1. **No.**

   FP01809115

2. **Title**

   Fundamental study for the establishment of novel prevention and treatment for depression after smoking cessation, which is based on the mechanism of exercise-induced antidepressant effects

3. **Period**

   2017-2019

4. **Summary**

   We recently demonstrated that the serotonin type 3 (5HT3) receptor is essential for exercise-induced hippocampal neurogenesis and antidepressant effects. In this study, we examined the 5HT3 receptor-mediated mechanism underlying hippocampal neurogenesis and antidepressant effects, and tried to establish novel prevention and treatment for depression after smoking cessation. Here, we show that the 5HT3 receptor agonist induces antidepressant effects as well as hippocampal neurogenesis independent of fluoxetine (a commonly used SSRI). Notably, our histological analysis reveals that the 5HT3 receptor and IGF1 are expressed in the same neurons in the hippocampal dentate gyrus. Furthermore, our *in vivo* microdialysis analysis shows that the 5HT3 receptor regulates hippocampal extracellular IGF1 levels, and we also show that the 5HT3 receptor-dependent hippocampal neurogenesis is mediated by increased IGF1 levels. Altogether, our results suggest a novel 5HT3 receptor-IGF1 mechanism that is distinct from fluoxetine-induced responses. Finally, we show that the 5HT3 receptor agonist exhibits antidepressant effects in mice with depressive-like behavior induced by LPS administration or withdrawal from chronic nicotine exposure. Our findings provide a new therapeutic target for depression after smoking cessation, which is based on the mechanism of exercise-induced antidepressant effects.