



Food Allergies Caused by Allergenic Lipid Transfer Proteins: What Is behind the Geographic Restriction?

M. J. Rial^{1,2} · J. Sastre^{1,2}

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Abstract

Purpose of Review To critically examine evidence suggesting that food allergy induced by lipid transfer proteins (LTPs) follows a geographic pattern.

Recent Findings LTP syndrome remains most common in the Mediterranean basin, with a clear gradient seen in prevalence of LTP sensitization between northern and southern Europe. We hypothesize that high levels of birch pollen seem to protect against LTP allergy, as these higher levels correlate with a lower prevalence of LTP hypersensitivity. Nevertheless, LTP food allergy cases still appear in areas having a high environmental level of birch pollen.

Summary Food allergy caused by LTP may be related to (1) primary sensitization to a food LTP allergen in the absence of pollinosis, (2) primary sensitization to LTP from a pollen source, and (3) co-sensitization to LTP from pollen and food.

Keywords Food allergy · Lipid transfer protein · LTP · Panallergen · Plant food

Background

In 1992, a small 8–10-kDa protein was described as the main peach allergen in Spain [1•]. This protein was characterized as a lipid transfer protein (LTP), belonging to the superfamily of prolamins and today is considered a relevant food allergen in the Mediterranean area.

LTPs are antigens involved in allergic reactions of varying severity to pollen, latex, and, of course, certain plant foods. LTPs are stabilized by disulfide bonds, giving them a high resistance to digestion, thereby allowing proteins to reach the intestine, where they cause sensitization [2]. There are two types of LTPs (1 and 2); of these, LTP1 is the most well-known and the main allergen in fruits, and there are 42 such proteins described in the IUIS database [3]. The high structural homology between LTP1s results in broad cross-

reactivity among these proteins. The 7-kDa lipid transfer proteins, LTP2s, share some amino-acid sequence, similar folds, and biological functions with the 9-kDa isoforms, LTP1, but are not important as allergens. LTP syndrome is defined as allergy to a minimum of two vegetable foods with no taxonomic relationship between them, with sensitization to LTPs as responsible for allergic reactions [4•].

LTP allergens from pollen also contribute significantly to primary sensitization. The existence of areas where there are pollens with high levels of LTP and food allergy suggests that pollinosis could trigger sensitization too [4•]. Interestingly, fruit LTPs from the plants of the *rosaceae* family were also found in the pollen of these trees [5••].

Pru 3, the main peach allergen and a non-specific LTP, is the most important allergen in Mediterranean area, where it is often associated with severe, sometimes life-threatening reactions, though in other cases oral allergy syndrome is the only adverse result [6]. Although sensitization to LTP is infrequent in central Europe and other regions, it does exist, despite a highly different aerobiology and climatology between this region and the Mediterranean basin [7]. In central European countries, diagnosing LTP allergy using plant extracts is difficult due to frequent co-sensitization with other allergens, especially birch Bet v 1 pollen and other panallergens such as profilins. Therefore, the apparent geographical pattern in food allergy due to LTPs merits further investigation.

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✉ J. Sastre
JSastre@fjd.es

¹ Allergy Department, Hospital Universitario Fundación Jiménez Díaz, Universidad Autónoma de Madrid, Av. de los Reyes Católicos, 2, 28040 Madrid, Spain

² CIBERES, Instituto Salud Carlos III, Madrid, Spain

An Effect of Pollinosis on Geographical Patterns of Allergy

In Europe, the pattern of allergy to plant foods shows a clear distinction between central and northern Europe on the one hand and the Mediterranean basin and southern Europe on the other. Allergy to plant foods in central and northern Europe is usually limited to oral allergy syndrome caused by sensitization to Bet v 1 and homologs (PR-10), while systemic reactions are much more frequent in southern and eastern Europe due to sensitization to LTP, with peach as the main culprit food [5••]; however, pediatric patients, from north and southern Europe are often sensitized to storage proteins from tree nuts [8]. In patients from northern and central Europe, primary sensitization to Bet v 1 generally occurs through the respiratory tract. The symptoms that develop after the ingestion of plant foods are usually mild, as the proteins responsible are thermolabile. Nevertheless, systemic reactions have been described by some PR-10 allergens such as Gly m 4 from soy [9] or Api g 1 [10] from celeriac. In southern Europe, on the other hand, allergic reactions to foods derived from plants are usually associated with systemic reactions due to a primary sensitization to LTPs, though thaumatin-like proteins (TLPs) have been also described as a cause of severe reaction to fruits in Spain [11]. Of note, LTPs have also been implicated in local reactions as OAS and even in asymptomatic sensitizations [12]. Currently, the explanation for this geographical distribution is a topic of debate, given that in central and northern Europe, plant foods that induce allergies also have high levels of LTP, and it appears that dietary habits and the different food-processing practices of the different regions alone do not offer a convincing explanation for this pattern.

In a cohort of 13 Austrian patients with a history of anaphylaxis after ingestion of plant foods, sensitization to LTP (Pru p 3) was demonstrated in ten of 13 patients, nine to Bet v 1, and two to profilin. This result showed that LTP sensitization may represent a risk factor for severe allergic symptoms in Central Europe [7]. Similar results were found by Azofra et al. in northern Spain [13], studying 72 patients with an unequivocal history of allergy to fruits, 96% had specific IgE to Pru p 3 and negative specific IgE for profilin and PR-10. Nevertheless, many patients included in the study were sensitized to mugwort and plane pollen, though in this geographic area, there is no environmental pollen from these trees. Inhibition studies showed that specific IgEs against mugwort and plane tree pollen were strongly inhibited by Pru p 3, whereas Pru p 3 was less inhibited by pollen extracts, which seems to point to peach Prup3 as the primary sensitizer. The clinical characteristics were quite similar to patients reported in the south of Spain (6), with a higher incidence of kiwi allergy (26%) and a lower importance of cofactors (21%) in the development of allergy. In these two studies [6, 13], it seems that food allergy is independent of the levels of

environmental pollens. However, studies of allergy to plant foods caused by LTP and its association with pollinosis indicate that most patients (> 75%) with allergy to peach LTP have a pollen sensitization and that most develop pollinosis [14]. The clinical relevance of sensitization to LTP of the *artemisia* pollen (Art v 3) was studied by Pastorello et al. [15], who used a selection of patients with allergy to Pru p 3. They analyzed the rate of sensitization to Art v 3 and its clinical consequences, concluding that sensitization to Art v 3 is an epiphenomenon due to cross-reactivity but without clinical relevance in symptoms induced by pollen. In contrast to this, studies carried out with *artemisia* [16] and plane tree [17] have found that Art v 3 and Pla a 3, both proteins of the LTP family, are responsible for primary sensitization to LTP. Palacín et al. studied patients with food allergy caused by LTP sensitization in Spain [18], observing that individuals from the northeastern part of peninsular Spain and the Canary Islands recognized a greater number of LTPs included in the 14-protein panel used (pollens: Art v 3, Ole e 7, rPar j 1; foods: Bra o 3, Cas s 8, Cit r 3, Jug r 3, Lac s 1, Lyc e 3, rMal d 3, Pha v 3, rPru p 3, rSin a 3, and rTri a 14) with respect to other areas such as Madrid, Málaga, Bilbao, Orense, or Alicante). The most strongly associated pollens were plane tree and *artemisia*. This is noteworthy given that Barcelona and the Canary Islands both have a comparatively high concentration of plane tree and *artemisia* pollen, respectively, which may modulate food allergy caused by LTP. The mugwort-peach syndrome found in southern Europe can explain food allergy in other continents, as in the case of China, where patients developed peach allergy by primary respiratory sensitization to mugwort Art v 3 [19]. Food allergy caused by LTP was also found in an Australian patient in whom sensitization to LTP was responsible for food allergy to apple seed and grape (Mal d 3 and Vit v 1, respectively) [26, 44]. Cross-reactivity of *cupresaceas* pollen with Pru p 3 has also been described in Spain, but its clinical significance is not well known [45]. In Table 1 is described different LTPs from food and its geographical distribution.

