

# Hypersensitivity to Tomato (*Lycopersicon esculentum*) in Peach-Allergic Patients: rPru p 3 and rPru p 1 Are Predictive of Symptom Severity

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## ■ Abstract

**Background:** The role of allergens in the severity of tomato allergy symptoms has not yet been studied.

**Objectives:** To evaluate the relationship between severe allergic reactions to peach and tomato and between tomato allergy symptoms and the pattern of IgE positivity for rPru p 1, rPru p 3, rPru p 4, rBet v 1, rBet v 2, rBet v 4, rPhl p 1, and rPhl p 12 in order to identify the role of recombinant allergens in the severity of reactions to tomato.

**Methods:** We studied peach-allergic patients with clinical reactions to tomato by performing an open food challenge, skin prick test, and determination of serum specific IgE to tomato and to recombinant peach, birch, and grass allergens. Statistical analysis was carried out to evaluate the relationship between the severity of tomato symptoms and IgE positivity to the different allergens and to peach-induced symptoms.

**Results:** We found a significant association between severe reactions to tomato and severe reactions to peach ( $P=.017$ ) and levels of IgE to rPru p 3 ( $P=.029$ ) and between mild tomato allergy symptoms and levels of IgE to rPru p 1 ( $P=.047$ ), anti-rBet v 1 ( $P=.0414$ ), anti-rBet v 2 ( $P=.0457$ ), and *Phleum pratense* ( $P=.0022$ ).

**Conclusion:** We observed a significant relationship between peach and symptoms of tomato allergy. IgE positivity for rPru p 3 seems to be a surrogate biochemical marker for severe tomato allergy, whereas the presence of anti-rPru p 1 IgE may be an indicator of mild tomato allergy.

**Key words:** Lipid transfer protein. LTP. Peach allergy. Pru p 3. Pru p 1.

## ■ Resumen

**Antecedentes:** La relevancia de los diferentes alérgenos del tomate, en relación a la severidad de los síntomas producidos tras su ingesta, no ha sido aún establecida.

**Objetivos:** Evaluar la relación entre las reacciones alérgicas graves inducidas por melocotón y tomate y entre los síntomas presentados tras ingesta de tomate, y el patrón de sensibilizaciones IgE mediadas frente a rPru p 1, rPru p 3, rPru p 4, rBet v 1, rBet v 2, rBet v 4, rPhl p 1 y rPhl p 12 con el fin de concretar la responsabilidad de cada uno de los alérgenos en la gravedad de las reacciones producidas por el tomate.

**Métodos:** Dentro de una población de pacientes alérgicos a melocotón seleccionamos aquellos pacientes con antecedentes de reacciones a tomate mediante una provocación oral abierta (OFC), pruebas cutáneas (SPT) e IgE específica a tomate, a alérgenos recombinantes de melocotón y gramíneas. La gravedad de los síntomas producidos por el tomate estaba relacionada con la presencia de IgE frente a los diferentes alérgenos así como a los síntomas causados por la ingesta de melocotón.

**Resultados:** Se halló una asociación significativa entre las reacciones alérgicas graves a tomate con las reacciones graves a melocotón ( $p = 0,017$ ) así como con los valores de IgE específica a rPru p 3 ( $p = 0,029$ ), en tanto que los valores de IgE específica a rPru p 1, rBet v 1,

rBet v 2 y *Phleum pratense* se relacionaban con síntomas leves tras ingesta de tomate ( $p = 0,047$ ,  $p = 0,0414$ ,  $p = 0,0457$ ,  $p = 0,0022$  respectivamente).

**Conclusión:** Existe una relación significativa entre los síntomas producidos por el melocotón y el tomate. La presencia de IgE específica frente a rPru p 3 parece ser un marcador de síntomas graves por alergia a tomate, en tanto que la presencia de IgE específica anti rPru p 1 parece ser un marcador de síntomas leves en los pacientes alérgicos a tomate.

