.e., a significant fraction of the linear dimension of the mouse or rat brain) away from a light source emitting light at modest irradiances (e.g., 100 mW/mm<sup>2</sup>).

We here present an optimized form of a red-light drivable halorhodopsin, which we have nicknamed Halo57, that we recently found in a genomic screen (Chuong et al., Society for Neuroscience, 2010). Halo57 has its action spectrum peak at 605 nm, and thus has a spectrum red-shifted relative to the *N. pharonis* halorhodopsin. Halo57 operates with ~65% of its peak photocurrent when irradiated with 633 nm light, and operates with ~40% of its peak photocurrent when irradiated with 660 nm light. Halo57 also expresses well in neurons, showing less aggregation than the *N. pharaonis* halorhodopsin.

The optimized form of Halo57 that we present, which bears several point mutations

as well as sequences to augment trafficking, exhibits photocurrents at 633 to 660 nm that are over 3x greater than those mediated by any previously publicly described opsin at 633 to 660 nm. We are now exploring the use of this red light drivable silencer to mediate long-distance, and less invasive, inactivation of neural activity in the mammalian brain.

Disclosures: **A.S. Chuong:** None. **N.C. Klapoetke:** None. **M.A. Henninger:** None. **L.C. Acker:** None. **B.Y. Chow:** None. **X. Han:** None. **E.S. Boyden:** None.

Keyword(s): opsin  
optical silencing  
optogenetic

Support: NIH Grants 1R01DA029639, 1DP2OD002002, 1RC1MH088182, 1RC2DE020919, 1R01NS067199 and 1R43NS070453  
NSF DMS 1042134, CAREER award, EFRI 0835878, DMS 0848804  
Paul Allen Distinguished Investigator Award

Google

MIT McGovern Institute Neurotechnology Award Program

[Authors]. [Abstract Title]. Program No. XXX.XX. 2011 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2011. Online.

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