

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

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Abstract

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 naive 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

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Note: This work is partly presented at 11th International Conference on ALLERGY, ASTHMA & CLINICAL IMMUNOLOGY, September 07-08, 2017 | Edinburgh, Scotland