An Animal Model Of Adult-Onset Allergic Asthma

J. Shin[1], A. Castaneda[1], D. Uyeminami[1, 2], J. Peake[1], I. Espiritu[1], P. Tornes[1], T. Kadir[1], Y. Cho[3], K. E. Pinkerton[1]
[1]University of California, Davis, Davis, CA, [2], [3]University of Montana, Missoula, MO

Corresponding author's email: jsh@ucdavis.edu

Rationale:
The mouse is the most widely used animal model for allergic asthma, with numerous studies using ovalbumin to induce asthma in young, juvenile mice. However, there is no established murine model for adult-onset asthma, a severe disease mainly affecting women and associated with a more rapid decline in lung function compared to childhood-onset asthma. House dust mite (HDM) is a ubiquitous allergen and can trigger allergic asthma. Using HDM to induce asthma in adult mice could provide a reasonable animal model for adult-onset allergic asthma. The goal of this study was to determine the degree of reactivity of young and mature female C57 Black/6 mice exposed to HDM.

Methods:
Three and nine month old female C57 Black/6 mice were randomized into two groups each, HDM (n=6-7) and PBS (phosphate buffered saline, n=5-6). An allergic response was induced via intranasal instillation. Sensitization was performed on days 1, 3, and 5, and challenge was performed on days 12, 13, and 14. On day 15, the mice underwent pulmonary function tests and methacholine challenges for EC200RL (effective concentration that leads to a two fold increase in resistance). Bronchoalveolar lavage (BAL) fluid was collected for cell differentials. The right lung lobes were fixed and stained for histopathology.

Results:
Pulmonary Function: Nine month old mice exposed to HDM had significantly decreased inspiratory capacity, decreased compliance, increased elastance, and increased small airway/peripheral tissue resistance while central airway resistance was not significantly different. EC200RL was significantly decreased, reflecting airway hyper-responsiveness. In contrast, Three month old mice exposed to HDM had no significant lung physiological changes.
Lung Inflammation (BAL): The total cell count was significantly higher in the HDM group compared to the PBS group for both three and nine month old mice. Of the cell differentials, the number of monocytes, neutrophils, lymphocytes, and eosinophils were significantly higher in nine month old mice, while the number of macrophages was not significantly different. For three month old mice, only esosinophils were significantly increased. This demonstrates a strong inflammatory/allergic response to HDM.
Histopathology: The HDM group showed marked perivascular inflammation in contrast to the lungs of PBS controls.

Conclusions:
Sensitization and challenge with HDM created a significant reactive airway response in nine month old female C57 Black/6 mice, but not in 3 month old mice. Both ages showed similar degrees of lung inflammation. These changes are consistent with adult-onset allergy, and potentially serve as a model of adult-onset asthma.

abstract figure.jpg

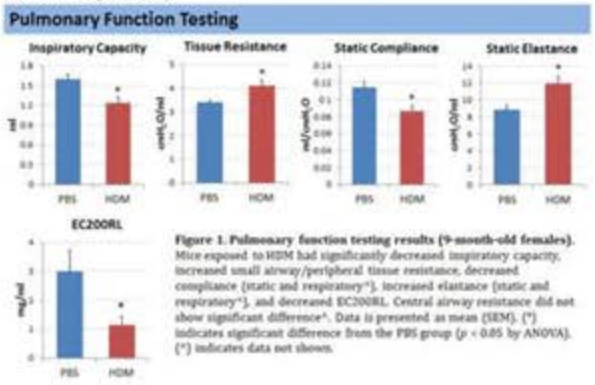

Figure 1. Pulmonary function testing results (9-month-old females). Mice exposed to HDM had significantly decreased inspiratory capacity, increased small airway/peripheral tissue resistance, decreased compliance (static and respiratory*), increased elastance (static and respiratory*), and decreased EC200RL. Central airway resistance did not show significant difference^. Data is presented as mean (SEM). (*) indicates significant difference from the PBS group ($p < 0.05$ by ANOVA). (^) indicates data not shown.

This abstract is funded by: National Institute for Occupational Safety and Health (NIOSH U54 0H07550)