The role of Pru p 7 in severe peach allergy

Insights about the connection between peach and cypress pollen allergy

The peach allergen Pru p 7 is a marker for severe fruit-induced allergy and might be a link between severe allergic reactions to fruits and Cupressaceae (cypress) pollen allergy.1,2 Pru p 7 is a gibberlin-regulated protein (GRP) and homologous, IgE cross-reactive proteins exist in several fruits. Testing of specific IgE (sIgE) to Pru p 7 may be especially useful to fill the gap in diagnosing patients who are peach-allergic but are not sensitized to the other peach allergens Pru p 1 (PR-10), Pru p 3 (LTP) and Pru p 4 (profilin). Patients with this allergic profile seem to be especially common in areas with high cypress pollen exposure.1

**Pru p 7 cross-reactivity may contribute to cypress-peach syndrome**

Patients with fruit-derived allergies often develop allergic responses to multiple fruits. With some fruits, cross-reactivity among different GRP allergens may be the culprit. Proven Pru p 7 cross-reactivities include the homologous GRP allergens Pru m 7 (Japanese apricot),3 Cit s 7 (orange)4 and Pun g 7 (pomegranate).5 Significant IgE-mediated cross-reactivities between Pru p 7 and the Cypress pollen allergens Cup s 7 and GRP BP14 have also been shown to be clinically important.2,6,7

**Pru p 7 immune response is linked to cypress pollen exposure**

Sensitization to Pru p 7 may be particularly prevalent in areas with high cypress pollen exposure. A recent study of the role of Pru p 7 in peach allergy analyzed 316 patients with suspected peach allergy from several regions across southern France.7 Pru p 7 sensitization was found in all geographic regions studied but was greater in regions with higher exposure to cypress tree pollen. In the study, patients were categorized as peach-tolerant or peach-allergic and examined for a range of responses associated with Pru p 7 sensitization. Pru p 7-sensitized patients who were peach-allergic exhibited higher concentrations of sIgE to Pru p 7 than patients who were peach-tolerant. Higher concentrations of sIgE were also associated with more severe reactions in response to peach exposure.

In comparison, about half of the Pru p 7-sensitized, peach-allergic patients did not exhibit significant sIgE response to several other tested allergens associated with peaches or pollens including Pru p 3 (peach peel), Pru p 1 (birch pollen), and Pru p 4 (grass pollen). Showing the potential utility of testing for sIgE to Pru p 7 in bridging the diagnostic gap for peach-allergic patients with unidentified peach allergen sensitization.

In the same study, Pru p 7 sensitization was found to be more frequent in peach-allergic patients who experienced more severe (grade 3) reactions than those who experienced lower grade 2 or grade 1 reactions. Pru p 7 sensitization was negatively related to grade 1 reactions. The severity of reactions was significantly associated with higher concentration of sIgE to Pru p 7. Allergic reactions were also more severe in regions with greater cypress pollen exposure and Pru p 7 was the only peach allergen that was associated with cypress pollen sensitization. In addition, in sIgE competition experiments, cypress pollen extract completely outcompeted Pru p 7.
Another recent study reveals additional evidence associating cypress pollen allergy with Pru p 7 sensitivity. This study identified a 7 kDa protein in three Cupressaceae species as being the pollen allergen involved in severe peach allergy. The protein is a GRP previously named Cup s 7. The study also shows that the sIgE binding capacity of patient sera was substantially higher to Cup s 7 than to Pru p 7. Additionally, the sera of 51 Pru p 7-sensitized peach-allergic patients contained higher levels of sIgE to Cup s 7 than sIgE to Pru p 7.

In these two independent studies, reciprocal inhibition experiments showed that cypress pollen extract1 and Cup s 72 completely outcompeted sIgE binding to Pru p 7 while in the inverse reaction only partial inhibition of sIgE binding by Pru p 7 occurred. The results of these studies suggest that cypress pollen, and specifically Cup s 7, may act as the predominant primary sensitizer in cypress pollen-associated Pru p 7-induced peach allergy.

