1. No.

   2019T009

2. Title

   Identification of driver gene in early lung adenocarcinoma in subjects with high risk alleles

3. Period

   2019-2023

4. Summary

Never-smokers' adenocarcinoma has several characteristics of mutation profile (EGFR mutations are dominant), ethnic profile (Asian female) and histological peculiarity (so-called lepidic pattern). The previous GWAS studies revealed recurrent predisposing genetic loci of modest odds ratio. We applied Japonica Array tuned for Japanese genetic profile to our case and controls. We confirmed previously identified loci and additional novel ones. Interestingly when we divide the cases into two having most common EGFR mutations (exon19 deletion and L858R mutation), the significant loci became changed. The risk loci including new ones were different according to the somatic EGFR mutations of the patients. The second hits in tumors occurring in the patients having new loci as risk alleles are being pursued; and the earliest changes of the genes among the panels in lung cancer having different EGFR driver changes would be intriguing.

When characterizing the nature of this entity of never-smokers' lung adenocarcinoma in Japan, genes involved with RNA modification behave uniquely in this subset of lung cancer, though the trend seems different in Western never-smoker's adenocarcinoma (we do not sufficient information on histological characteristics). *FAF1* is another potentially related markers of the EGFR mutant lung adenocarcinoma.

International consortiums, most famous one is "Sherlock" lead by Dr. Landi in NCI, also found various unusual EGFR mutations in South America, China and other areas, thus geographical and environmental aspects such as reliable exposure markers should be considered into future prospect of search for never-smokers' lung cancer etiologies, pathogenesis, and prevention.