1. **No.**

   FP01911172

2. **Title**

   Molecular Epidemiological Study of Cigarette Smoking Effect on Metabolome and Inflamentaiton-related Biomarkers

3. **Period**

   2018-2020

4. **Summary**

[Background] The aim of this study is to clarify the effects of smoking on the risk of lifestyle-related diseases based on immune- and inflammation-related biomarkers, lipid and water-soluble metabolites, and genetic polymorphisms.

[Methods] Immune- and inflammation-related biomarkers were measured by ELISA using human stored serum, and lipid and water-soluble metabolites were measured by liquid chromatography-tandem mass spectrometry. Genetic polymorphisms were identified by the TaqMan 5' nuclease method.

[Results] Targeted metabolomics analysis using mass spectrometry of lipid and water-soluble metabolites in serum was possible. Serum CRP levels were increased in smokers, especially in the smoking group with *IL6R-A/A* genotype. Serum IFN-γ levels were significantly lower in smokers and decreased with increasing age, especially IFN-γ levels were decreased in the smoking group with *IL6R-A/A* genotype. Metabolomic analysis showed that unsaturated fatty acids and sphingolipids increased in the smoking group, while fatty acid metabolites and oxylipids tended to be low. In addition, nicotine and its metabolites (cotinine, hydroxycotinine, nornicotine, etc.) were detected as compounds present in high concentrations in the serum of the smoking group, and could be evaluated as tobacco-derived biomarkers. Lysophospholipid such as glycerophospholipid (lysophosphatidic acid ;LPA, lysophosphatidyl glycerol; LPG, lysophosphatidyl serine; LPS) and gangliosides were significantly increased, and lysophosphatidylcholine (LPC), platelet-activating factor (PAF) and sphingolipids were significantly decreased in the smoking group with *IL6R-A/A* genotype.

[Conclusion] It was found that serum IFN-γ levels were significantly decreased in the smoking group with a specific *IL6R* genotype, and that the effects of smoking on lipid metabolites differed according to *IL6R* genotype.