Immunologic Response with Venom Immunotherapy

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Allergic diseases including atopic dermatitis, food allergy, allergic rhinitis, asthma and anaphylaxis have significant associated morbidity along with large health-care expenditures. Allergen-specific immunotherapy (SIT) has been used as a desensitizing therapy for allergic diseases and may represents a curative and specific way of the treatment. Hymenoptera venom allergy is a major cause for severe andpotentially fatal anaphylaxis.1 Immunotherapy with hymenopteravenoms was shown to be highly effective. However, inpatients with honeybee venom (BV) allergy, it might cause systemic allergic side effects in up to 20% to 40%, mainly during the dose-increase phase. For this reason, preventive medication with antihistamines is often used during the initial phase of honeybee venom immunotherapy (BVIT) and was shown to significantly reduce large local and generalized cutaneous reactions in several double-blind, placebo-controlled trials. The mechanism by which immunotherapy induces protection is associated with changes in the fine balance between allergenspecific regulatory T cells and TH2 cells, TH1 cells, or both. Histamine, originally considered a mediator of acute inflammatory and immediate hypersensitivity responses, has also been demonstrated to regulate antigen-specific TH1, TH2, and regulatory T cells, as well as related antibody isotype responses. Histamine enhances TH1-type responses by triggering HR1, whereas both TH1- and TH2-type responses are negatively regulated by HR2. Human CD41 TH1 cells predominantly express HR1 and CD41 TH2 cells predominantly express HR2, which results in their differential regulation by histamine. The significantly decreased value of the HR1/HR2 ratio in the placebo group indicates HR2 dominance during venom immunotherapy. The induction of a tolerant state in peripheral T cells represents an essential step in allergen-specific immunotherapy. Peripheral T cell tolerance is characterized mainly by suppressed proliferative and cytokine responses against the major allergens and its T cell recognition sites. It is initiated by autocrine action of IL-10 and/or TGF-b, which are increasingly produced by the antigen-specific T Regulatory (Treg) cells. Tolerized T cells can be reactivated to produce either distinct Th1 or Th2 cytokine patterns thus directing allergen-SIT towards successful or unsuccessful treatment. Treg cells directly or indirectly influence effector cells of allergic inflammation, such as mast cells, basophils and eosinophils. In addition, there is accumulating evidence that they may suppress IgE production and induce IgG4 and IgA production against allergens. By the application of the recent knowledge in mechanisms of allergen SIT, more

rational and safer approaches are awaiting for the future of prevention and possibly cure of allergic diseases.