Is Pru p 7 (Peamaclein) Sensitization a Predominant Cause of Cypress Pollen–Associated Peach Allergy in Spain?

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The *Cupressaceae* tree family includes about 160 different species of trees distributed in 5 genera worldwide [1]. *Cupressus sempervirens* is the most common species in the Mediterranean. The prevalence of sensitization to cypress pollen has increased in recent decades, ranging from 9% to 65% [1,2]. Madrid has one of the highest prevalence values in Spain [3,4], with a cumulative rate of 11 023 grains/m^3 in 2021, ie, twice that of 2020 (www.polenes.com).

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

In 2013, peamaclein (Pru p 7) was identified as the first gibberellin-regulated protein and registered as a peach allergen (www.allergen.org). Peach allergy has been associated with cypress pollen allergy in certain areas, such as France [7,8] and Japan [9], owing to cross-reactivity between Cup a 7 and Pru p 7. In these areas, 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 (nonspecific lipid transfer protein), 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 were collected from 153 consecutive patients with *Cupressus* pollen allergy who had been treated at Fundación Jiménez Díaz Hospital, Madrid, Spain from September 2021 to June 2022. The methods are summarized in Supplementary Table I.

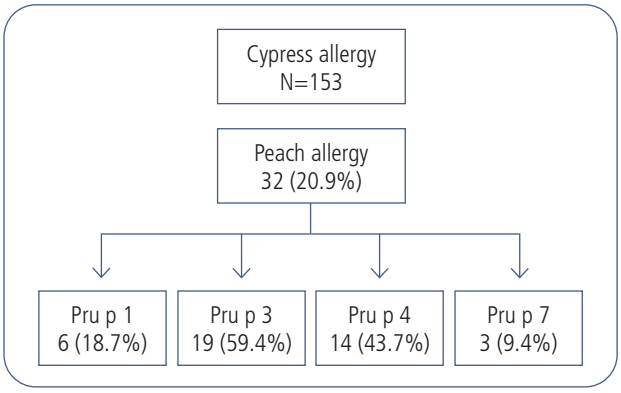

Figure. Molecular pattern of patients allergic to peach and cypress pollen in Madrid, Spain.

We evaluated 153 consecutive patients allergic to *Cupressus arizonica*. Patient characteristics are given in Supplementary Table II.

Of the 153 *Cupressus*-allergic patients, 64 (41.8%) were allergic to fruits: 32 (50.0%) to peach, 28 (43.7%) to melon/watermelon, 17 (26.6%) to kiwi, 15 (23.4%) to banana, 11 (17.1%) to citrus 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%) (Figure).

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

Of the 153 *Cupressus*-allergic patients, 12 (7.8%) were sensitized to Pru p 7. There was no significant difference in sex or age between those sensitized and those not sensitized to Pru p 7.

Of the 12 patients sensitized to Pru p 7, 8 (66.6%) had fruit allergy: 2 (16.6%) to peach and melon/watermelon, 2 (16.6%) to citrus fruit, 1 (8.3%) to citrus fruit 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 observed in 3 patients, Pru p 3 alone in 1 patient, and PR-10 in 1 patient. Therefore, 4 patients (33.3%) were not allergic to plant-derived foods.

None of the 3 peach-allergic patients were monosensitized to Pru p 7. One was also sensitized to Pru p1 and the other 2 to both Pru p 3 and Pru p 4.

It has been proposed that purified Pru p 3 extract from natural sources could be contaminated by Pru p 7, leading to false positivity and overdiagnosis of allergy [11]. Moreover, Klingebiel et al [8] demonstrated a high frequency of sensitization to Pru p 7 among peach-allergic patients in an area with high concentrations of cypress pollen, thus calling into question the real frequency of sensitization to Pru p 3.

We found that only 7.8% (95%CI, 3.6%-12.1%) of *Cupressus*-allergic patients were sensitized to Pru p 7 and confirmed that Pru p 3 was a major peach allergen in Madrid. Our findings are remarkable, first, because the study was performed using recombinant allergens, both Pru p 3 and Pru p 7, thus avoiding the possibility of contamination, and second, the frequency of sensitization was evaluated among cypress-allergic patients, a population prone to sensitization to Pru p 7 [8].

A high Pru p 7 sensitization rate was demonstrated in Japan [9] and southern France, mostly in Mediterranean areas such as Marseille and Toulouse (up to 66%), compared with continental areas such as Lyon (about 30%) [8]. Our results contrast strongly with both. *Cryptomeria japonica* pollen, which is predominant in Japan belongs to other genera of the *Cupressaceae* family, thus implying that its allergens might have a lower sequence identity and cross-reactivity.

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

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

The limitations of our study are summarized in Supplementary Table III.

We can conclude that sensitization to peamaclein (Pru p 7) was not a predominant cause of cypress pollen–associated peach allergy in central Spain. Pru p 3 was the major peach allergen.

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Conflicts of Interest

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