Clinical relevance and testing
Sensitization to Pru p 7 is a risk factor for severe fruit-induced allergic reactions with the severity of reactions significantly associated with sIgE levels.1 Pru p 7 sensitization seems to be a characteristic of a subtype of cypress pollen allergy, in which cypress pollen is the primary sensitizer that causes severe peach allergy.1,2 In areas with high cypress pollen exposure Pru p 7 sensitization seems to be especially common in peach-allergic patients who are not sensitized to other known peach allergens including Pru p 1 (PR-10), Pru p 3 (LTP) and Pru p 4 (profilin).1,8

Pru p 7 has an unusually high cysteine content (19% of total residues) with six cysteine bridges that stabilize the protein against heat and intestinal digestion,9 indicating that it may be a true food allergen.6 Peach-induced clinical manifestations related to Pru p 7 sensitization can include some common symptoms of severe food-induced allergic reactions like anaphylaxis with urticaria. However, Pru p 7 allergy also exhibits several peculiar symptoms including swelling of the face, especially the eyelids, and laryngeal tightness. Moreover, the onset of Pru p 7 allergic reactions can be enhanced by cofactors such as exercise or aspirin intake.1,3

Multiple approaches are available to assist in the diagnosis of peach allergy. Commonly used skin prick tests with commercially available purified native Pru p 3 extracts may yield inconsistent results, potentially due to Pru p 7 contamination. Pru p 7 and Pru p 3 have similar mass and pl, which can make complete separation difficult during extract purification.9 However, testing for sIgE to Pru p 7 is another approach that can be useful to reveal undetermined causes of peach allergy. A number of peach allergen components, produced as recombinant proteins, are now available for component-resolved diagnostics (CRD), offering improved diagnostic work-up (Figure 1), especially for patients sensitized to Pru p 7 who are at risk for severe reactions.

Figure 1

Negative* (<0.1 kU/L)
Consider alternative investigations. If clinical suspicion persists, consider component testing or a controlled peach challenge.

Positive* (≥0.1 kU/L)

Negative* (<0.1 kU/L)
Positive* (≥0.1 kU/L)

ImmunoCAP™ Whole Allergen Peach (f95)

ImmunoCAP™ Allergen Components

f421 rPru p 41 (PR-10)
f419 rPru p 11 (PR-10)
f420 rPru p 33 (LTP)
f454 rPru p 72 (GRP)

Cross-reaction, rarely associated with clinical symptoms or severe reactions10,11
Management considerations: further investigation to identify primary allergen.

Risk of local and in rare cases systemic reactions10,11
Management considerations: in regions where birch is common, consider testing with Bet v 1 (t215) to confirm primary sensitization.

High risk of severe, systemic symptoms1,2,10-12
Management considerations: testing with Cypress (t23 and t222) if Pru p 7 is positive, and other LTPs if Pru p 3 is positive.

* Results should be interpreted in the context of a patient’s clinical symptoms and history. Patients can be sensitized to more than one component.
** Full product names available on page 3.
† E.g. Ara h 9† (f427), Art v 3† (w233), Cor a 8† (f425), Jug r 3† (f442), Mal d 3 (f435), Pia a 3†, Tri a 14† (f443).”
‡ Available on ImmunoCAP™ ISAC111 multiplexing test.
Product List

**ImmunoCAP™ Allergens:**
- ImmunoCAP Allergen f95, Peach; ImmunoCAP Allergen f419, Allergen Component rPru p 1 PR-10, Peach; ImmunoCAP Allergen f420, Allergen Component rPru p 3 LTP, Peach; ImmunoCAP Allergen f421, Allergen Component rPru p 4 Profilin, Peach; ImmunoCAP Allergen f454, Allergen Component rPru p 7 Peach; ImmunoCAP Allergen f427, Allergen Component rAra h 9 LTP, Peanut; ImmunoCAP Allergen f425, Allergen Component rCor a 8 LTP, Hazelnut; ImmunoCAP Allergen f442, Allergen Component rJug r 3 LTP, Walnut; ImmunoCAP Allergen f435, Allergen Component rMal d 3 LTP, Apple; ImmunoCAP Allergen f443, Allergen Component rTri a 14 LTP, Wheat; ImmunoCAP Allergen f215, Allergen Component rBet v 1 PR-10, Birch; ImmunoCAP Allergen f233, Allergen Component Art v 3 LTP, Mugworth.

References


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