1. **No.**

   FP01812205

2. **Title**

   Study of the clearance mechanism of the protein aggregates through the nicotinic receptor

3. **Period**

   2017-2019

4. **Summary**

Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS) have increasingly been realized to have common cellular and molecular mechanisms including protein aggregation and inclusion body formation. In the present study, to examine whether nicotine has neuroprotective effect against ALS-associated mutant Cu / Zn superoxide dismutase (SOD1)-induced aggregation and neurotoxicity in a cellular model, we used PNU 282987, an α7 nicotinic receptor agonist. PNU 282987 significantly reduced the intracellular aggregates of mutant SOD1. In addition, PNU282987 significantly prevented mutant SOD1-related neurotoxicity. The reduction of intracellular aggregates of mutant SOD1 caused by PNU 282987 was significantly abolished by treatment of chloroquine, an autophagy inhibitor. In addition, PNU 282987 activated AMPK – mTOR pathway. Moreover, PNU 282987 increased the expression of autophagy-related genes via TFEB activation. These results suggest that PNU 282987 reduced intracellular aggregate via the activation of autophagy. PNU 282987 against mutant-SOD1-induced aggregation via the activation of autophagy are an efficient source of new treatment and prevention for ALS.