1. No.

   2021Y008

2. Title

   Investigation of cigarette smoke-induced goblet cell hyperplasia mechanism using human iPS cells

3. Period

   2021-2023

4. Summary

Airway remodeling caused by habitual cigarette smoking is characterized by structural changes of goblet cell hyperplasia, submucosal gland hyperplasia, subepithelial fibrosis, and smooth muscle cell hyperplasia. In particular, excessive mucus caused by the goblet cell hyperplasia leads to sever airway obstruction, resulting in the destruction of lung tissues. However, the mechanism of goblet cell differentiation and mucus production caused by cigarette smoking has not yet been fully clarified. The aim of this study is to generate goblet cell hyperplasia model *in vitro* by the use of human iPS cell-derived airway epithelium and cigarette smoke solution (CSS) in order to elucidate the mechanism of goblet cell hyperplasia.

In 2021, I was able to establish several human iPS cell lines that conditionally expresses the transcriptional factor FOXJ1, which is assumed to be involved in the suppression of goblet cell hyperplasia. From 2022 to 2023, I was able to induce human iPS cells cultured with mouse embryonic fibroblasts into definitive endoderm, anterior intestinal endoderm, and ventralized anterior foregut endoderm, which is the expected region for the development of airway epithelium, by the use of several growth factors, cytokines, and chemical compounds.

As a next study, I will induce human iPS cell-derived ventralized anterior foregut endoderm into airway epithelium, and try to generate human-specific goblet cell hyperplasia model *in vitro* by the use of human iPS cell-derived airway epithelium and CSS in order to elucidate the mechanism of goblet cell hyperplasia.