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Presentation Abstract

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Presentation Title: Optogenetic projection targeting with AAV5 in non-human primates

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Abstract: Optogenetics enables cell-type specific control of defined neuronal populations *in vivo*. Cell type-specificity can be achieved with promoters in viruses or transgenic animals, or with Cre-inducible viruses used in combination with Cre-driver mouse lines. With a paucity of specific promoters small enough to package into viruses, and in animals that are less amenable for transgenic techniques, cell-type specificity is often difficult to achieve with genetic methods. In addition, for many studies, targeting specific connections between two brain areas is more desirable than local cell-type specific targeting. We report here an analysis of projections in a non-human primate that we were able to label with unilateral injections of AAV5 in combination with the promoters hSyn and hThy-1 in premotor, motor and somatosensory cortex. We found strong cortical expression in fibers ipsilateral and contralateral to the injection site. We also found labeled fibers in subcortical projections coursing from cortex over very long distances, as far as the red nucleus. Surprisingly, while transduced cell bodies were virtually never observed away from the injection site, we found a substantial group of labeled cell bodies in the ventro-posterior-lateral (VPL) thalamic nucleus, suggesting possible specific traveling of AAV5 between cortex and thalamus. To further investigate whether AAV5 can travel between other brain areas with known strong connections we explored several well-characterized circuits in rodents. Using a highly sensitive

Cre-lox based assay, in either mouse interhemispheric hippocampal connections or the projection from the ventral tegmental area to the nucleus accumbens, we were able to show that AAV5 transduced local cells almost exclusively in these circuits, with only extremely rare exceptions of single labeled cell bodies outside the injected sites. In summary, AAV5 seems to be suited for three purposes: (1) In studies of neocortical function, local expression in cell bodies guarantees virtually no retrograde traveling from cortex to other cortical brain areas, and allows stimulation of local cell bodies while eliminating confounding (e.g. antidromic) effects from retrogradely-labeled axons projecting back to the injection site. (2) By relying on fiber stimulation in non-injected areas that receive projections from the injected site, AAV5 may be suited for targeting even long-range projections between connected brain areas. (3) By making use of projection-specific traveling of the virus between cortex and thalamic nuclei, specific stimulation of the VPL cortical projection neurons may be possible with a thalamic illumination strategy.

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VIRUS

SOMATOSENSORY CORTEX

Support: HFSP

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