

# ASP—AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY GERIATRIC DEVELOPMENT INITIATIVE JUNIOR FACULTY DEVELOPMENT AWARD

## *Award Recipient:*



PAULA BUSSE, MD  
MOUNT SINAI SCHOOL OF MEDICINE

## PROJECT:

THE ROLE OF CHRONIC ALLERGEN EXPOSURE ON THE EXPRESSION OF THE MAJOR MUCUS PRODUCING GENE IN THE AIRWAYS, MUC-5AC, IN OLDER MICE, AND DEVELOPMENT OF A MURINE MODEL OF ELDERLY-ONSET ATOPIC ASTHMA

## MENTORSHIP TEAM:

STEVEN ITZKOWITZ, MD	XIU-MIN LI, MD
LLOYD MAYER, MD	HUGH A. SAMPSON, MD
ALBERT L. SIU, MD	

After completion of my fellowship training in allergy and immunology at Mount Sinai Hospital in 2001, I joined the division of clinical immunology as an instructor. My long-term goal is to become a full professor and to continue my research in the pathophysiology of asthma, especially late-onset asthma, and the consequences of long-term inflammation in the airways. Although my proposal to the T. Franklin Williams Scholars Program is based upon murine models, I plan on translating this research to human asthmatics. In addition, I would like to generate sufficient data to make an application for a K-08 grant by the year 2004.

My project focuses upon the consequences of long-term airway inflammation in asthma and developing a murine model of late-onset asthma. Asthma is frequently thought of as a childhood illness, but it can affect patients of all ages. Estimates of the prevalence of asthma in the elderly are between four and eight percent of the total population of individuals over the age of 65. "Elderly" asthmatics consist of those with disease onset in their childhood and those who develop it later in life without a history of childhood asthma. Unfortunately, the research into the pathogenesis of asthma has focused mostly upon younger populations. This gap may be partly due to lack of recognition of asthma in the elderly but also to the difficulty of obtaining lung tissue from these patients. However, over the past years, the interest in airway remodeling from chronic inflammation may have sparked further interest into the pathology of longstanding asthma past the age of 65 years. One particular aspect of airway

remodeling that remains unclear is the pathogenesis of mucus cell hyperplasia/hypertrophy. The gene, MUC-5AC, that controls the major airway protein in mucus has been recently identified and is increased in expression in animal models of asthma and in the lung tissue from asthmatic subjects. The regulation of the MUC-5AC gene by chronic airway inflammation is important for the elderly asthmatic as it may help to explain loss of reversibility of their asthma and may be a target for therapy. In addition to not fully understanding the effects of chronic airway inflammation on mucus production in the elderly, the pathology of elderly-onset asthma is not well understood, and there are no animal models of adult or elderly-onset asthma. This study will use an established model of conalbumin-induced asthma with subsequent exposure to this same antigen for different periods of time to explore the contribution of chronic antigen exposure in the expression of MUC-5AC. In addition, this study will develop a murine model of late-onset asthma. This model will offer insight into the pathogenesis of asthma in this population. Finally, this study will investigate the effect of a murine anti-TNF- $\alpha$  antibody on MUC-5AC expression and airway hyperactivity in sensitized mice. Establishing a relationship between MUC-5AC and TNF- $\alpha$  would provide a rationale for a new treatment of asthma by blocking TNF- $\alpha$ . This type of treatment of asthma could be beneficial for the elderly population in whom corticosteroids have an increased side-effect potential.