1. **No.**

   FP01809117

2. **Title**

   Genome-wide analysis of copy number variations in individual differences in vulunerablility to and severity of substance dependence regarding nicotine and other addictive substances

3. **Period**

   2017-2019

4. **Summary**

   To date, several candidate single nucleotide polymorphisms (SNPs) have been identified to be genome-widely associated with smoking behaviors mainly in subjects with European ancestry. We comprehensively explored genetic contributors of copy number variations (CNVs) to smoking behavior, particularly nicotine dependence, in a total of 300, followed by 240 and 192, Japanese patients who visited Iwata City Hospital.

   [Methods] A genome-wide CNV study was conducted for the genotype data obtained by whole-genome genotyping with iScan System (Illumina K.K.) and BeadChip HumanCytoSNP-12 approximately targeting 300,000 markers or HumanCoreExome approximately targeting over 500,000 markers. From among several smoking-related traits, the Fagerström Test for Nicotine Dependence (FTND), the Tobacco Dependence Screener (TDS), and the numbers of cigarettes smoked per day (CPD), were analyzed.

   In a genome-wide analysis, several CNVs were selected to be possibly associated with these traits. Among them, a ~20 kbp CNV mapped at 22q13.1, which is located in the region of the APOBEC3B gene, and a ~3 kbp CNV mapped at 17q12, which is located at the neighboring region of the PLXDC1 gene, showed genome-wide significant association with FTND score in the initial 300 samples and TDS score in the following 192 samples, respectively.

   Although future studies with larger sample size are required, these results will serve to discover genetic factors contributing to smoking behavior specific to Japanese population in addition to those common to other populations.