1. No.
   2025Y002

2. Title
   Understanding the Mechanism of Smoking-Induced Y-Chromosome Loss in Oral Cancer and Its Role in Cancer Progression

3. Period
   2025-2025

4. Summary
   In this study, we focused on the loss of Y-chromosome (LOY), which a sex chromosome found exclusively in males—due to aging and smoking, and performed research aimed at elucidating its biological significance in cancer progression. Using RNA sequencing data from head and neck squamous cell carcinoma cases included in the TCGA, we analyzed the mRNA expression levels of Y-chromosome genes and their correlation with prognosis. We found that downregulation of several Y chromosome genes expressed in cancer tissues was strongly correlated with shorter survival times in cancer patients. In fact, in the mouse oral cancer cell line NOOC1, established from the 4NQO drinking water model, which is a mouse model reported as mimic the genetic abnormalities of oral cancer caused by smoking. We observed reduced expressions of Y-chromosome genes, but they were not completely lost. Therefore, we performed single-cell cloning using NOOC1 and revealed the existence of cell clones that maintained high mRNA expression of the Y-chromosome genes and cell clones that were completely deficient in it. In the future, we plan to use these unique cell clones to conduct a detailed *in vivo* analysis of the relationship between LOY and cancer progression.