Interleukin (IL)-15 immunotherapy: A novel non-steroidal approach to treat allergen-induced airway obstructions

Allergen-induced airway obstruction is a physiologic feature of asthma and IL-15 deficiency is reported in asthmatic patients. Therefore, we tested the hypothesis that regulation of IL-15 is critical for the preservation of allergen-induced airway hyper responsiveness (AHR), airway resistance and compliance. Accordingly, airway inflammation, AHR, resistance and compliance were assessed in IL-15- gene deficient mice and IL-15 overexpressing mice in an allergen-induced murine model of asthma. Herein, we report that IL-15 deficiency promotes baseline airway resistance in naïve mice. Moreover, rIL-15 delivery to the lung down regulates expression of proinflammatory cytokines, and improves allergen-induced AHR, resistance and compliance. These observations were further validated in DOX-inducible CC-10-IL-15 transgenic mice. DOX exposed Aspergillus extract challenged CC-10-IL-15 bi-transgenic mice exhibited significantly reduced levels of pro inflammatory cytokines (IL-4, IL-5, IL-13) and decreased goblet cell hyperplasia. Airway obstruction including AHR and resistance was diminished in allergen challenged DOX exposed mice compared to non-DOX exposed CC-10-IL-15 bi-transgenic mice. Mechanistically, we observed that IL-15-mediated protection of airway obstruction is associated with induced IL-10-producing regulatory CD4+CD25+Foxp3+ T cells. Additionally, we found that a human IL-15 agonist (ALT-803) improved airway resistance and compliance in an experimental asthma model. Taken together, our studies conclude that IL-15 has a potent inhibitory effect on the airway obstruction that occurs in response to environmental allergens.

Biography
Anil Mishra is a Professor of Medicine. He is also the Director of Tulane Eosinophilic Disorder Center in the section of pulmonary diseases at Tulane University School Of Medicine. His research established that eosinophils are the resident cells of the gastrointestinal tract that home prenatally. He showed that eosinophil active chemokine eotaxin-1 constitutively expressed and has significant role for eosinophils homing into the gastrointestinal tract. He developed the first murine model of eosinophilic esophagitis (EoE). His findings implicated aerallergen in the etiology of EoE and suggested that esophageal eosinophilic inflammation is mechanistically associated with pulmonary inflammation. Recently, he reported that rIL-15 is a therapeutic molecule for the allergen-induced airway hyperactivity and fibrosis for chronic asthma and other pulmonary functional impairment. He is an Elected Fellow of American Academy of Allergy Asthma Immunology (FAAAAI) and American Gastrointestinal Association (FAGA). He has published over 72 articles, book chapters and reviews on molecular mechanisms of pulmonary and gastrointestinal allergic responses in high impact factor journals. His research is supported by National Institutes of Health via NIDDK and NIAID institutes. He is also a member of several NIH study sections and serving as Editor and Editorial Board Member in a number of international journals.

Anil Mishra
Tulane University School of Medicine, USA

amishra@tulane.edu

Notes: