

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.¹ 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.

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Another recent study reveals additional evidence associating cypress pollen allergy with Pru p 7 sensitivity.² 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

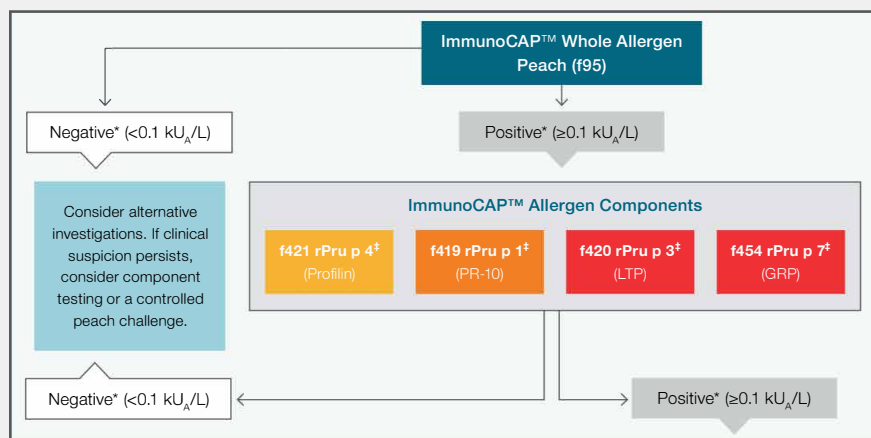
Sensitization to Pru p 7 is a risk factor for severe fruit-induced allergic reactions with the severity of reactions significantly associated with sIgE levels.¹ Pru p 7 sensitization seems to be a characteristic of a subtype of cypress pollen allergy, in which cypress pollen is the primary sensitizer 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.⁸ 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 pI, 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



* 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.

Cross-reaction, rarely associated with clinical symptoms or severe reactions^{10,11}

Management considerations: further investigation to identify primary allergen.

Risk of local and in rare cases systemic reactions^{10,11}

Management considerations: in regions where birch is common, consider testing with Bet v 1 (t215)** to confirm primary sensitization.

High risk of severe, systemic symptoms^{1,2,10-12}

Management considerations: testing with Cypress (t23 and t222)** if Pru p 7 is positive, and other LTPs[^] if Pru p 3 is positive.

[^] E.g. Ara h 9[†] (f427), Art v 3[†] (w233), Cor a 8[†] (f425), Jug r 3[†] (f442), Mal d 3 (f435), Pla a 3[†], Tri a 14[†] (f443).**

[†] Available on ImmunoCAP™ ISAC_{E12i} 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 t215, Allergen Component rBet v 1 PR-10, Birch; ImmunoCAP Allergen t23, Italian/Mediterranean/Funeral cypress; ImmunoCAP Allergen t222, Arizona cypress; ImmunoCAP Allergen w233, Allergen Component Art v 3 LTP, Mugwort.

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