1. No.
   2018G014

2. Title
   Role of cellular senescence in smoking-induced pathology

3. Period
   2018-2021

4. Summary
   Chronic obstructive pulmonary disease (COPD) is third leading cause of death worldwide, and one of its major causes is the cigarette smoking. Pulmonary emphysema is a main component of COPD. Emphysema is characterized by permanent alveolar destruction, and there is currently no cure for this disease. Cellular senescence is accelerated in lung of patients with emphysema; however, it was unknown whether and how cellular senescence is involved in the emphysema-associated pathologies. We firstly analyzed the roles of senescent cells in emphysema pathology, and found that elimination of senescent cells (senolysis) alleviated the emphysema-associated pathologies including alveolar inflammation and destruction. These results suggested that lung senescent cells exacerbate the pathology and are potential therapeutic target for this disease. However, the elimination of senescent cells had no therapeutic effect on animal already established emphysema, suggesting that senolysis by itself is insufficient to restore the pulmonary function in emphysematous lung.

   While the senolysis did not have therapeutic effect in the emphysematous animals, we found that transplantation of lung progenitor cells in conjunction with senolysis restored the pulmonary function. Our analyses further revealed that senescent cells non-cell autonomously affected the regenerative activity. Together, these findings are expected to lead the development of innovative therapies for emphysema.