The pattern of allergy to a given food varies by area. The study by Hansen et al. [29], which describes the sensitization profile in hazelnut-allergic patients from Spain, Switzerland, and Denmark demonstrated that IgE to the lipid transfer protein rCor a 8 was clearly more prevalent in Spain (Spain, 71%; Switzerland, 15%; Denmark, 5%), whereas sensitization to rCor a 1 was more common in Denmark and Switzerland (Switzerland/Denmark, 100%; Spain, 18%). The same phenomenon occurs with peanut sensitization. When comparing the profile of sensitization between Spain, the USA, and Sweden, Spanish peanut-allergic patients had greater sensitization to LTP rAra h 9, while Swedes and Americans were found to be more commonly sensitized to rAra h 1, 2, and 3 than their Spanish counterparts [8••]. Other example of geographical variation in sensitization pattern is the case of kiwi allergy. Patients from Iceland were mainly sensitized to Act d 1; those from

Table 1 LTPs from different food, their geographic distribution and the bibliographic reference

Food	LTP allergen (UIIS)	Geographical areas	Reference for first description
Apple	Mal d 3	Predominantly in southern Europe, also described in northern Europe and Australia	Pastorello, JACI 1999 [20] Gülsen A [21]
Asparagus	Aspa o 1	Predominantly in southern Europe	Tabar AI. Clin Exp Allergy. 2004 [22]
Cabbage	Bra o 3	Predominantly in southern Europe	Palacín, JACI 2006 [23]
Chestnut	Cas s 8	Predominantly in southern Europe, also described in USA	Sánchez-Monge, JACI 2006 [24]
Grape	Vit v 1	Predominantly in southern Europe, also described in Australia and Germany	Pastorello, JACI 2003 [25] Schäd IAAI [26]
Green bean	Pha v 3	Predominantly in southern Europe	Zoccatelli, Mol Immunol 2010 [27]
Hazelnut	Cor a 8	Predominantly in southern Europe, also described in Switzerland and Denmark	Pastorello, JACI 2002 [28] Hansen, JACI 2009 [29]
Kiwi	Act d10	Predominantly in southern Europe	Lee et al. JACI 2013 [30]
Lentil	Len c 3	Predominantly in southern Europe	Akkerdaas et al. IAAI 2012 [31]
Lettuce	Lac s 1	Predominantly in southern Europe	San Miguel-Moncin, Allergy 2003 [32]
Linseed		Predominantly in southern Europe	Antolin et al. JIACI 2016 [33]
Maize		Southern Europe	Guillen, Clin Exp Allergy. 2004 [34]
Mandarin	Cit r 3	Predominantly in southern Europe	Ebo, Int Arch Allergy Immunol 2007 [35]
Mustard	Sin a 3	Predominantly in southern Europe	Sirvent, Clin Exp Allergy 2009 [36]
Mustard	Sin a 3	Predominantly in southern Europe	Vereda et al. JACI 2011 [37]
Orange	Cit s 3	Predominantly in southern Europe	Ahrazem O, Int Arch Allergy Immunol. 2005 [38]
Peach	Pru p 3	Predominantly in southern Europe, but also described in China, the Netherlands, the USA, and Australia	Lleonart R. Ann Allergy 1992 [1•]
Peanut	Ara h 9	Predominantly in southern Europe, also described in the USA	Krause, JACI 2009 [39] Vereda A, JACI 2009 [8]
Pomegranate	Pun g 1	Predominantly in southern Europe	Enrique et al. AAAI 2006 [40]
Tomato	Lyc e 3	Predominantly in southern Europe	Le LQ. Plant Biotechnol J. 2006 [41]
Walnut	Jug r 3	Predominantly in southern Europe, but also described in the USA.	Pastorello, JACI 2004 [42]
Wheat	Tri a 14	Predominantly in southern Europe	Palacin, JACI 2007 [43]

western/central and eastern Europe were mainly sensitized to Act d 8 (pathogenesis-related class 10 protein), and those from southern Europe were mainly sensitized to Act d 9 (profilin) and Act d 10 (nonspecific lipid transfer protein) [30].

