1. **No.**

   FP01811131

2. **Title**

   Genome epidemiology of smoking-related respiratory disease

3. **Period**

   2017-2019

4. **Summary**

   In a case-control study on lung cancer (462 cases and 379 controls), HIF1A rs11549467, HIF1A rs11549465, HIF1A rs2057482, HIF2A rs13419896 and VEGFA rs833061 using TaqMan real-time PCR assay were evaluated. After adjustment for age, sex, education, smoking status and drinking status, the AA genotype of HIF2A rs13419896 (odds ratio (OR) = 0.54, 95 % confidence interval (CI) = 0.30–0.99) and the CC genotype of VEGFA rs833061 (OR = 0.42, 95 % CI = 0.24–0.75) were significantly associated with a decreased risk of lung cancer. Additive interactions between the rs13419896 and rs833061 polymorphisms and cigarette smoking were also statistically significant.

   Similarly, in a case-control study on chronic lung diseases (830 cases and 379 control), TERT rs2736100, TERC rs1881984, OBFC1 rs11191865, CYP1A1 rs4646903, GSTM1 deletion polymorphism, AKAP13 rs62025270 and DSP rs12076295 were genotyped with real-time PCR using TaqMan fluorescent probes. TERT rs2736100 was significantly associated with the risk of CLD; increases in the number of this risk allele increased the risk of IPF (P trend = 0.013). In regard to the combined action of the three loci, increasing numbers of "at-risk" genotypes did not increased the risk of CLD in a dose-dependent manner. The CC genotype of CYP1A1 rs4646903 was significantly associated with the risk of CLD (OR = 1.86, 95% CI = 1.06–3.25).

   [Conclusions] TERT rs2736100 and CYP1A1 rs4646903 may be associated with the risk of CLD in a Japanese population. Re-analysis may be required after a definitive diagnosis of such as COPD and IPF.