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Presentation Abstract

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Presentation Title: Development of a squirrel monkey model for nonhuman primate optogenetics

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Abstract: Since their introduction, optogenetic techniques have been used with substantial success and versatility in rodent models. However, while promise therefore exists for important applications in nonhuman primate models, no study has yet reported a useful behavioral effect in primate. We previously reported functionality of excitatory (ChR2, SFO) and inhibitory (eNpHR2.0) optogenetic tools in rhesus macaque cortex (Diester et al., 2011), but overall development of nonhuman primate opsins has been limited, in part due to long timescales of rhesus research. Primate optogenetics may be advanced by a primate model more closely matched to the rapid timescale of opsin development so that newer and more potent tools may be tested more quickly. In addition, while promoter-based approaches allow highly specific circuit selection in transgenic mice, highly specific circuit selection in primates will likely require projection-targeting techniques including axonal membrane expression, transsynaptic tracer proteins, and retrograde travelling viruses (Mattis, et al; SFN 2010). These techniques may not translate directly from rodent to rhesus, pointing to the need for development of an intermediate primate optogenetic model that could provide both histological and electrophysiological data rapidly and with larger sample sizes. Finally, demonstrating efficacy across multiple primate species may yield a more robust primate optogenetic toolkit. In

this study, we present a squirrel monkey model for histological analysis of primate optogenetic constructs. Using stereotactic techniques, we intraoperatively injected optogenetic constructs in multiple cortical and subcortical sites in squirrel monkeys. After allowing adequate time for expression, we analyzed injection sites histologically for fluorescent cells using confocal laser microscopy. We present evidence of the first nonhuman primate expression of two advanced opsins, a modification of the excitatory opsin ChR2 and the highly potent inhibitory opsin eNpHR3.0, under control of the CaMKIIα promoter using the AAV5 vector system, in squirrel monkey hippocampus and somatosensory cortex respectively. Use of this new model for optogenetics may improve development of nonhuman primate optogenetics by allowing rapid translation from rodents to primates and expanding the diversity of primate species available for optogenetic intervention.

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