

## **Is Pru p 7 (peamaclein) sensitization a predominant cause of cypress pollen-associated peach allergy in Spain?**

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*Cupressaceae* tree family includes about 160 different species of trees worldwide distributed in five genera [1]. *Cupressus sempervirens* (*Cupressus spp*) is the most common species in Mediterranean areas. The prevalence of sensitization to cypress pollen has increased in the last decades and varies from 9 to 65% [1,2]. Madrid is among the cities with the highest prevalence in Spain [3,4]. In 2021, it has an accumulated rate of 11,023 grains/m<sup>3</sup>, the doubled compared to 2020 ([www.polenes.com](http://www.polenes.com)).

Four allergens from *Cupressus spp* have been characterized ([www.allergen.org](http://www.allergen.org)): Cup s 1, pectate lyase; Cup s 2, polygalacturonase; Cup s 3, thaumatin-like and Cup s 7 gibberellin-regulated protein. High sequence identity and cross-reactivity among *Cupressaceae* pollen allergens have been demonstrated [5,6]

Peamaclein (Pru p 7) was the first gibberellin-regulated protein identified and registered as peach allergen in 2013 ([www.allergen.org](http://www.allergen.org)). Peach allergy has been associated to cypress pollen allergy in certain areas, such as France [7,8] or Japan [9] due to cross-reactivity between Cup a 7 and Pru p 7. There, Pru p 7 was established as a major peach allergen. In Spain, peach was the most frequent fruit eliciting allergy and Pru p 3 was reported to be the major peach allergen [10].

The aim of this study was to assess the frequency of sensitization to Pru p 7 (peamaclein) and Pru p 3 (nsLTP), as well as other peach allergens (Pru p 1 and Pru p 4) among cypress allergic patients from Madrid (Spain), an area with high exposure to *Cupressus* tree pollen.

Sera from 153 consecutive patients with *Cupressus* pollen allergy, who had been attending at Fundación Jiménez Díaz Hospital, Madrid (Spain) from September 2021 to June 2022, were collected. Methods are summarized in supplementary I.

153 consecutive patients allergic to *Cupressus arizonica* were evaluated. Patient characteristics are given in supplementary II

#### **Peach allergy among *Cupressus* allergic patients:**

Sixty-four (41.8%) out of 153 *Cupressus* allergic patients were allergic to fruits: 32 (50.0%) were allergic to peach, 28 (43.7%) to melon/watermelon, 17 (26.6%) to kiwi, 15 (23.4%) to banana, 11 (17.1%) to citric fruits, 10 (15.6%) to pineapple, 9 (14.1%) to apple and 3 (4.7%) to avocado.

In the subgroup of 32 peach-allergic patients: Pru p 3 was the most predominant allergen eliciting sensitization in 19 patients (59.4%), followed by Pru p 4 in 14 (43.7%), Pru p 1 in 6 (18.7%) and Pru p 7 in 3 (9.4%) (Fig 1).

The median specific IgE concentration to Pru p 3 was 156.5 kU/L (Q1-Q3: 23.6-405.3kU/L), to Pru p 4 was 8.0 kU/L (Q1-Q3: 0.0-191.0kU/L), to PR-10 was 1.0 kU/L (Q1-Q3: 0.0-11.0kU/L) and to Pru p 7 was 3.0 kU/L (Q1-Q3: 2.0-6.0kU/L),

#### **Sensitization to Pru p 7 (peamaclein) in *Cupressus* allergic patients:**

Twelve (7.8%) out of 153 *Cupressus* allergic patients were sensitized to Pru p 7. There was no significant difference in sex or age compared to general studied patients.

Of these 12 patients sensitized to Pru p 7, 8 (66.6%) have food allergy: 2 (16.6%) to peach and melon/watermelon, 2 (16.6%) to citrics, 1 (8.3%) to citrics and peach, 1

(8.3%) to melon/watermelon, 1 (8.3%) to melon and banana and 1 (8.3%) to kiwi. Three patients were monosensitized to Pru p 7. Cosensitization with Pru p 3 and Pru p 4 was present in 3 patients, just Pru p 3 in 1 patient and PR10 in another patient. Therefore, 4 (33.3%) were non-food allergic patients

None of the 3 peach-allergic patients were monosensitized to Pru p 7. One was also to Pru p 1 and the other 2 to both Pru p 3 and Pru p 4.

It has been proposed that Pru p 3 purified extract from natural source could be contaminated by Pru p 7, causing false positivity and Pru p 3 overdiagnosis [11]. Moreover, Klingebiel et al. [8] demonstrated a high frequency of Pru p 7 sensitization among peach allergic patients in an area with high concentration of cypress pollen, questioning the real frequency of sensitizations to Pru p 3.

Our study found that only a 7.8% (CI95%: 3.6-12.1) of patients allergic to *Cupressus* were sensitized to Pru p 7 and confirmed that Pru p 3 was a major peach allergen in Madrid (Spain). We would like to highlight some characteristics of this study. The first one was that the study was performed by using recombinant allergens, both Pru p 3 and Pru p 7, avoiding the possibility of contamination. Secondly, the frequency of sensitization was evaluated among cypress allergic patients, a population prone to be sensitized to Pru p 7 [8].

High Pru p 7 sensitization rate has been demonstrated in Japan [9] and southern France, mostly in Mediterranean areas as Marseille and Toulouse (up to 66%), compared to continental areas as Lyon (about 30%) [8]. Our results strongly contrast with both. *Cryptomeria japonica* pollen, predominant in Japan belongs to other genera of the

*Cupressaceae* family which implies that its allergens might have a lower sequence identity and cross-reactivity.

Pru p 3 was characterized as a major peach allergen in Italy [13] and Spain [10]. Our results agree with them and reinforce those reported by Asero et al. [14]. They found that 77.9% of cypress and peach sensitized patients had positive result for Pru p 3 and less than 10.7% to Pru p 7 with no geographical difference inside Italy. Both Asero et al. [14] and our research emphasize the conclusion that Pru p 3 is a major peach allergen, even among cypress allergic patients.

The controversial results obtained in different areas prove the existence of different allergenic patterns depending on local factors (genetic, environmental, dietary etc.) attending to major peach allergens: Northern and Central European patients sensitized to Pru p 1 [15], French and Japanese sensitised to Pru p 7 [8,9] and Spanish and Italian sensitised to Pru p 3 [7,14].

This study has some limitations. They are summarized in supplementary III

In summary, we can conclude that peamaclein (Pru p 7) sensitization was not a predominant cause of cypress pollen-associated peach allergy in the central area of Spain, being Pru p 3 the major peach allergen.

**Conflict of interests**

*The authors have no conflicts of interest* directly related to the present manuscript to declare.

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**FIGURE LEGENDS**

**Figure.** Molecular pattern of patients allergic to peach and cypress pollen in Madrid (Spain).

