1. No.
   2021G005

2. Title
   Elucidation of functional conversion mechanisms of nicotinic receptors by endogenous neurotoxin-like proteins.

3. Period
   2021-2023

4. Summary
   Previously, we have proposed that Ly6H is an endogenous antagonist of nAChR in *in vitro* experiments. In this study, we successfully generated Ly6H KO mice using the CRISPR/Cas9 system and found that Ly6H KO mice showed increased susceptibility to nicotine-induced tremor, indicating that Ly6H suppresses nAChR function as an antagonist *in vivo*. Using Ly6H KO mice, we generated a monoclonal antibody against Ly6H detectable by Western blot and IHC, and further succeeded in human chimerism of the antibody. IHC analysis using this human chimeric antibody revealed that Ly6H is expressed in the hippocampus, prefrontal cortex, paracerebellar peduncular nucleus, bed nucleus of the stria terminalis, and hypothalamus. Behavioral experiments revealed that Ly6H KO mice exhibit increased anxiety and reduced progression of cognitive dysfunction in old age.