1. No.
   2017G023

2. Title
   Elucidation of the pulmonary emphysema suppressant mechanism by a novel surfactant protein

3. Period
   2017-2021

4. Summary

The objectives of this study were to demonstrate the ameliorative effect of SCGB3A2 on COPD, particularly to understand the molecular mechanisms of development of pulmonary emphysema, and to evaluate the activity of the SCGB3A2 peptides. First, histological analysis of COPD mouse models of cigarette smoke exposure generated using *Scgb3a2*-WT, -KO, and -TG mice was performed. Pulmonary emphysema was worse in the lungs of KO mice while normal morphology was maintained in the lungs of TG mice, suggesting an association of pulmonary emphysema with SCGB3A2 expression level. The mechanism by which SCGB3A2 suppresses emphysema was examined using cultured mouse lung cell line; SCGB3A2 phosphorylates STAT1 and STAT3, however, only phosphorylated STAT3 migrates to the nucleus and promotes *Serpina1a* transcription. In parallel, changes in the lungs of WT and KO mice during aging were investigated. The results showed that SCGB3A2 deficiency increases the risk of developing emphysema with aging. In KO mouse lungs, Serpina1a gene was barely detectable at 8 weeks of age, and immune system-related gene expression was significantly altered when examined at 3 months of age. For the application of SCGB3A2 to peptide drugs, the activity of SCGB3A2 peptides was evaluated with a focus on cell proliferation and apoptosis inhibition and improvement of lung inflammation, Type A peptides were shown to have similar activity to SCGB3A2.