1. **No.**

   FP01907128

2. **Title**

   Redox-signal Regulation by Nicotine in Neuronal Cells

3. **Period**

   2017-2020

4. **Summary**

Nicotine modulates neuronal functions by binding to the nicotinic acetylcholine receptors. However, the mechanisms underlying this phenomenon have not been completely elucidated. In this study, to elucidate the impact of reactive sulfur species (RSS) on the nicotine-induced redox signal in neuronal cells, we investigated the effects of nicotine and RSS on nerve growth factor (NGF)-induced neurite outgrowth and extracellular signal-regulated kinase (ERK) phosphorylation.

In this study, we demonstrated that nicotine signals were regulated by RSS, and the redox signal was involved in the action of nicotine. Furthermore, we showed that NGF-induced neurite outgrowth was enhanced by nicotine, neuronal nitric oxide synthase (nNOS) and RSS, which was mediated by the ERK phosphorylation cascade. We constructed a quantitative analysis method for RSS using a novel alkylating-agent (N-iodoacetyl tyrosine methyl ester), and clarified that NGF treatment promotes the production of RSS in a NOS-dependent manner. These results for the first time showed that nicotine-induced nNOS redox signal was involved in neural differentiation and maturation through endogenous RSS regulation.