1. No.
   2021T008

2. Title
   Effects of Novel Molecules Related to Dopaminergic Regulation in the CNS on Nicotine-Induced Addictive Behaviors

3. Period
   2021-2025

4. Summary
   Formation of smoking habits is recently assumed to require the acquisition of preference to smoking-related behaviors, in addition to the substance dependence on nicotine. In 5-year-study, we investigated the brain region and responsible genes related to nicotine-intake behavior in mice to reveal the mechanism of formation of smoking dependence. To elucidate the mechanisms underlying nicotine addiction-related behavior, we established a two-bottle choice paradigm in which mice could freely select nicotine-containing water. By providing nicotine in the drinking water for seven days prior to the two-bottle test (nicotine priming), many mice exhibited a high preference for nicotine (preference ≥ 70%). Immunohistochemical analysis of the neuronal activity marker FosB revealed that CaMKII-positive pyramidal neurons in the basolateral amygdala (BLA) are involved in this addiction-related behavior. In mice with a high preference for nicotine consumption, neuronal activity in the posterior BLA (pBLA) was higher than that in the anterior BLA (aBLA). Furthermore, chemogenetic activation of pyramidal neurons in the pBLA enhanced nicotine preference behavior. These findings suggest that pyramidal neurons in the pBLA play a role in regulating nicotine addiction-related behavior.