1. No.
   2020G005

2. Title
   Carcinogenic Risk Assessment of Interstitial Pneumonia Patients - Molecular Pathological Analyses of Influence of Smoking Habit and Chronic Inflammation

3. Period
   2020-2022

4. Summary
   Interstitial lung disease (IP) is a risk factor for lung cancer. In this study, we hypothesized and tested that IP-associated lung adenocarcinoma may arise from bronchial metaplasia of honeycombs. Bronchial epithelialization products in 13 IP lung biopsies and KRAS mutation frequencies in 46 non-IP lung biopsies were analyzed using digital PCR. The results showed that KRAS G12C/G12V accumulated in bronchial epithelialization products. It was suggested that the bronchial epithelializing component may be the origin of IP-related lung adenocarcinoma. The results were published in an international journal.

   Based on this result, we used next-generation sequencing to comprehensively examine cancer-related gene mutations in 5 cases of remarkable bronchial metaplasia among resected lung biopsy materials that have stored frozen sections. searched. As a result, three kinds of gene mutations (KMT2C/c2228t, KMT2C/c2291t, FANCD2/a1214g) were found as common mutations in multiple cases of bronchial metaplasia. Mutations in KMT2C and FANCD2 were found in multiple cases. These two genes are molecules that regulate histone methylation and DNA repair, respectively. These mutation-induced dysfunctions may cause changes in cellular methylation status and accumulation of gene mutations and may be involved in the promotion of bronchial epithelial metaplasia to cell carcinogenesis.

   In the future, we would like to further investigate the possibility of identifying gene mutations characteristic of bronchial epithelial metaplasia through comprehensive gene analysis such as deeper all-exon sequencing. If we can identify a group of gene mutations that are characteristic of bronchial metaplasia, it is expected to lead to the development of a gene panel test that predicts the risk of developing IP-related lung cancer. A more in-depth, comprehensive genetic analysis targeting larger number of cases may be able to achieve this goal.