Abstract

Thesis title: New T cell target genes in peanut allergy.

Name	Aziza Saidova
E-mail	aziza.saidova@icloud.com aziza_84s@rambler.ru
Home Institute address	Bagishamal str., 223. Yunusabad region, Tashkent 100140, Uzbekistan Tel: +99871 262-34-03 Fax: +99871 262-33-14 Email: interdep@tashpmi.uz
Host Institute address	Klinische Abteilung für Pädiatrische Pulmologie, Allergologie und Endokrinologie, Allergielabor, Level 4 Universitätsklinik für Kinder- und Jugendheilkunde Medizinische Universität Wien Währinger Gürtel 18-20, 1090 Wien Tel.: +43-1-40400-34940 / 34530

Introduction

Peanut allergy one of the serious IgE mediated food allergies. The prevalence of food allergy is increasing [Sicherer S.H., et al., JACI 2018]. Allergic patients may experience life-threatening systemic allergic reactions affecting the skin, the gastrointestinal tract, the respiratory tract and the cardiovascular system upon exposure [Valenta R., et al., Gastroenterology 2015].

T helper cells play a key role in the process of allergic sensitization and have the ability to drive and control allergen specific inflammation. A better understanding of T helper cells in the context of peanut allergy may provide novel diagnostic options and help to design novel, innovative treatment approaches. Therefore, we aimed to delineate specific proteins that are specific for allergen specific T cells from peanut allergic individuals and contribute to the generation of treatment attempts with fewer

side effects. This is needed since oral immunotherapy (OIT) is effective in elevating the threshold, however only 10-15% of patients undergoing OIT develop tolerance or sustained unresponsiveness. Moreover, side effects due to allergic reactions upon ingestion of the allergen during OIT are frequent. Thus, we characterized hypoallergenic variants of Ara h 2 and Ara h 6 with the potential to be used for the treatment of peanut allergy.

Methods and results

We executed whole human genome oligo microarray analyses of sorted Ara h 2 specific ($CFSE^{low}CD3^{+}CD4^{+}$) T cells. By using a two-step bioinformatic approach, we identified markers that were specific for peanut allergy, regardless T cell activation status. Gene expression profiles of markers identified from whole mRNA array analyses were confirmed in 2 different cell compartments (allergen specific CD4+ T cells and peripheral blood mononuclear cells (PBMCs)) by quantitative real time PCR. The potential marker TAB3 is involved in the NFκB activation pathway.

In our next study, we aimed to create mutated versions of Ara h 2 and Ara h 6 proteins with a reduced ability to bind IgE and to maintain T cell immunogenicity for the activation and modulation of regulatory T cells. Thus, the structure of the Ara h 2 and Ara h 6 proteins was modified by altering sequential and conformational IgE epitopes. Accordingly, generated hypo-allergens displayed a decreased ability to activate basophils from peanut allergic individuals and showed a reduced Th2 and increased Treg responses *in vitro*.

Conclusion

Targeting T cells may be a promising approach to treat peanut allergy. Our data provided new markers and potential ways that may help to diagnose or to treat peanut allergy in the future. We observed a peanut allergy associated regulation of the TGF-β activated kinase 1 and MAP3K7 binding protein 3, which is essential for NFκB activation pathway. In addition, we created hypoallergenic variants of the peanut proteins Ara h 2 and Ara h 6, which showed a favorable response compared to their recombinant wild type and native counterparts.

Key words: food allergy, peanut allergy, Ara h 2, Ara h 6, basophil activation, desensitization, T cells, hypoallergen, IgE