1. No.
   2021G025

2. Title
   Elucidation of suppression mechanism of nicotine addiction targeting epigenome factor and novel therapeutic strategy.

3. Period
   2021-2023

4. Summary
   We have developed various histone acetyltransferase inhibitors such as DNP derivatives and various glycosides of curcumin and anacardic acid with permeability to the blood-brain barrier through this research project, and as a result of administration experiments of these agents to mice, we have obtained the phenomenon that the decrease in mesencephalic syntaxin 1A expression is accompanied by the suppression of syntaxin 1A neural function of releasing mesencephalic dopamine vesicles, resulting in a decrease in nicotine dependence. On the other hand, we found that administration of amlexanox, a known inhibitor of the NFκB signaling pathway, did not alter midbrain syntaxin 1A expression, dopamine vesicle release function, and nicotine dependence. Furthermore, the nicotine place preference of syntaxin 1A knockout mice, in which syntaxin 1A gene expression was completely lost, was verified, and it was found that nicotine dependence was predominantly reduced. Based on these results, to date, the suppressive effect of histone acetyltransferase inhibitor treatment on nicotine dependence is not mediated by the NFκB signaling pathway but by the syntaxin 1A-histone acetyltransferase pathway, which is mediated by a reduction in midbrain syntaxin 1A expression and its neural function, dopamine vesicle releasing function may occur, resulting in reduced nicotine dependence.