1. No.
   2020G014

2. Title
   Analysis of New Serine-Type Proteinase Inhibitor upon the Pathogenesis of Chronic Obstructive Lung Disease due to Smoking

3. Period
   2020-2024

4. Summary
   We identified WAP as a molecule that is expressed in adult hematopoietic stem cells and spermatogonial stem cells, that disappears when these cells differentiate. WAP is also reported to have stem cell activity in the lung epithelial cells such as basal cells, club cells, and type II alveolar epithelial cells. In order to investigate its function in adult mice, we created a conditional knockout mouse (hereafter referred to as a KO mouse) in which gene deletion can be induced at any desired time by administering tamoxifen. Using these mice, we found that when the WAP gene is deleted in adults, the KO mice show both chronic bronchitis and emphysema. In the KO mice were there increases in lung volume and many phagocytic macrophages and neutrophils in the bronchoalveolar lavage fluid observed. In the HE staining images, when followed from 12 to 51 weeks after the start of gene deletion, inflammatory cell infiltration into the bronchial lumen and alveolar destruction were observed over time. Furthermore, the abnormal tight junction protein distribution observed in the bronchi *in vivo* was not observed in the epithelial cells in the bronchial alveolar interface culture. Thus, we speculated that the increase in bronchial wall permeability was secondary effects. On the other hand, abnormalities were observed in the differentiation pathway from basal cells to club cells and ciliated epithelial cells via the progenitor cell fraction.