**Palabras clave:** Alergia a tomate. Proteína de transferencia de lípidos. LTP. Alergia a melocotón. Pru p 3. Pru p 1.

## Introduction

Tomato (*Lycopersicon esculentum*), a member of Solanaceae family, is a well-known allergen in pollen-sensitized patients [1-4]. The correlation between grass pollen and tomato-specific IgE is well established, even in barely symptomatic patients [1,2]. The self-reported frequency of tomato allergy is about 3% worldwide [5]. Differences in frequency are reported between northern and southern Europe, ranging from about 1.3% in England [6] to 6.5% on the Mediterranean coast of Spain, where, surprisingly, most sensitized patients tolerate ingestion of tomato [4]. In an Italian multicenter observational study, of 351 patients with type I food allergy, only 2 had tomato allergy, and only 1 of these patients reported systemic symptoms [7]. More recently, Asero [8] studied 96 patients with plant food allergy and found that 32 were sensitized to tomato (33% prevalence); most patients were sensitized to type 10 pathogenesis-related (PR) protein and profilin, while 12% were sensitized only to lipid transfer protein (LTP) [8]. Our group demonstrated that tomato LTP, albeit a minor allergen, was clinically relevant in Italian patients and was recognized in 15% of patients who experienced more severe reactions to tomato [9]. We also detected different allergenic LTPs in tomato peel, pulp, and seeds, which were all allergenic [9]. LTP is the main allergen involved in plant food allergy in Mediterranean countries, as demonstrated by Spanish and Italian studies of allergy to peach [10] and tomato [7,11]. In patients with multiple sensitizations to plant foods and pollens, component-resolved diagnosis is a useful tool for diagnosing LTP syndrome [12]. In Italian children, however, the presence of specific IgE to Pru p 3 was not associated with systemic reactions [13]. In a study on peach-allergic patients [14], we showed that simultaneous positivity for anti-Pru p 3 and anti-Pru p 1 IgE was associated with milder symptoms than positivity for anti-Pru p 3 IgE alone, which was associated with severe symptoms. Given the high number of peach-allergic patients with tomato allergy symptoms in our previous study [14], we investigated the possible relationship between severe peach allergy symptoms and allergic reactions to tomato, as well as the correlation between tomato allergy and IgE positivity for the major peach allergens rPru p 3 and rPru p 1.

## Methods

### Study Design

The objective of the present study was proposed as a secondary objective in a previously published trial on peach

allergy [14] approved by the Ethics Committee of Niguarda Ca'Granda Hospital and registered at ClinicalTrials.gov (protocol ID: NCT00715156). We aimed to evaluate the relationship between severe reactions to peach and plant food allergens, in particular, whether sensitization to rPru p 3 could be a possible marker of severe reactions to other plant food allergens.

### Patients

The study population comprised 148 peach-allergic patients who were enrolled in a clinical study [14] and investigated for a clinical history of tomato allergy. The type of reaction and its severity were investigated. Symptoms were recorded using a case report form as part of the previously described protocol [14]. Tomato-induced symptoms were classified into 4 possible grades of severity as previously described for peach; in particular, we defined mild oral allergy syndrome (OAS grade I) as reactions localized only in the oral mucosa and severe OAS (OAS grades II, III, or IV) as reactions including OAS grade I plus systemic symptoms [14]. Patients who reported symptoms to tomato were divided into 2 groups: patients with mild symptoms (OAS grade I) and patients with severe symptoms (OAS grades II, III, and IV), according to an OAS score of symptom severity [14]. Patients with mild OAS and grade II OAS underwent an open food challenge (OFC) with the "Galeon" cultivar to test for the presence of local symptoms. When there was a history of very severe reactions (OAS grade III and IV), the clinical documentation was carefully reviewed, and patients did not undergo challenge [15]. In these 2 groups of patients, we also reported the severity of peach symptoms, as all the patients had experienced clinical reactions to peach. All of the patients admitted to the study had positive skin test results to fresh tomato, as confirmed using the prick-prick method [16].

### In Vitro Test

All of the patients' sera were tested for specific IgE to peach, tomato, birch (*Betula verrucosa*), timothy grass (*Phleum pratense*), rPru p 1, rPru p 3, rPru p 4, rBet v 1, rBet v 2, rBet v 4, rPhl p 1, and rPhl p 12. Sera were tested for total IgE using the ImmunoCAP System (Thermo Fisher Scientific), according to the manufacturer's instructions. IgE levels were considered positive when a value greater than 0.10 kU<sub>A</sub>/L was obtained.