Geographically, specific sensitization to LTP by inhalation has also been confirmed in cases of occupational asthma, as in sensitization to the LTP Tria 14 in baker's asthma, a sensitization was found to be more common in workers from Spain than from Germany [43, 46]. Other studies involving patients with occupational asthma who were sensitized to the LTPs described in Spain include asparagus collectors (Aspa o 1), peach harvesters (Pru p 3, contained in peach leaves), and maize-LTP sensitization causing rhinoconjunctivitis in an employee working in a snack-processing facility [22, 34, 47].

Taking all these findings into account, Zuidmeer and van Ree [48•] have established three mechanisms by which patients develop food allergy caused by LTP: (1) primary sensitization to a LTP of food without pollinosis, (2) primary sensitization to LTP from pollen, and (3) co-sensitization to LTP from pollen and food sources.

For reasons yet to be explained, the prevalence of LTP syndrome is mostly focused in the Mediterranean basin and Mediterranean countries, primarily in Spain and Italy, and a clear gradient is seen in the prevalence of LTP sensitization between northern and southern regions [21, 49–51]. We hypothesize that the presence of high levels of birch pollen protects against LTP allergy, as higher levels of birch pollen are correlated with a lower prevalence of LTP hypersensitivity independently of the area; however, cases of LTP food allergy still appear in areas with high environmental levels of birch [21].

Conclusions

Currently, three main challenges remain in LTP allergy research. First, information on whether the geographic distribution of this type of allergy may be related to how sensitization occurs is lacking. Second, we do not know why some sensitized subjects only react to the culprit food in the presence of cofactors, while others develop reactions independently of

these factors. Lastly, our ability to offer reliable recommendations on avoidance diets is limited by the partial predictability of cross-reactivity. Most patients will only have cross-reactivity with members of the *prunoideae* or *rosaceae* families; however, as can be seen in the most insightful studies on tolerance to plant food, this is not always the case [4•, 13, 51], even in some patients citrus allergy may be included in this list of allergens causing cross-reactivity, among others [38]. Knowledge of allergy to LTP is growing, which will undoubtedly help answer these and other questions while increasing the rate with which this type of allergy is diagnosed outside the Mediterranean basin. Simultaneously, new strategies are being developed to approach this problem, such as oral immunotherapy with purified Pru p 3 [52]; available in some countries such as Spain, these initiatives look to increase the threshold of tolerance in individuals with severe systemic reactions, potentially enabling patients from any part of the world who are allergic to LTP to reach full tolerance.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

