

Antigen-Fixed Leukocytes Tolerize Th2 Responses in Mouse Models of Allergy

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Abstract

Allergic diseases, including asthma and food allergies, are an increasing health concern. Immunotherapy is an effective therapeutic approach for many allergic diseases but requires long dose escalation periods and has a high risk of adverse reactions, particularly in food allergy. New methods to safely induce Ag-specific tolerance could improve the clinical approach to allergic disease. We hypothesized that Ag-specific tolerance induced by the i.v. injection of Ags attached to the surface of syngeneic splenic leukocytes (Ag-coupled splenocytes [Ag-SPs]) with the chemical cross-linking agent ethylene-carbodiimide, which effectively modulate Th1/Th17 diseases, may also safely and efficiently induce tolerance in Th2-mediated mouse models of allergic asthma and food allergy. Mice were tolerized with Ag-SP before or after initiation of OVA/alum-induced allergic airway inflammation or peanut-induced food allergy. The effects on disease pathology and Th2-directed cytokine and Ab responses were studied. Ag-SP tolerance prevented disease development in both models and safely tolerized T cell responses in an Ag-specific manner in presensitized animals. Prophylactically, Ag-SP efficiently decreased local and systemic Th2 responses, eosinophilia, and Ag-specific IgE. Interestingly, Ag-SP induced Th2 tolerance was found to be partially dependent on the function of CD25⁺ regulatory T cells in the food allergy model, but was regulatory T cell independent in the model of allergic airway inflammation. We demonstrate that Ag-SP tolerance can be rapidly, safely, and efficiently induced in murine models of allergic disease, highlighting a potential new Ag-specific tolerance immunotherapy for Th2-associated allergic diseases.

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