### Open Food Challenge

OFC was performed with "Galeon" fresh tomato by administering doses at 15-minute intervals, as previously described [9]. Testing was performed outside the birch and

Table. Demographic Data, Clinical Symptoms, and Specific IgE Results

Mild Tomato Allergy Symptoms		Tomato		Peach		Birch		Timothy		Specific IgE for Recombinant Allergens								Total IgE	
Patient	Age	Gender	OAS <sup>s</sup>	IgE	OAS <sup>s</sup>	IgE	Symptoms	IgE	Symptoms	IgE	Prup1	Prup3	Prup4	Betv1	Betv2	Betv4	Phlp1	Phlp12	
1	31	Female	I	23.8	I	44.5	Yes	100.0	Yes	100	74.4	0.2	12.1	100.0	14.6	40.7	100.0	20.5	1816
2	25	Female	I	1.3	I	0.1	Yes	100.0	Yes	100	10.8	0.1	4.3	35.3	4.2	0.0	38.5	7.2	908
3	38	Male	I	0.9	I	4.6	Yes	28.5	No	26.8	11.4	0.0	1.0	22.7	1.1	4.4	3.4	0.4	133
4	45	Male	I	1.4	I	5.3	Yes	100.0	Yes	59	25.6	0.0	0.0	42.0	0.0	0.0	27.6	0.0	316
5	28	Female	I	4.7	I	5.4	Yes	13.2	Yes	30.5	2.4	0.3	7.6	7.1	8.9	0.0	27.4	9.0	125
6	43	Female	I	0.9	I	1.0	Yes	1.3	No	19.9	0.0	0.0	0.9	0.0	1.2	0.0	4.3	0.6	214
7	18	Female	I	4.5	I	9.6	Yes	2.2	Yes	90.9	0.2	8.7	0.6	0.6	0.5	0.0	48.4	1.2	351
8	30	Female	I	6.4	I	0.7	No	35.8	Yes	78.3	12.9	0.0	2.5	37.4	1.6	0.0	57.1	4.1	547
9	29	Male	I	16.0	I	64.9	No	100.0	Yes	100	75.5	34.4	15.2	100.0	15.2	0.0	100.0	16.2	832
10	42	Female	I	0.3	I	7.1	No	0.1	No	86	0.0	2.4	0.0	0.0	0.0	0.0	6.7	0.0	194
11	49	Male	I	1.1	I	7.5	Yes	0.1	No	0.34	0.0	8.6	0.0	0.2	0.0	0.0	0.2	0.0	285
12	32	Female	I	0.1	I	2.1	Yes	19.5	Yes	25.2	11.3	0.0	0.0	17.7	0.0	0.0	12.8	0.0	162
13	61	Female	I	0.1	I	2.4	Yes	40.0	Yes	39.4	10.1	0.0	0.0	48.2	0.0	0.0	22.7	0.2	915
14	48	Female	I	0.2	I	5.9	Yes	35.7	No	0.0	9.3	0.0	0.0	16.5	0.0	0.0	NT	NT	232
15	21	Male	I	0.0	I	0.6	Yes	48.5	No	0.0	9.8	0.0	0.0	53.4	0.0	0.0	NT	NT	75.7
16	31	Male	I	0.0	I	3.1	No	36.2	Yes	25.3	10.0	1.9	1.3	32.6	1.2	0.0	14.0	1.4	249
17	49	Female	I	0.0	I	6.0	Yes	26.1	No	0.16	10.4	0.0	0.0	17.9	0.0	0.0	0.5	0.0	68.7
18	55	Male	I	8.8	II	19.4	No	0.0	Yes	8.0	0.0	14.5	0.0	0.0	0.0	0.0	8.5	0.2	1076
19	58	Male	I	0.3	III	3.5	Yes	22.5	No	1.4	6.8	2.3	0.0	17.2	0.0	0.0	1.2	0.0	476
20	38	Male	I	0.6	IV	2.8	No	0.0	Yes	44.2	0.0	4.1	0.0	0.0	0.0	0.0	26.8	0.0	353
21	30	Female	I	16.8	III	3.7	No	5.7	Yes	50.9	0.0	6.9	14.5	0.0	19.8	12.9	76.8	23.9	908
22	44	Female	I	3.0	III	56.7	No	100.0	No	9.9	98.5	0.2	0.0	100.0	0.0	0.0	3.5	0.0	672
23	24	Female	I	3.8	IV	0.7	Yes	5.9	Yes	100.0	0.0	0.4	4.4	0.0	5.3	0.0	NT	NT	364
24	42	Female	I	3.4	III	6.7	No	0.0	No	0.0	0.0	10.2	0.0	0.0	0.0	0.0	NT	NT	587
25	63	Female	I	0.0	III	26.8	No	0.0	No	0.0	0.0	21.7	0.0	0.0	0.0	0.0	NT	NT	333
Severe Tomato Allergy Symptoms																			
26	57	Male	III	9.9	III	7.4	Yes	98.0	Yes	45.4	12.9	0.1	10.6	80.6	14.0	0.0	49.2	10.4	1215
27	39	Female	III	39.5	III	91.5	Yes	100.0	Yes	100.0	55.2	100.0	32.1	100.0	54.2	96.9	88.5	23.3	4459
28	32	Female	III	3.1	III	9.5	No	0.0	No	81.5	0.0	10.8	0.0	0.0	0.0	0.0	25.0	0.0	234
29	22	Male	IV	4.3	III	29.7	No	0.0	No	0.0	0.0	22.4	0.0	0.0	0.0	0.0	NT	NT	64.2
30	26	Male	III	4.6	III	12.0	No	1.0	No	0.0	0.0	13.1	0.0	0.0	0.0	0.0	NT	NT	294
31	34	Female	II	2.5	II	7.1	No	0.0	No	0.0	0.0	10.7	0.0	0.0	0.0	0.0	NT	NT	58.6
32	17	Male	IV	2.1	III	20.0	No	0.0	No	0.0	0.0	34.7	0.0	0.0	0.0	0.0	NT	NT	387

