



Letter to the Authors Concerning the Published Manuscript by Rial and Sastre: Food Allergies Caused by Allergenic Lipid Transfer Proteins: What Is Behind the Geographic Restriction?

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Published online: 25 October 2018

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To the Editor,

We read with great interest the manuscript by M. J. Rial and J. Sastre [1] about the geographical distribution of sensitization to non-specific lipid transfer proteins (ns-LTPs). In present day, this is an interesting topic, and therefore we would like to raise some issues and questions, especially concerning the prevalence of ns-LTP sensitization outside the Mediterranean area. The authors report that sensitization to ns-LTPs is infrequent in Central Europe and other non-Mediterranean regions; however, it appears that the authors have overlooked a large Belgian survey performed in 718 patients [2]. As a matter of fact, we demonstrated that the prevalence of sIgE reactivity towards ns-LTP(s) is demonstrable in about one-quarter of Belgian patients presenting with symptoms of a pollen and/or plant food allergy. In this survey, all patients were systematically screened for ns-LTP sensitization using a panel of six different ns-LTPs; four food ns-LTPs respectively rPru p 3 of peach (*Prunus persica*), rMal d 3 of apple (*Malus domestica*), rCor a 8 of hazelnut (*Corylus avellana*), and rAra h 9 of peanut (*Arachis hypogaea*) and two weed pollen ns-LTPs specifically nArt v 3 of mugwort (*Artemisia vulgaris*) and rPar j 2 of wall pellitory (*Parietaria judaica*). To the best of our knowledge, this study is the largest prevalence study focusing on ns-LTP sensitization in north-western Europe.

Moreover, this study also demonstrated that in a north-western European country, patients with ns-LTP sensitization

can exhibit distinct phenotypes that are not readily predictable by the sIgE results. Although, similar to initial observations in the Mediterranean basin [3–5], some of our patients demonstrated systemic reactions, the majority of patients with sIgE reactivity towards ns-LTPs did not report any clinical reaction to the respective plant food(s). A possible explanation for the absence of overt allergy could be the high prevalence of sensitization to the major allergen of birch pollen, Bet v 1 (*Betula verrucosa*) [6–8]. However, for the time being, this explanation is highly speculative, but relies on observations from the Mediterranean basin on sensitization to Bet v 1 (PR10 molecule) to protect for ns-LTP-related allergies. In other words, patients co-sensitized to Bet v 1 and Bet v 1 homologues report milder clinical symptoms compared to patients without co-sensitization to PR10 molecules. Clearly, more studies are needed to fully elucidate the protective effect of PR10 molecules.

The exact reason(s) for the high prevalence of ns-LTP sensitization in our country remain(s) elusive. Although we cannot exclude our findings (in part) to reflect our methodology (usage of multiple sensitive single-plexed assays), we believe that in most patients, ns-LTP sensitization is genuine and might result from various sensitization routes that extend beyond pollen and plant-derived foods. Actually, we observed that Can s 3, the ns-LTP from *Cannabis sativa*, is a major allergen in cannabis allergy in our regions [9]. Moreover, it appears that sensitization to Can s 3 can result from both active and passive exposure to marijuana smoke [10] and that the Can s 3 cross-reactivity syndrome extends beyond fruits and vegetables but can also involve beverages and latex [11].

In conclusion, sensitization towards ns-LTP, although historically predominantly described in the Mediterranean basin, is not uncommon in north-western Europe and can result in clinically distinct phenotypes. Further collaborative studies are required to obtain insight into sensitization routes, clinical

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phenotypes, and the influence of pollen sensitization and to improve the predictive capacity of diagnostic tests for ns-LTP-related allergies.

References

- Rial MJ, Sastre J. Food allergies caused by allergenic lipid transfer proteins: what is behind the geographic restriction? *Curr Allergy Asthma Rep.* 2018;18(11):56.
- Faber MA, Van Gasse AL, Decuyper II, Uyttebroek A, Sabato V, Hagendorens MM, et al. IgE- reactivity profiles to nonspecific lipid transfer proteins in a northwestern European country. *J Allergy Clin Immunol.* 2016.
- Pascal M, Vazquez-Ortiz M, Folque MM, Jimenez-Feijoo R, Lozano J, Dominguez O, et al. Asymptomatic LTP sensitisation is common in plant-food allergic children from the Northeast of Spain. *Allergol Immunopathol (Madr).* 2016;44(4):351–8.
- Faber MA, Van Gasse AL, Decuyper, II, Uyttebroek A, Sabato V, Hagendorens MM, et al. IgE- reactivity profiles to nonspecific lipid transfer proteins in a northwestern European country. *The J Allergy Clin Immunol* 2017;139(2):679–82 e5.
- Gonzalez-Mancebo E, Gonzalez-de-Olano D, Trujillo MJ, Santos S, Gandolfo-Cano M, Melendez A, et al. Prevalence of sensitization to lipid transfer proteins and profilins in a population of 430 patients in the south of Madrid. *J Investig Allergol Clin Immunol.* 2011;21(4):278–82.
- Fernandez-Rivas M, Bolhaar S, Gonzalez-Mancebo E, Asero R, van Leeuwen A, Bohle B, et al. Apple allergy across Europe: how allergen sensitization profiles determine the clinical expression of allergies to plant foods. *J Allergy Clin Immunol.* 2006;118(2): 481–8.
- Scala E, Till SJ, Asero R, Abeni D, Guerra EC, Pirrotta L, et al. Lipid transfer protein sensitization: reactivity profiles and clinical risk assessment in an Italian cohort. *Allergy.* 2015;70(8):933–43.
- Pastorello EA, Farioli L, Pravettoni V, Scibilia J, Mascheri A, Borgonovo L, et al. Pru p 3- sensitised Italian peach-allergic patients are less likely to develop severe symptoms when also presenting IgE antibodies to Pru p 1 and Pru p 4. *Int Arch Allergy Immunol.* 2011;156(4):362–72.
- Ebo DG, Swerts S, Sabato V, Hagendorens MM, Bridts CH, Jorens PG, et al. New food allergies in a European non-Mediterranean region: is Cannabis sativa to blame? *Int Arch Allergy Immunol.* 2013;161(3):220–8.
- Decuyper II, Faber MA, Sabato V, Bridts CH, Hagendorens MM, Rihs HP, et al. Where there's smoke, there's fire: cannabis allergy through passive exposure. *J Allergy Clin Immunol Pract.* 2017;5(3):864–5.
- Faber MA, Sabato V, Bridts CH, Nayak A, Beezhold DH, Ebo DG. Clinical relevance of the Hevea brasiliensis lipid transfer protein Hev b 12. *J Allergy Clin Immunol.* 2015;135(6):1645–8.