A mechanistic study of cigarette smoke-induced COPD and cessation effects in C57BL/6 mice

Introduction

Chronic obstructive pulmonary disease (COPD) is defined by the WHO as a lung disease that is characterized by chronic obstruction of lung airflow that interferes with normal breathing and is associated with narrowing of the small airways, chronic bronchitis, and the development of alveolar emphysema. In developed countries cigarette smoking is the main etiological factor in the pathogenesis of COPD. However, the underlying pathogenesis of the disease is not fully understood. Identification of a murine model is a prerequisite for the development of treatment options for COPD. We have established a model of smoke-induced emphysema in C57BL/6 mice that mimics many of the characteristics of human COPD.

Materials and Methods

Animals
- Female C57BL/6 mice 8–10 weeks old were used.
- The animals were randomly allocated to the following 3 exposure groups just prior to the start of the exposure:
  1) Sham – fresh air control group
  2) 3R4F Reference cigarette, University of Kentucky (for specifications see University of Kentucky, http://www.ca.uky.edu/refcig) – Cigarette smoke exposure
  3) Cessation – 2 months cigarette smoke followed by up to 5 months fresh air

Exposure
- Whole-body exposure chambers
  - 3R4F – Health Canada Intense Puffing Regime
  - Target concentration – 750 μg TPMP, 4 hours per day, 5 days per week
  - This exposure regime was selected as similar exposure conditions have resulted in the progression of emphysematous changes in the lungs in C57BL/6 mice (1, 2)

Results

Body weight progression during the exposure period. CS exposure resulted in a lower rate of body weight increases relative to fresh air (sham)-exposed animals, with differences seen from 20 days after exposure start. Following a switch from cigarette smoke to fresh air (Cessation), the body weight gain was rapid, and reached the body weight of sham animals within approximately 2 weeks.

Discussion

1. We have established a model of smoke-induced emphysema in C57BL6 mice that mirrors many of the characteristics of human COPD.
2. Cigarette smoke exposure resulted in increased infiltration of inflammatory cells and mediators into the lung which were quantified in the bronchoalveolar lavage fluid.
3. Pulmonary function was decreased by cigarette smoke and resulted in the leftward-shift of the PV loops following exposure.
4. Histopathological and morphometric assessment of lung tissue showed time-dependent progression of pulmonary emphysema in response to cigarette smoke exposure.
5. Cessation following 2 months of cigarette smoke exposure resulted in the amelioration of the above mentioned parameters to near sham levels as soon as within 1 month of cessation.

References