Mild Tomato Allergy Symptoms	Tomato		Peach		Birch		Timothy		Specific IgE for Recombinant Allergens											
	Patient	Age	Gender	OAS*	IgE	OAS*	IgE	Symptoms	IgE	Symptoms	Prup1	Prup3	Prup4	Betv1	Betv2	Betv4	Phlp1	Phlp12	Total IgE	
																				OAS*
33	28	Female	III	13.2	III	25.7	No	0.6	Yes	0.0	23.3	0.0	0.0	0.0	0.0	0.0	NT	NT	146	
34	24	Male	III	18.5	III	53.5	No	0.2	No	0.0	42.0	0.0	0.0	0.0	0.0	0.0	NT	NT	632	
35	58	Female	III	0.7	III	5.1	No	0.0	No	0.0	11.2	0.0	0.0	0.0	0.0	0.0	NT	NT	451	
36	18	Female	IV	0.4	III	4.9	No	15.3	No	0.0	5.3	0.0	0.0	15.1	0.0	0.0	NT	NT	46.5	
37	26	Female	III	0.3	II	1.3	No	10.6	Yes	5.2	2.9	0.0	0.0	10.2	0.3	0.0	4.5	0.5	106	
38	44	Female	II	0.2	III	1.0	No	0.0	Yes	0.2	1.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	15	
39	57	Female	III	0.0	III	2.9	No	0.0	No	0.0	1.9	0.0	0.0	0.0	0.0	0.0	NT	NT	45.7	
40	29	Female	II	0.0	II	2.4	No	0.6	No	0.0	0.3	2.9	0.0	1.8	0.0	0.0	NT	NT	140	
41	57	Female	II	0.0	IV	3.3	No	0.0	No	0.0	3.7	0.0	0.0	0.0	0.0	0.0	NT	NT	88.1	
42	20	Female	III	0.0	III	7.7	No	0.0	No	0.0	0.0	0.0	0.0	0.0	0.0	0.0	NT	NT	86.5	
43	24	Female	III	0.0	I	1.2	No	0.0	No	0	1.2	0.0	0.0	0.0	0.0	0.0	NT	NT	34.7	
44	71	Female	III	0.2	I	11.8	Yes	21.2	No	0.71	16.0	0.0	0.0	23.2	0.0	0.0	0.6	0.0	110	
45	34	Female	III	3.9	I	7.0	Yes	3.7	Yes	25.8	7.4	0.0	3.6	0.0	0.0	0.0	18.0	0.0	235	
46	39	Female	III	8.6	I	28.8	Yes	100.0	Yes	100	3.4	10.8	100.0	8.5	0.0	0.0	38.1	6.3	1537	
47	40	Female	II	1.2	I	2.9	No	0.3	Yes	20.9	4.2	0.0	0.0	0.0	0.0	0.0	29.0	0.0	255	
48	38	Female	II	0.5	I	5.3	No	0.0	No	0.0	5.3	0.0	0.0	0.0	0.0	0.0	NT	NT	70.5	
49	6	Female	III	0.0	I	1.0	Yes	44.8	Yes	12.7	1.6	0.0	4.3	0.0	0.0	0.0	8.1	0.0	121	
50	48	Female	III	0.0	I	3.0	Yes	11.8	No	0.0	6.6	0.0	9.4	0.0	0.0	0.0	NT	NT	191	

Abbreviation: NT, not tested; OAS, oral allergy syndrome.

\*Oral allergy syndrome severity: grade I, only OAS symptoms; grade II, OAS and urticaria/angioedema; grade III, OAS with gastrointestinal symptoms and asthma; grade IV, OAS with life-threatening symptoms such as edema of the glottis, hypotension, and shock.

grass pollen seasons. The test result was considered positive when objective symptoms appeared; in the case of subjective symptoms, the challenge result was considered positive when similar symptoms occurred twice [15].

