1. No.
   2021G002

2. Title
   Multi-Omics Characterization of Smoking-Accociated Laryngeal Cancer

3. Period
   2021-2024

4. Summary
   Smoking is one of the major causes of epithelial malignancies of the laryngeal mucosa, but the details of gene regulation mechanisms in precancerous lesions remain unclear. The aim of this study is to elucidate the mechanisms of laryngeal carcinogenesis induced by smoking using a multi-omics analysis in a mouse model. Focusing on the subregions of the larynx (supraglottis, vocal cords and subglottis), gene expression and epigenetic changes were comprehensively analyzed using RNA-seq, ATAC-seq and RRBS. In RNA-seq, increased expression of the oxidative stress response factor Nrf2 and its downstream genes was prominent in the smoking exposure group and in vocal cords was suggested to be particularly associated with demethylation. Histological evaluation and electron microscopy showed few clear morphological changes, but fine structural changes were observed. The establishment of immortalized lines from primary cultured cells derived from the human larynx is being developed as a basis for future *in vitro* validation in humans with smoking exposure; Nrf2 knockout mice and patient specimens will also be utilized for more comprehensive mechanistic elucidation.