1. **No.**

   FP01801020

2. **Title**

   Establishment of Immunohistochemical Marker for Mutation Burden in NSCLC

3. **Period**

   2016-2018

4. **Summary**

In the first year of the project, we analyzed endoreticulum (ER) stress genes, since accumulation of mutation should stimulate ER stress associated genes. Unexpectedly, all of analyzed genes (PERK, ATF6, IRE1, ERO1L) by us were highly expressed in the cohort having better prognosis. Therefore, we analyzed relationship between all genes and mutation using cancer cellline encyclopedia (CCLE) of the Broad institute of MIT. Among six candidate of genes, endoplasmic reticulum aminopeptidase 2 (ERAP2) was suppressed in heavy smoker's lung adenocarcinoma, in which more mutations would be happen. To compare mutation status and loss of ERAP2, we performed whole exon sequencing of three smokers' lung adenocarcinoma, they showed loss of expression of ERAP2 and three non-smokers' lung adenocarcinoma that expressed ERAP2. All three smokers' lung adenocarcinoma showed more than 10/Mb mutations, and all three non-smokers' lung adenocarcinoma showed no tumor mutation burden (TMB). As ERAP2 is involved in antigen presentation mechanism, we are performing case control study with expression status of ERAP2 by immunohistochemistry in clinical sample from who showed good response to immune check point inhibitor or not.