1. **No.**

   FP01812189

2. **Title**

   Cigarette smoke-induced starvation of bronchioalveolar stem cells (BASCs) and exacerbation of chronic obstructive pulmonary disorder (COPD)

3. **Period**

   2017-2019

4. **Summary**

   Although cigarette smoking is proposed as the leading cause of COPD, stop smoking exerts little effect to repair the injured alveoli or to ameliorate its symptoms. In this study, we hypothesized that a mechanism underlying cigarette smoke-induced worsen of COPD would be exhaustion of bronchoalveolar stem cells (BASCs) and abnormal signaling via LPAR3. Compared to WT mice, LPAR3-/- mice exhibited emphysema-like phenotype with age, and aberrant destruction of alveolar walls by inhalation of elastase as well. In addition, the percentage of bronchoalveolar stem cells (BASCs) in aged LPAR3-/- mice was significantly lower than those in age-matched WT mice, and BASCs collected from LPAR3-/- mice exhibited shortened telomere length, one of the characteristics of cellular senescence, compared to those collected from WT mice. In accordance, BASCs collected from LPAR3-/- mice had significantly lower capacity to form spheroid by 3D sphere-forming assay compared to those from WT mice. Also, the capacity of BASCs to form spheroid was strongly impaired by exposure of cigarette smoke.

   From our study, it was suggested that impaired self-renewing of BASCs by decreased LPAR3 signaling as well as cigarette smoking could be a mechanism that deteriorate COPD and a selective LPAR3 agonist could be a promising for treatment of COPD.