ASP-American Academy of Allergy, Asthma, and Immunology Geriatrics Development Initiative Junior Faculty Development Award

AWARD RECIPIENT

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PROJECT

"Identification and Impact of Age-Related Changes in Neutrophils During an Asthma Exacerbation"

MENTORSHIP TEAM

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As the US population ages, the prevalence of asthma in the elderly is expected to increase significantly. The aging population has the highest hospitalization and mortality rates for asthma, yet it is under-diagnosed and undertreated. In comparison to younger asthmatics, elderly asthmatics have a higher rate of severe exacerbations, emergency department visits, and hospitalizations, which can have a significant impact on disease impairment and risk.

Neutrophils have a well-known role in inflammation in the airway, as they are one of the first inflammatory cells recruited to the airway after exposure to infection or allergen. Neutrophil mediators such as leukotriene B4 (LTB4) and neutrophil elastase (NE) have been shown to play a role in the pathogenesis of asthma by causing cholinergic airway hyper-responsiveness and mucus hyper-secretion, respectively. In asthma exacerbations, neutrophil activation and degranulation likely contribute to airway obstruction and lower respiratory tract symptoms through neutrophil protease induced mucus secretion by airway gland serous cells.

Previous studies have shown that both older non-asthmatic and asthmatic subjects at baseline disease have a significant increase in airway neutrophils. Our preliminary data revealed differences in the baseline levels of both sputum LTB4 and NE activity of older asthma subjects. A decrease in sputum LTB4 production was found in older asthma subjects, which we hypothesize may impair an effective immune response, as LTB4 aids in neutrophil superoxide anion generation and recruitment of other inflammatory cells. Furthermore, we found increased NE activity in the sputum of older asthmatics, which could lead to airway epithelial cell damage and in turn to an increased susceptibility to infection and asthma exacerbation. It is not known if alterations in these neutrophil mediators are present or further enhanced during an asthma exacerbation.

The goal of this project is to identify age-related changes that occur in the neutrophils of asthmatics and the impact it has during an asthma exacerbation. This will be pursued in the following specific aims:

1. Assess age-related changes in the in vitro and in vivo production of neutrophil inflammatory mediators.
2. Assess correlation of neutrophil dysfunction with the length and severity of asthma exacerbations in older asthma subjects.

Identifying the differences seen in asthma in the growing elderly population will be important in the diagnosis of the disease, improvement in the morbidity and mortality, as well as determining optimal therapies for this growing population.

At the completion of this project we expect to identify changes in the neutrophil that occur during an exacerbation to help us understand why older asthmatics have more severe exacerbations. The information obtained from the proposed study will provide preliminary data for future grant applications, address the mechanistic role of dysfunctional airway neutrophils during an asthma exacerbation, and identify potential therapies for overcoming these deficiencies in the growing elderly population. Furthermore, it will provide valuable support to facilitate my successful transition to an independent investigator in aging research, so that I may make significant contributions to improve the health of the growing elderly population.