

Sensitization to Pru p 7 in Peach-Allergic Patients Sensitized to Pru p 3 in Areas of High Exposure to Cypress Pollen

Tomás-Pérez M^{1,2*}, Vera-Berrios RN^{3*}, Casas-Saucedo R⁴, Galleani C^{5,6}, González-Bravo L⁷, Gonzalo-Fernández A³, González-Pérez A⁸, Rodríguez-Mazariego E⁹, Ruano-Zaragoza M^{10,11}, Zambrano-Ibarra G⁹, Bartra-Tomás J^{10,11,12}

¹Allergy Department, Hospital Universitario La Paz, Madrid, Spain

²Instituto de Investigación (IDiPAZ), Madrid, Spain

³Allergy Department, Hospital Clínico San Carlos, IdISSC, Madrid, Spain

⁴Allergy Department, Hospital General Granollers, Barcelona, Spain

⁵Allergy Department, Hospital Universitario 12 Octubre, Madrid, Spain

⁶Instituto de Investigación Sanitaria Hospital 12 Octubre (IMAS12), Madrid, Spain

⁷Allergy Department, Hospital Príncipe de Asturias, Madrid, Spain

⁸Allergy Department, Hospital Universitario del Vinalopó, Elche, Spain

⁹Allergy Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

¹⁰Allergy Department, Hospital Clínic, Barcelona, Spain

¹¹Clinical and Experimental Respiratory Immunoallergy (IDIBAPS), Barcelona, Spain

¹²RETIC Asma, Reacciones Adversas y Alergia (ARADyAL) and RICORS Red de Enfermedades Inflamatorias (REI), Madrid, Spain

*Both authors contributed equally as first authors.

All the authors are members of AliAdos, a group of young emerging allergologists belonging to the Food Working Group of the Spanish Society of Allergology and Clinical Immunology (SEAIC)

J Investig Allergol Clin Immunol 2025; Vol. 35(4)
doi: 10.18176/jiaci.1065

Key words: Peach allergy. Pru p 3. Pru p 7. Cosensitization. Gibberellin.

Palabras clave: Alergia al melocotón. Pru p 3. Pru p 7. Co-sensibilización. Giberelina.

The prevalence of confirmed food allergy in Europe is estimated at 0.2% to 4.1% [1].

In the Mediterranean area, allergy to rosaceous fruits, particularly peach, is predominant [2]. To date, according

to the WHO/IUIS Allergen Nomenclature Sub-Committee, 7 peach allergens have been described, as follows: Pru p 1 (PR-10), Pru p 2 (thaumatin-like protein), Pru p 3 (nonspecific lipid transfer protein [nsLTP] 1), Pru p 4 (profilin), Pru p 7 (gibberellin-regulated protein [GRP]), Pru p 9 (PR-1), and Pru p 10 (polygalacturonase).

Pru p 3, the peach nsLTP, is generally considered the primary sensitizer and the most important allergen in peach allergy in the Mediterranean area and is a known risk factor for severe allergic reactions, given its resistance to heat and acid degradation [3]. Pru p 7 (or peamaclein), a protein belonging to the GRP family, was recently described in an Italian study, in which the authors reported a 2.8% prevalence of sensitization to Pru p 7 among cypress pollen-allergic patients, of whom 71% also had a history of food allergy, predominantly related to peach ingestion [4]. Pru p 7 has also been described as a risk factor for severe peach allergy [5]. A recent study [6] with peach-allergic patients from Madrid, Spain revealed the frequency of sensitization to Pru p 7 in peach-allergic patients to be 16%. However, the prevalence of cosensitization to Pru p 3 and Pru p 7 in Spain is unknown.

We performed a multicenter, cross-sectional study in 6 Spanish hospitals located in Madrid, Barcelona, and Elche between July 2022 and June 2024. The study was approved by the local ethics committees. All the participants or their legal representatives gave their written informed consent to participate and for the results to be published.

Given the unknown prevalence of cosensitization to peach LTP and gibberellin in Spain, the sample size was calculated based on a worst-case scenario (50% prevalence), resulting in 97-385 patients with a $\pm 5\%$ -10% margin of error, respectively, and a 95%CI.

The study population comprised patients of both sexes aged ≥ 12 years reporting immediate allergic reactions (≤ 2 hours) after eating peach, with positive skin prick test (SPT) and sIgE results to Pru p 3.

Patients were excluded if they had received treatment with biologics or allergen immunotherapy in the previous 3 years or were pregnant, breastfeeding, or immunosuppressed.

The data collected included demographics, family and personal history of atopy, detailed information on allergic reactions to peach, and the results of an allergology study.

SPT with peach, Pru p 3, and pollen extracts (Roxall, ALK) (Supplementary Table 1) and determinations of total IgE and sIgE to Pru p 3, Pru p 4, and Pru p 7 (ImmunoCAP, Thermo Fisher Scientific Phadia) were performed. A mean wheal diameter ≥ 3 mm and sIgE ≥ 0.35 kU_A/L were considered positive.

Severity was graded using the ordinal Food Allergy Severity Score (oFASS-5) and the numerical Food Allergy Severity Score (nFASS) [7].

Descriptive statistics were reported. Univariate comparisons were conducted using the Mann-Whitney test,

Spearman correlations, and the χ^2 test. The analysis was performed using IBM SPSS Statistics (IBM Corp). Statistical significance was set at $P=.05$.

