1. **No.**

   FP01912216

2. **Title**

   Elucidation of the Pathogenesis of Asthma and COPD Overlap (ACO) Model Mice by Use of Cigarette Smoke

3. **Period**

   2020-2020

4. **Summary**

   In the previous study, we found that co-exposure of CS to asthma model mice produced by OVA exposure induced steroid-resistant airway inflammation, which is one of the characteristics of ACO. In the present study, we aimed to establish a mice model for ACO and to elucidate the pathogenesis of ACO. We found that OVA and CS co-exposed mice showed mixed neutrophila-eosinophila airway inflammation and increased production of inflammatory cytokines, similar to ACO. In addition, downregulation of gene and protein expression of HDAC2 and GRα and increased phosphorylation of Akt indicating activation of the PI3K pathway were also observed in lung tissue, which have been reported to be involved in the development of steroid resistance. These findings suggest that mice that co-exposed to OVA and CS might be used as an animal model of ACO that exhibits mixed airway inflammation in asthma and COPD and steroid resistance. Furthermore, the results suggest that the down-regulation of HDAC2 and GRα by PI3K activation might be involved in the mechanism of steroid resistance in this mouse model.