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

Award Recipient:

Sameer K. Mathur, MD, PhD
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Project:

Effects of Atopy and Immunosenescence on Regulation of T-cell Activity

Mentorship Team:

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Asthma is a chronic disease characterized by airway hyperresponsiveness, subepithelial fibrosis, and goblet cell hyperplasia. These properties are, in part, the consequence of airway inflammation. Inflammation in asthma is a multicellular process including neutrophils, T-cells, and eosinophils. There is evidence to suggest that immune function declines with aging. For example, there is increased frequency and greater severity of infections in the geriatric population. The impairment in immunity has been attributed to diminished function of immune cells with age, termed "immunosenescence." In contrast to microbial immunity, there is often a continued presence or new onset of asthma in the geriatric population, which suggests that allergic airway inflammation in asthma can persist into old age. It is unclear why anti-microbial inflammation and allergic inflammation apparently differ in their responses with aging.

Allergic inflammation is a process classically described as a Th2 response. This implies that the inflammation is mediated by Th2 cells, which are characterized by the CD4 cell surface marker and the secretion of cytokines including IL-4, IL-5, and IL-13. In addition, it is recognized that other T-cell subsets, Th1 and T-regulatory cells, may impact the function of Th2 cells and modulate allergic inflammation. Itis unknown whether immunosenescence alters the distribution or function of these particular subsets of T-cells.

We are interested in understanding the influence of aging on immune function in allergic inflammation and propose to address this issue in the context of asthma by exploring the interaction between atopy and immunosenescence in young adults and the geriatric population. A particular focus of these studies will be the regulation of T-cell activity. We propose to examine the relationship of allergic status, or atopy, and immunosenescence in vitro by analyzing T-cell populations in young versus elderly asthma subjects, with and without atopy, and to characterize the differences in the cellular composition in the airway and markers for immunosenescence with age. We will also examine T-cell activity and an in vitro model for immunoregulation of the T-cell activity in asthma with the co-culture of eosinophils. Taken together, these studies will clarify the relationship between atopy, immunosenescence, and T-cell function.

The ASP-American Academy of Allergy, Asthma and Immunology-ASP Geriatric Development Initiative Junior Faculty Award will provide valuable support for my training as an independent investigator in geriatric research. The transition into a junior faculty position will be guided by the mentoring committee and participation in the University of Wisconsin Clinical Investigator Preparatory Program, which will provide core training in research design, ethics, statistical analysis, manuscript writing, and oral presentations. The award will enable implementation of the research proposal, which will lead to new knowledge about asthma in the geriatric population. This work will facilitate the education of general internists and subspecialists on the unique features of asthma in the geriatric population. Further training in the care of geriatric patients and participation in educational outreach activities will be accomplished in association with the University of Wisconsin Institute on Aging. Finally, this award will provide the financial support to launch my career in geriatric research and will establish a "track record" of funding in geriatric research, which will be beneficial in seeking future support.