Orally administered hydrolysed ovalbumin as an immunotherapeutic agent in a mouse model of egg allergy

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Background: At present, the main treatment for egg allergic patients is based on food avoidance, which poses a risk, since egg is used as an ingredient in a wide range of food products. Oral immunotherapy (OIT) is a promising treatment option, although the use of intact allergens produces frequent side effects. In this respect, egg white protein hydrolysates are thought to be safer to induce protective mechanisms leading to oral tolerance. The aim of this study was to determine the immunomodulatory effects of pepsin-hydrolyzed ovalbumin (OVA) administered as OIT in a BALB/c model of egg allergy.

Methods: BALB/c mice were orally sensitized during 6 weeks with 5 mg of raw egg white (EW) using cholera toxin as adjuvant. On week 7, mice underwent an immunotherapy protocol with either intact or pepsin-hydrolyzed OVA during 3 weeks and were subsequently challenged with EW. The severity of the anaphylactic response was evaluated (clinical signs and body temperature drop) and serum levels of mMCP-1 were determined by ELISA. Allergen-specific antibodies, IgE and IgG1, were monitored throughout the OIT. The expression of the genes TSLP, IL-33, IL-25, TGF-β and IL-10 was analyzed by RT-qPCR in the small intestine. Furthermore, cytokine responses were measured in allergen-stimulated splenocytes and changes in cellular populations (Th1, Th2 and T reg) were assessed in the mesenteric lymph nodes (MLNs) using flow cytometry.

Results: Mice orally treated with pepsin-hydrolyzed OVA were significantly protected from anaphylactic reactions compared with the groups of untreated mice and mice treated with intact OVA, which showed anaphylactic signs and a marked decrease of body temperature. Similarly, serum levels of mMCP-1 were lower in mice treated with the hydrolyzate. Desensitization of the allergic mice induced by the hydrolyzate was accompanied by a significant reduction in the levels of EW-specific IgE and IgG1. Administration of hydrolyzed OVA also downregulated the intestinal expression of TSLP, IL-33 and IL-25, and led to higher levels of IL-10 expression. However, the group that received intact OVA showed similar expression levels than untreated control mice. Desensitization by pepsin-hydrolyzed OVA was associated with a shift in the Th2 profile, as shown in ex vivo stimulated splenocytes and flow cytometry analysis of T cell subsets in the MLNs.

Conclusion: OIT with pepsin-hydrolyzed OVA desensitizes and prevents allergen-induced anaphylaxis in mice allergic to EW more effectively than the intact protein.