IL-12 expression on allergen-laden VNP enhances their Th1 priming activity and reduces Th2 responses in a humanized preclinical model of mugwort allergy

B. Kratzer[1], *S. Hofer*[1], *P. Tauber*[1], *D. Trapin*[1], *M. Schaar*[1], *G. Hofer*[2], *W. Keller*[2], *G. Gadermaier*[3], *W. Pickl*[1,4]

[1]Medical University of Vienna, Center for Pathophysiology, Infectiology and Immunology, Institute of Immunology, Vienna, Austria, [2]University of Graz, Institute of Molecular Biosciences, BioTechMed, Division of Structural Biology, Graz, Austria, [3]Paris Lodron University of Salzburg, Department of Biosciences and Medical Biology, Salzburg, Austria, [4]Karl Landsteiner University, Krems, Austria

Type selection

Choose your preferred presentation format: Oral presentation

General data

Track: Adaptive Immunity

Topic: Allergy

Abstract text

Text: Encapsulation of allergens inside of Virus-like nanoparticles (allergen-laden, AL-VNP) leads to allergen-specific activation of tolerogenic T cells in the absence of sensitization, a feature which may be further improved by decoration of AL-VNP with Th1-priming cytokines.

N-terminal fusion of the major mugwort pollen allergen Art v 1 to the viral matrix protein MoMLV-MAp15 was used for the loading of VNP and to shield the allergen, while C-terminal fusion of single-chain (p35::p40) mIL-12 to the minimal CD16b GPI-anchor was applied to allow surface decoration of VNP with this cytokine. A humanized mouse model of mugwort pollen allergy was used to investigate the immunomodulatory capacities of such VNP *in vitro* and *in vivo*. Notably, allergen-expressing IL-12$^+$ AL-VNP significantly increased IFN-g, moderately increased IL-10, but reduced IL-4, IL-5, IL-13 and IL-17A production and cellular proliferation of allergen-specific splenocytes. Incubation of naïve allergen-specific T cells with IL-12$^+$ AL-VNP and bone marrow-derived dendritic cells (BMDC) differentiated them into IFN-g$^+$CD4$^+$ Th1 cells, comparable to classical Th1 polarization (IL-2, IL-12, anti-IL-4), whose phenotype remained stable after secondary allergen stimulation. In contrast, co-incubation of IL-12$^+$ AL-VNP with Th2-differentiated cells diverted them from IL-13 production and strongly inhibited the further expansion of allergen-specific IL-13$^+$ Th2 cells. In vivo, prophylactic treatment with IL-12+ AL-VNP followed by bona fide allergen challenge via the airways reduced the expansion of IL-4$^+$ and IL-13$^+$ CD4$^+$ T cells compared to treatment with control AL-VNP decorated with a constitutively inactive form of IL-12.

In summary, IL-12 decoration of AL-VNP enhances their Th1-priming potential, leading to reduced Th2 expansion in vitro and may thus prove useful for the treatment of allergies in the future.

Conflict of Interest statement

Do you have any conflict of interest to declare?: Yes

Conflict of Interest statement: This work was supported by the Federal State of Lower Austria, Danube Allergy Research Cluster (Danube ARC, project no. 10) and the Medical University of Vienna.

Affirmation

1. Consent to participate and present onsite: Yes

2. Consent to publication publication: Yes

3. Consent on treatment of contact details saved in this system: Yes