1. No.
   2019T010

2. Title
   The Elucidation of the Oncogenic Mechanisms of KRAS-mutated Carcinomas Based on the Whole Genome Analysis of Early Lung Cancers.

3. Period
   2019-2022

4. Summary
   Whole exome analysis of 43 lung adenocarcinoma cases with non-TRU type histology revealed that the majority of non-TRU type lung adenocarcinomas were HNF4α-positive adenocarcinomas with gastrointestinal differentiation and a high prevalence of KRAS mutations. No abnormalities in EGFR, ALK, RET, etc. were found. TFF-1 is inversely correlated with TTF-1 expression in lung adenocarcinoma cell lines, and immunostaining for TFF-1 in primary lung adenocarcinoma cases revealed that TFF-1-positive adenocarcinomas are HNF4α positive and frequently harbor KRAS mutations, and that high TTF-1 expression is an independent prognostic poor prognosis in advanced cancers. In lung adenocarcinoma cell lines with HNF4α-positive and KRAS mutations, KD of TFF-1 suppressed cell proliferation and soft-agar colony formation, and induced apoptosis of cancer cells, indicating that TFF-1 is not just a non-TRU type TFF-1 is not only a marker of non-TRU type but also a molecular target of non-TRU type lung adenocarcinoma. We also found that HNF4α-positive poorly differentiated adenocarcinomas are an extremely malignant group with a poor prognosis.