1. No.

   2022G034

2. Title

   Elucidation of the Effect of Heated Tobacco Products on Lung Cancer Metastasis and Recurrence

3. Period

   2022-2024

4. Summary

   In the first year, we identified biomarkers that objectively reflect the impact of cigarette smoking on the recurrence risk of lung cancer. A group with high peaks of three types of phosphatidylcholine (PC) structural isomers in adenocarcinoma - namely, PC (14:0_18:2), PC (16:1_16:1), and PC (16:0_16:2) - showed a significantly shorter recurrence-free survival period and a high odds ratio for T factors (≥pT2) and pleural invasion. In squamous cell carcinoma, a low *m/z* 736.5276 group had a shorter recurrence-free survival period and a high odds ratio for recurrence.

   In the second year, we demonstrated that the overall survival period after surgery for lung cancer in smokers of non-small cell lung cancer with negative EGFR mutations was significantly shorter compared to non-smokers.

   In the third year, we comprehensively explored the impact of heated tobacco on the lipid profiles of lung adenocarcinoma tissue and normal lung tissue, showing that PC (14:0_18:2), identified as a recurrence risk in the first year with cigarette smoking, also increased in lung adenocarcinoma tissue with heated tobacco. This was a cancer tissue-specific change not observed in non-cancerous tissue. Screening for metabolites with median relative amounts more than twice as high in heated tobacco smokers compared to non-smokers revealed that the highest level in lung adenocarcinoma tissue was acylcarnitine (4.1 times). Coenzyme Q10 showed high levels in lung cancer tissue (3.1 times), normal lung tissue (2.1 times), and spontaneous pneumothorax (2.7 times). Triglycerides were elevated in both tumor tissue (3.1 times) and normal lung tissue (8.8 times) of lung adenocarcinoma cases. Phosphatidylethanolamine was elevated only in the tumor tissue of lung adenocarcinoma cases (2.3 times), while monohexosylceramide was elevated only in the normal lung tissue of lung adenocarcinoma cases (3.6 times).