1. Leonart R, Cisteró A, Carreira J, Batista A, Moscoso del Prado J. Food allergy: identification of the major IgE-binding component of peach (*Prunus persica*). *Ann Allergy*. 1992;69:128–30. **First description of an LTP as major allergen in peach.**
2. Tordesillas L, Gómez-Casado C, Garrido-Arandia M, Murua-García A, Palacín A, Varela J, et al. Transport of Pru p 3 across gastrointestinal epithelium an essential step towards the induction of food allergy? *Clin Exp Allergy*. 2013;43:1374–83.
3. Radauer C, Nandy A, Ferreira F, Goodman RE, Larsen JN, Lidholm J, et al. Update of the WHO/IUIS allergen nomenclature database based on analysis of allergen sequences. *Allergy*. 2014;69:413–9.
4. Pascal M, Muñoz-Cano R, Reina Z, Palacín A, Vilella R, Picado C, et al. Lipid transfer protein syndrome: clinical pattern, cofactor effect and profile of molecular sensitization to plant-foods and pollens. *Clin Exp Allergy*. 2012;42:1529–39. **Description of LTP syndrome in Mediterranean area.**
5. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, et al. EAACI molecular allergology user's guide. *Pediatr Allergy Immunol*. 2016;27:1–250. **A compendium of molecular diagnosis.**
6. Flores E, Cervera L, Sanz ML, Diaz-Perales A, Fernández J. Plant food allergy in patients with pollinosis from the Mediterranean area. *Int Arch Allergy Immunol*. 2012;159:346–54.
7. Mothes-Luksch N, Raith M, Stingl G, Focke-Tejkl M, Razzazi-Fazeli E, Ziegelmayer R, et al. Pru p 3, a marker allergen for lipid transfer protein sensitization also in Central Europe. *Allergy*. 2017;72:1415–8.
8. Vereda A, van Hage M, Ahlstedt S, Ibañez MD, Cuesta-Herranz J, van Odijk J, et al. Peanut allergy: clinical and immunologic differences among patients from 3 different geographic regions. *J Allergy Clin Immunol*. 2011;127:603–7. **An article which compare different pattern of sensitization to peanut in different populations.**
9. Kleine-Tebbe J, Vogel L, Crowell DN, Haustein UF, Vieths S. Severe oral allergy syndrome and anaphylactic reactions caused by a Bet v 1-related PR-10 protein in soybean, SAM22. *J Allergy Clin Immunol*. 2002;110:797–804.
10. Ballmer-Weber BK, Vieths S, Lüttkopf D, Heuschmann P, Wüthrich B. Celery allergy confirmed by double-blind, placebo-controlled food challenge: a clinical study in 32 subjects with a history of adverse reactions to celery root. *J Allergy Clin Immunol*. 2000;106:373–8.
11. Palacín A, Tordesillas L, Gamboa P, Sanchez-Monge R, Cuesta-Herranz J, Sanz ML. Characterization of peach thaumatin-like proteins and their identification as major peach allergens. *Clin Exp Allergy*. 2010;40:1422–30.
12. Ballmer-Weber BK, Lidholm J, Fernández-Rivas M, Seneviratne S, Hanschmann KM, Vogel L, et al. IgE recognition patterns in peanut allergy are age dependent: perspectives of the EuroPrevall study. *Allergy*. 2015;70:391–407.
13. Azofra J, Berroa F, Gastaminza G, Saiz N, Gamboa PM, Vela C, et al. Lipid transfer protein syndrome in a non-Mediterranean area. *Int Arch Allergy Immunol*. 2016;169:181–8.
14. Cuesta-Herranz J, Barber D, Blanco C, Cistero-Bahima A, Crespo JF, Fernández-Rivas M, et al. Differences among pollen-allergic patients with and without plant food allergy. *Int Arch Allergy Immunol*. 2010;153:182–92.
15. Pastorello EA, Robino AM. Clinical role of lipid transfer proteins in food allergy. *Mol Nutr Food Res*. 2004;48:356–62.
16. Lombardero M, García-Sellés FJ, Polo F, Jimeno L, Chamorro MJ, García-Casado G, et al. Prevalence of sensitization to Artemisia allergens art v 1, art v 3 and art v 60 kDa. Cross-reactivity among art v 3 and other relevant lipid-transfer protein allergens. *Clin Exp Allergy*. 2004;34:1415–21.
17. Lauer I, Miguel-Moncin MS, Abel T, Foetisch K, Hartz C, Fortunato D, et al. Identification of a plane pollen lipid transfer protein (Pla a 3) and its immunological relation to the peach lipid-transfer protein, Pru p 3. *Clin Exp Allergy*. 2007;37:261–9.
18. Palacín A, Gómez-Casado C, Rivas LA, Aguirre J, Tordesillas L, Bartra J, et al. Graph based study of allergen cross-reactivity of plant lipid transfer proteins (LTPs) using microarray in a multicenter study. *PLoS One*. 2012;7(12):e50799.
19. Gao ZS, Yang ZW, Wu SD, Wang HY, Liu ML, Mao WL, et al. Peach allergy in China: a dominant role for mugwort pollen lipid transfer protein as a primary sensitizer. *J Allergy Clin Immunol*. 2013;131:224–6.
20. Pastorello EA, Pravettoni V, Farioli L, Spano M, Fortunato D, Monza M, et al. Clinical role of a lipid transfer protein that acts as a new apple-specific allergen. *J Allergy Clin Immunol*. 1999;104:1099–106.
21. Gülsen A, Jappe U. Lipid transfer protein sensitization in an apple-allergic patient: a case report from northern Europe. *Eur Ann Allergy Clin Immunol*. 2018; <https://doi.org/10.23822/EurAnnACI.1764-1489.63>.
22. Tabar AI, Alvarez-Puebla MJ, Gomez B, Sanchez-Monge R, García BE, Echechipia S, et al. Diversity of asparagus allergy: clinical and immunological features. *Clin Exp Allergy*. 2004;34:131–6.

