1. No.
   2021T001

2. Title
   The Role of DOPA and Dopaminergic Transmission in Nicotine Addiction

3. Period
   2021-2025

4. Summary
   Nicotine induces 3,4-L-dihydroxyphenylalanine (DOPA) and dopamine (DA) via mecamylamine-sensitive nicotinic receptors from Nucleus Accumbens or dorsal striatum in rodent animal models. G-protein coupled receptor GPR143, a gene product of ocular albinism1, was identified as a receptor for DOPA. In this study, we examined the possible role of GPR143 in regulating the function of DA receptors. In *Gpr143*-gene deficient mice, quinpirole, a DA D2 receptor agonist-induced behavioral action was attenuated whereas SKF81297, a DA1 receptor agonist-induced action was not modified. Quinpirole-induced increase in the phosphorylation of GSK3β (S9) was enhanced in Chinese hamster ovary cells coexpressing the long form of DA D2 receptors (D2Rs) (D2L) and GPR143 compared with cells expressing D2L alone. On the contrary, the effect of quinpirole was suppressed in cells coexpressing the short form D2S and GPR143 compared with D2S alone. Thus GPR143 positively regulates D2L but negatively regulates D2S. Since it was suggested that D2L mainly functions as postsynaptic receptors while D2S functions as presynaptic autoreceptors to negatively regulated DA release, GPR143 may reinforce D2R-mediated DA transmission via both pre- and postsynaptic mechanisms.