Poster

Structure-based IgE-epitope investigation of the major cat allergen Fel d 4

N. Todorovic[1], D. Trifonova[2,3], M. Curin[2], L. Schooltink[1], T. Sagmeister[1], C. Grininger[1], N. Gottstein[1], R. Kiss[2], T. Pavkov-Keller[1], A. Karaulov[3], R. Valenta[2,3], W. Keller[1]

[1]Institute of Molecular Biosciences, University of Graz, Graz, Austria, [2]Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria,[3]Laboratory for Immunopathology, Department of Clinical Immunology and Allergology, Sechenov First Moscow State Medical University, Moscow, Russian

nikolina.todorovic@uni-graz.at

Pets have been recognized as one of the major sources of indoor allergens posing a great risk for the development of IgE-mediated diseases such as rhinitis and asthma [1]. To date, the WHO/IUIS database reports eight cat allergens, among which the frequency of IgE recognition and allergen-specific IgE reactivity is found to be the highest for Fel d 1, Fel d 4 and Fel d 7 making them clinically the most important cat allergens [2]. The cat allergen Fel d 4 belongs to the lipocalin protein family and shares a high sequence identity with the lipocalin allergens from dog (Can f 6) and horse (Equ c 1). IgE cross-reactivity to these allergens contributes to polysensitization triggering allergic responses caused by contact with different animals [3]. The structural analysis of allergens together with epitope studies are important for the improvement of diagnostic approaches as well as the development of specific immunotherapies. We generated recombinant Fel d 4 allergens using two different expression systems and employed X-ray crystallography to reveal the structures that confirmed that Fel d 4 has a typical lipocalin fold, consisting of an 8-stranded β-barrel and one α-helix, and shares high structural similarity to Can f 6 and Equ c 1. Based on the obtained structural data we performed immunological studies using indirect epitope mapping with antisera raised in rabbits against synthetic Fel d 4 peptides for competing with IgE binding of allergic patients. Results of the IgE competition studies showed that the C terminal region of the allergen harbors conformational IgE epitopes or is part of a region containing conformational IgE epitopes. Uncovering the specific IgE binding sites of Fel d 4 contributes to the understanding of allergen recognition by IgE, helps to understand the basis for IgE cross-reactivity and is important for the rational design of active and passive allergen-specific treatment forms such as vaccines and therapeutic antibodies.

[1] Nwaru, B., I., Suzuki, S., Ekerljung, L., Sjölander, S., Mincheva, R., Rönmark, E., P., Rådinger, M., Rönmark, E., Borres, M., P., Lundbäck, B., Lötvall, J. (2019). *J. Allergy Clin. Immunol. Pract.*, **7**, 1230–1238.e4.

[2] Trifonova, D., Curin, M., Riabova, K., Karsonova, A., Keller, W., Grönlund, H., Käck, U., Konradsen, J., R., van Hage, M., Karaulov, A., Valenta, R. (2023) *Int. J. Mol. Sci.*, **24**, 16729.

[3] Nilsson, O., B., Binnmyr, J., Zoltowska A., Saarne, T., van Hage, M., Grönlund, H. (2012) *Allergy*., **67(6)**, 7517.

The work is supported by the Austrian Science Fund, DocFund Biomolecular structures and interactions, grant no. Doc130, and in part by the Danube Allergy Research Cluster of the Country of Lower Austria and by grant no. 23-75-30016 from the Russian Science Foundation in its part related to allergen characterization.