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2. Title
   Genomic alteration of early lung cancer and its clinicopathological significance

3. Period
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4. Summary
Since the development and introduction of next-generation sequencing (NGS), whole genomes have been sequenced in various cancers, and in lung cancer, genomic alterations in adenocarcinoma, squamous cell carcinoma, and small cell carcinoma have been reported in detail. In lung adenocarcinoma, mutations in oncogenes such as *EGFR* and *STK11* were found at high rates, and the major genetic mutations in lung adenocarcinoma are now largely understood. On the other hand, "evolution" within tumors has recently been postulated, and evolutionary concepts such as "neutral evolution" and "selection" have been applied to understanding cancer progression. Although this remains a hypothetical bioinformatics study, computational attempts have also been made to depict how driver mutations that arise early in cancer development become predominant in all tumors, and how mutations that arise further along the way gradually become dominant. If this is how the "evolution" of tumors is viewed, then the mutations that predominate in advanced cancers are not necessarily the mutations that occurred early in the development of the cancer. Therefore, we performed sequencing (WES) of early-stage lung adenocarcinoma lesions to detect characteristic gene mutations in early-stage lung adenocarcinoma lesions and to clarify the relationship between smoking history and other factors. We completed WES of formalin-fixed, paraffin-embedded specimens from 67 cases of early-stage lung adenocarcinoma and analyzed the following data: 1) somatic mutation profiling, 2) comparison of gene mutation frequency with invasive lung adenocarcinoma, 3) somatic mutation burden, 4) mutation signatures, and 5) genomic copy number changes. Correlating these results with smoking history and other clinical characteristics, we obtained interesting findings, including a) involvement of the APOBEC3 pathway in carcinogenesis in non-smoker EGFR mutant cases, b) differences in somatic mutation burden accumulation between smoker and non-smoker EGFR mutant cases, and c) a higher incidence of whole genome doubling in EGFR mutant cases.