23. Palacín A, Cumplido J, Figueroa J, Ahrazem O, Sánchez-Monge R, Carrillo T, et al. Cabbage lipid transfer protein Bra o 3 is a major allergen responsible for cross-reactivity between plant foods and pollens. *J Allergy Clin Immunol*. 2006;117:1423–9.
24. Sánchez-Monge R, Blanco C, López-Torrejón G, Cumplido J, Recas M, Figueroa J, et al. Differential allergen sensitization patterns in chestnut allergy with or without associated latex-fruit syndrome. *J Allergy Clin Immunol*. 2006;118:705–10.
25. Pastorello EA, Farioli L, Pravettoni V, Ortolani C, Fortunato D, Giuffrida MG, et al. Identification of grape and wine allergens as an endochitinase 4, a lipid-transfer protein, and a thaumatin. *J Allergy Clin Immunol*. 2003;111:350–9.
26. Schad SG, Treka J, Vieths S, Scheurer S, Conti A, Brocker EB, et al. Wine anaphylaxis in a German patient: IgE-mediated allergy against a lipid transfer protein of grapes. *Int Arch Allergy Immunol*. 2005;136:159–64.
27. Zoccatelli G, Pokoj S, Foetisch K, Bartra J, Valero A, Del Mar San Miguel-Moncin M, et al. Identification and characterization of the major allergen of green bean (*Phaseolus vulgaris*) as a non-specific lipid transfer protein (Pha v 3). *Mol Immunol*. 2010;47:1561–8.
28. Pastorello EA, Pravettoni V, Farioli L, Rivolta F, Conti A, Ispano M, et al. Hypersensitivity to mugwort (*Artemisia vulgaris*) in patients with peach allergy is due to a common lipid transfer protein allergen and is often without clinical expression. *J Allergy Clin Immunol*. 2002;110:310–7.
29. Hansen KS, Ballmer-Weber BK, Sastre J, Lidholm J, Andersson K, Oberhofer H, et al. Component-resolved in vitro diagnosis of hazelnut allergy in Europe. *J Allergy Clin Immunol*. 2009;123:1134–41.
30. Le TM, Bublin M, Breiteneder H, Fernández-Rivas M, Asero R, Ballmer-Weber B, et al. Kiwifruit allergy across Europe: clinical manifestation and IgE recognition patterns to kiwifruit allergens. *J Allergy Clin Immunol*. 2013;131:164–71.
31. Akkerdaas J, Finkina EI, Balandin SV, Santos Magadán S, Knulst A, Fernandez-Rivas M, et al. Lentil (*Lens culinaris*) lipid transfer protein Len c 3: a novel legume allergen. *Int Arch Allergy Immunol*. 2012;157:51–7.
32. San Miguel-Moncin M, Krail M, Scheurer S, Enrique E, Alonso R, Conti A, et al. Lettuce anaphylaxis: identification of a lipid transfer protein as the major allergen. *Allergy*. 2003;58:511–7.
33. Antolin-Amerigo D, Rodríguez-Rodríguez M, Barbarroja-Escudero J, Sánchez-González MJ, Haroun-Díaz E, Cuesta-Herranz J, et al. Linseed Allergy Due to LTP: Another Food for LTP Syndrome. *J Investig Allergol Clin Immunol*. 2016;26:376–7.
34. Guillen D, Barranco P, Palacín A, Quirce S. Occupational rhinoconjunctivitis due to maize in a snack processor: a cross-reactivity study between lipid transfer proteins from different cereals and peach. *Allergy Asthma Immunol Res*. 2014;6:470–3.
35. Ebo DG, Ahrazem O, Lopez-Torrejón G, Bridts CH, Salcedo G, Stevens WJ. Anaphylaxis from mandarin (*Citrus reticulata*): identification of potential responsible allergens. *Int Arch Allergy Immunol*. 2007;144:39–43.
36. Sirvent S, Palomares O, Vereda A, Villalba M, Cuesta-Herranz J, Rodríguez R. nsLTP and profilin are allergens in mustard seeds: cloning, sequencing and recombinant production of sin a 3 and sin a 4. *Clin Exp Allergy*. 2009;39:1929–36.
