Characterization of a transgenic mouse model to investigate Bet v 1-specific T cell responses and PR-10 cross-reactivity in birch pollen allergy

M. Schaar[1], B. Kratzer[1], A.N.A. Sehgal[1], D. Trapin[1], A. Neunkirchner[1], B. Bohle[2], U. Wiedermann[3], R. Valenta[2,4,5,6], W. Pickl[1,7]

[1]Medical University Vienna, Center for Pathophysiology, Infectiology & Immunology, Institute of Immunology, Vienna, Austria, [2]Medical University Vienna, Center for Pathophysiology, Infectiology & Immunology, Institute of Pathophysiology and Allergy Research, Vienna, Austria, [3]Medical University Vienn, Center for Pathophysiology, Infectiology and Immunology, Institute of Specific Prophylaxis and Tropical Medicine, Vienna, Austria, [4]Karl Landsteiner University, Center for Molecular Allergology, Krems, Austria, [5]Sechenov First Moscow State Medical University, Laboratory for Immunopathology, Department of Clinical Immunology and Allergology, Moscow, Russian Federation, [6]Life Improvement by Future Technologies (LIFT) Center, Moscow, Russian Federation, [7]Karl Landsteiner University, Krems, Austria

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Abstract text

Text: Sensitization to birch (*Betula verrucosa*) pollen is one of the main causes of pollinosis in the Northern hemisphere. Bet v 1 represents the major allergen, to which over 95% of birch pollen allergic patients are sensitized. Bet v $1_{142\text{-}153}$ had been identified as the immunodominant T-cell epitope in birch pollen allergic individuals previously.To study allergic sensitization and organ-specific manifestations upon exposure to birch pollen, we here generated a transgenic mouse model expressing a human Bet v $1_{142\text{-}153}$-specific T cell receptor (TCR), human CD4, and HLA-DR7**.** Primary and secondary lymphoid organs of $hCD4^+TCR^+HLA\text{-}DR7^+$ transgenic (tg) mice were analyzed by flow cytometry. The functionality of T cells of allergen-naïve hCD4 $^+TCR^+HLA\text{-}DR7^+$ tg mice was assessed and confirmed in splenocyte proliferation and cytokine secretion assays. Additionally, a panel of peptides from Bet v 1-homologs, derived from tree and food allergens, was screened to determine their potency to activate Bet v $1_{142\text{-}153}$-specific T cells and to bind to the restricting HLA-DR7 molecule, revealing their cross-reactive and immunomodulatory potential.Of the $CD3^+CD4^+$ T cells, 90.1±8.4% co-expressed hCD4, and 61.6±9.8% of those $CD3^+mCD4^+hCD4^+$ cells co-expressed the human Bet v $1_{142\text{-}153}$-specific TCR. Of $CD19^+$ B cells, 60.1±8.0% co-expressed HLA-DR7. *In vitro*, specific T cell proliferation upon co-incubation of splenocytes with full-length rBet v 1 and Bet v $1_{142\text{-}153}$ peptide could be induced, along with the elaboration of a mixed cytokine pattern. In addition, we identified several cross-reactive PR-10 peptides derived from different tree, nut, and fruit allergens among the 26 Bet v 1-homologs tested and determined their differential binding characteristics to HLA-DR7. The novel TCR- and HLA-transgenic humanized mouse model for birch pollen allergy presented herein represents a valuable platform for the study of birch pollen allergy and for development of prophylactic and therapeutic strategies once *in vivo* sensitization and treatment protocols are established.

Conflict of Interest statement

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

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