1. **No.**

   FP01807094

2. **Title**

   The effects of smoking exposure during early developmental stages on brain development via alteration of DNA methylation

3. **Period**

   2017-2019

4. **Summary**

Maternal smoking is reported to cause an increased risk of neurodevelopmental disorder such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) in children. However, little is known about molecular mechanisms. The purpose of this study was to clarify the effects of cigarette smoke extract (CSC) exposure on epigenetic gene expression dysregulation and neuronal differentiation and neuronal function using human iPS cells (hiPSCs). In hiPSCs, cell morphology was changed by exposure to 40 μg/mL CMC, and cell proliferation was suppressed. Analysis of pluripotent stem cell-related genes showed that SOX2 and OCT4 did not change, but GDF3 expression decreased. Comprehensive gene expression analysis revealed that 3 genes were significantly altered at 2.5 μg/mL CMC exposure and 7 genes were altered at 10 μg/mL, whereas 229 genes were significantly altered at 40 μg/mL CSC exposure. CYP1A1 and LRAT expression showed a significant concentration-dependent increase in CSC exposure of 0.4 μg/mL or more. As a result of DNA modification analysis in CSC exposure, DNA methylation significantly increased and DNA hydroxymethylation decreased in 10 μg/mL CSC exposure. Exposure of iPSCs to CSC at 40 μg/mL induced cell death in neural progenitor cells and did not allow continued differentiation into neural cells. It was suggested that exposure to 40 μg/mL CSC did not show cell death in iPSCs, but had a significant effect on differentiation induction.