A total of 110 peach-allergic patients sensitized to Pru p 3 (Madrid, 81; Barcelona, 21; Elche, 8) were included (73 women and 37 men; mean [SD] age, 33.7 [12.7] years). All patients had a personal history of atopy. Allergic rhinoconjunctivitis was recorded in 78.2%, cypress allergy in 65.1%, asthma in 40.9%, and atopic dermatitis in 19.1%.

Table. Characteristics of Peach-Allergic Patients Sensitized to Pru p 3.

| Demographic characteristics | N=110 |
|---|-------------------|
| Female sex, No. (%) | 73 (66.4%) |
| Mean (SD) age, y | 33.70 (12.7) |
| Personal history of atopy, No. (%) | |
| Atopic dermatitis | 21 (19.10%) |
| Allergic rhinitis | |
| Cypress | 55 (50%) |
| Other pollens | 34 (30.90%) |
| Other allergens ^a | 19 (17.30%) |
| Asthma | 45 (40.90%) |
| Other food allergies | |
| Other Rosaceae | 70 (63.60%) |
| Citrus/pomegranate | 4 (3.60%) |
| Other plant foods | 84 (76.40%) |
| Animal source foods | 5 (4.50%) |
| Peach allergy | |
| Mean (SD) age at first reaction, y | 21.20 (13.90) |
| oFASS-5, No. (%) | |
| Grade 1 | 12 (10.90%) |
| Grade 2 | 58 (52.70%) |
| Grade 3 | 15 (13.60%) |
| Grade 4 | 15 (13.60%) |
| Grade 5 | 10 (9.10%) |
| nFASS, median (IQR) | 2.71 (2.11-3.47) |
| Mean (SD) SPT, mm | |
| Peach | 7.40 (2.70) |
| Pru p 3 | 7.50 (2.90) |
| Median (IQR) sIgE, kU _A /L | |
| Peach | 4.43 (1.53-9.31) |
| Pru p 3 | 5.08 (1.68-11.43) |
| Pru p 7 | 0.03 (0.01-0.05) |
| Pru p 4 (n=52) | 0.005 (0-0.02) |
| Median total IgE, kU/L | 143 (58.30-335) |

Abbreviations: FASS, Food Allergy Severity Score; nFASS, numerical FASS; oFASS-5, ordinal FASS in 5 grades; SPT, skin prick test.

^aDust mites, fungi, dog and cat dander

Moreover, 90% of patients reported allergy to other fruits and/or vegetables. Regarding a history of peach allergy, the median (SD) age at the first reaction was 21.2 (13.9) years. The median (IQR) sIgE to Pru p 3 was 5.07 (1.68-11.43) kU_A/L (Table). Only 3 patients were also sensitized to Pru p 7, giving a prevalence of cosensitization to Pru p 3 and Pru p 7 of 2.7% with a $\pm 3.03\%$ margin of error at a 95%CI.

Severe reactions (oFASS grades 4-5) were reported for 22.7% of patients, cardiovascular/neurological involvement (Grade 5) for 9.1%, and lower respiratory symptoms (Grade 4) for 13.6%. The reactions reported by the 3 cosensitized patients were Grade 2, Grade 3, and Grade 4 (Supplementary Table 2).

No correlations were found between the severity of the reactions and Pru p 3 sIgE values, sensitization to profilin, demographic characteristics, cypress allergy, or history of atopy. Given the low prevalence of cosensitization to Pru p 7, no correlations could be explored in this regard.

The allergens Pru p 7 and Pru p 3 play a key role in peach allergy and are associated with severe clinical symptoms. However, the prevalence of cosensitization to both has not been reported in Spain.

The clinical and demographic characteristics of the patients included in our study did not differ from those that are usually reported in patients sensitized to Pru p 3. The same applies to the 2.7% sensitized to both Pru p 3 and Pru p 7. We highlight the high percentage of patients cosensitized to Cupressaceae pollen (65.1%), which is similar to percentages reported elsewhere [6,8,9], and the finding that a large percentage of the reactions were severe (22.7%).

The frequency of cosensitization we reported (2.7%) was much lower than the 16.3% reported for Pru p 7 by Vilchez-Sánchez et al [6]. This disparity in Pru p7 sensitization rates between the rates we report and the literature may result from our inclusion criterion of requiring prior sensitization to Pru p 3 and could also be influenced by demographic factors, such as age, or environmental factors, such as climate and pollen season. Consistent with Betancor et al [9], this low percentage of sensitization to Pru p 7 was recorded in patients highly exposed to Cupressaceae pollen and of whom most were sensitized. Although other LTPs were not evaluated in our study, most patients reported allergic reactions to other fruits of the Rosaceae family and other plant foods, partly owing to sensitization to LTP as part of LTP syndrome. Moreover, given that sensitization to multiple LTPs, higher levels of sIgE to Pru p 3, and sensitization to profilin have been reported to influence severity [10], we searched for possible associations in this regard. The fact that we found none is likely due to different sensitization patterns in our population that require further testing. Consequently, a more comprehensive study is necessary in patients sensitized to LTP in clinical practice, including testing for other allergens and other LTPs and assessment of clinical reactivity. Our study was limited by the low number of patients sensitized to Pru p 7 among those sensitized to Pru p 3, which prevented us from establishing an association between sensitization to peach and clinical severity. It would be very interesting to extend the study to more regions of Spain in order to further analyze this association and identify the various sensitization patterns and clinical phenotypes in peach allergy, investigate

a possible association with the severity of reactions, and determine the possible implications for patient management in clinical practice.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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■ Manuscript received October 22, 2024; accepted for publication January 20, 2025.

Margarita Tomás Pérez

Allergy Department

La Paz University Hospital

Madrid, Spain

E-mail: margui.tomas@gmail.com