Pathway-selective optogenetic and chemogenetic manipulation to study the sensorimotor and cognitive functions in macaque monkeys

Department of Neuroscience, Graduate School of Medicine, Kyoto University, Japan
Tadashi Isa

Selective manipulation of particular pathways in the central nervous system either is critical to demonstrate their causal contribution to particular brain functions in the systems neuroscience studies. Introduction of optogenetics and chemogenetics enabled such selective manipulation in experimental studies and nowadays, it is becoming a common experimental paradigm in mice or other model animals. However, it is still difficult in nonhuman primates, especially in the macaques, because of its huge brain and poorer gene expression efficiency of target genes by currently available viral vectors.

Our group first succeeded in the selective manipulation of a spinal motor circuit by combination of retrograde and anterograde vectors under control of Tet activator system, and succeeded in manipulating the behavior of macaque monkeys (Kinoshita et al. 2012; Tohyama et al. 2017). After that, we gradually improved the technique, and succeeded in manipulation more wider brainstem pathway (Kinoshita et al. 2019), basal ganglia pathway (Vancraeyenest et al. 2020) and more recently, the interhemispheric cortico-cortical pathway by using DREADDs (Mitsuhashi et al. 2024). On the other hand, we recently succeeded in the optogenetic manipulation of the meso-cortical dopamine pathway to demonstrate its contribution to the flexible decision (Sasaki et al. 2024).

I would like to explain how we developed these techniques in the macaques.