37. Vereda A, Sirvent S, Villalba M, Rodríguez R, Cuesta-Herranz J, Palomares O. Improvement of mustard (*Sinapis alba*) allergy diagnosis and management by linking clinical features and component-resolved approaches. *J Allergy Clin Immunol*. 2011;127:1304–7.
38. Ahrazem O, Ibáñez MD, López-Torrejón G, Sánchez-Monge R, Sastre J, Lombardero M, et al. Lipid transfer proteins and allergy to oranges. *Int Arch Allergy Immunol*. 2005;137:201–10.
39. Krause S, Reese G, Randow S, Zennaro D, Quarantino D, Palazzo P, et al. Lipid transfer protein (Ara h 9) as a new peanut allergen relevant for a Mediterranean allergic population. *J Allergy Clin Immunol*. 2009;124:771–8.
40. Enrique E, Utz M, De Mateo JA, Castelló JV, Malek T, Pineda F. Allergy to lipid transfer proteins: cross-reactivity among pomegranate, hazelnut, and peanut. *Ann Allergy Asthma Immunol*. 2006;96:122–3.
41. Le LQ LY, Scheurer S, Fötisch K, Enrique E, Bartra J, et al. Design of tomato fruits with reduced allergenicity by dsRNAi-mediated inhibition of ns-LTP (Lyc e 3) expression. *Plant Biotechnol J*. 2006;4:231–42.
42. Pastorello EA, Farioli L, Pravettoni V, Robino AM, Scibilia J, Fortunato D, et al. Lipid transfer protein and vicilin are important walnut allergens in patients not allergic to pollen. *J Allergy Clin Immunol*. 2004;114:908–14.
43. Palacín A, Quirce S, Armentia A, Fernández-Nieto M, Pacios LF, Asensio T, et al. Wheat lipid transfer protein is a major allergen associated with baker's asthma. *J Allergy Clin Immunol*. 2007;120(5):1132–8.
44. Murad A, Katelaris CH, Baumgart K. A case study of apple seed and grape allergy with sensitisation to nonspecific lipid transfer protein. *Asia Pac Allergy*. 2016;6:129–32.
45. Sánchez-López J, Asturias JA, Enrique E, Suárez-Cervera M, Bartra J. Cupressus arizonica pollen: a new pollen involved in the lipid transfer protein syndrome? *J Investig Allergol Clin Immunol*. 2011;2:522–6.
46. Palacín A, Varela J, Quirce S, del Pozo V, Tordesillas L, Barranco P, et al. Recombinant lipid transfer protein tri a 14: a novel heat and proteolytic resistant tool for the diagnosis of baker's asthma. *Clin Exp Allergy*. 2009;39(8):1267–76.
47. Pérez-Calderón R, Gonzalo-Garijo MÁ, Rodríguez-Velasco FJ, Sánchez-Vega S, Bartolomé-Zavala B. Occupational respiratory allergy in peach crop workers. *Allergy*. 2017;72:1556–64.
48. Zuidmeer L, Van Ree R. Lipid transfer protein allergy: primary food allergy or pollen/food syndrome in some cases. *Curr Opin Allergy Clin Immunol*. 2007;7:269–73. **A review article on LTP allergy.**
49. Asero R, Antonicelli L, Arena A, Bommarito L, Caruso B, Crivellaro M, et al. EpidemAAITO: features of food allergy in Italian adults attending allergy clinics: a multicentre study. *Clin Exp Allergy*. 2009;39:547–55.
50. Haroun-Díaz E, Azofra J, González-Mancebo E, de Las Heras M, Pastor-Vargas C, Esteban V, et al. Nut allergy in two different areas of Spain: differences in clinical and molecular pattern. *Nutrients*. 2017;21:9.
51. Asero R, Piantanida M, Pravettoni V. Allergy to LTP: to eat or not to eat sensitizing foods? A follow-up study. *Eur Ann Allergy Clin Immunol*. <https://doi.org/10.23822/EurAnnACI.1764-1489.57>.
52. Fernández-Rivas M, Garrido Fernández S, Nadal JA, Díaz de Durana MD, García BE, González-Mancebo E, et al. Randomized double-blind, placebo-controlled trial of sublingual immunotherapy with a Pru p 3 quantified peach extract. *Allergy*. 2009;64:876–83.