### Statistical Analysis

After validation, all the data were analyzed using appropriate descriptive methods, and the association between severity of symptoms to peach and tomato was verified using Mantel-Haenszel OR measures together with their *P* values. The Mann-Whitney test was used to compare rPrup3 IgE. For each patient, we compared the severity of tomato symptoms with the severity of peach symptoms using the Mann-Whitney test. For each patient, we compared the rPru p 3, rPru p 1, rPru p 4, rBet v 1, rBet v 2, rBet v 4, rPhl p 1, and rPhl p 12 IgE levels between the 2 groups of mild and severe tomato-induced symptoms using the Mann-Whitney test. Furthermore, we used linear regression to investigate the correlation between tomato-specific IgE levels and *P pratense* IgE levels.

## Results

### Patients

We selected 50 of 148 peach-allergic patients (34%) who had been enrolled in our previous study [14]. The patients had a documented history of tomato allergy and positive prick-prick results [16] for fresh tomato. The sample comprised 14 males (28%) and 36 females (72%), with a mean age of 37 years; no differences in age ( $P=.3973$ , *t* test) or in OAS severity ( $P=.173$ , Mann-Whitney test) were found with respect to gender. The Table shows demographic data, symptoms to allergens (tomato, peach, and pollen), serum specific IgE levels (tomato, peach, birch, timothy, rPru p [1, 3, and 4], rBet v [1, 2, and 4], rPhl p [1 and 12]) and total IgE levels for both groups (mild symptoms and severe symptoms). We found 25 patients with mild symptoms (Table, patients 1-25) and 25 patients with severe symptoms (Table, patients 26-50).

### Open Food Challenge

All of the 25 patients with mild symptoms underwent OFC with fresh tomato, which elicited clinical symptoms corresponding to those reported in the clinical histories (OAS grade I), except for 4 patients (patients 19, 21, 24, and 25 [Table]), who also complained of nausea and abdominal pain. If only subjective symptoms of OAS were reported, the OFC was repeated twice; the result was considered positive when the same symptoms were elicited during both challenges. As for the 25 patients with severe symptoms, only those presenting grade II OAS underwent OFC (patients 31, 38, 40, 41, 47, and 48 [Table]); again, the symptoms observed during OFC were grade II OAS. Patients with grade III or IV OAS did not undergo OFC for ethical and safety reasons.

### Statistical Analysis

*Association between peach and severity of tomato symptoms.* Most patients with mild peach OAS also had mild symptoms with tomato (17/25; 68%). Only 8 out of 25

patients (32%) with mild OAS to peach had severe symptoms with tomato. In contrast, most patients with severe reactions to peach had severe symptoms with tomato (17/25; 68%). On the basis of these data, we observed a significant association between patients with mild peach symptoms and mild tomato symptoms ( $P=.0189$ , Mann-Whitney test).

*Association between total IgE levels and severity of tomato symptoms.* We found that total IgE levels were significantly higher in the group with mild tomato symptoms than in the group with severe tomato symptoms ( $P=.0101$ , Mann-Whitney test).

*Association between rPrup 3, rPrup 1, and rPrup 4 IgE levels and severity of tomato allergy symptoms.* We found that the rPru p 3 IgE levels were significantly lower in the group with mild symptoms than in the group with severe symptoms ( $P=.0291$ , Mann-Whitney test), whereas rPru p 1 IgE levels were significantly higher than in the group with severe symptoms ( $P=.0461$ , Mann-Whitney test). No significant differences were found for rPru p 4 IgE levels ( $P=.0769$ , Mann-Whitney test).

*Association between rBet v 1, rBet v 2, and rBet v 4 IgE levels and severity of tomato symptoms.* We found significantly higher levels of rBet v 1 IgE and rBet v 2 IgE in the group with mild symptoms than in the group with severe symptoms ( $P=.0414$  and  $P=.0457$ , respectively, Mann-Whitney test). No differences were found for rBet v 4 IgE levels (Mann-Whitney test,  $P=.3325$ ).

*Association between symptoms to *P pratense*, specific IgE levels to *Phleum pratense*, specific IgE levels to rPhl p 1 and rPhl p 12, and severity of tomato allergy symptoms.* We found significantly higher *P pratense* IgE levels in the group with mild symptoms than in the group with severe symptoms ( $P=.0022$ , Mann-Whitney test). No differences were found between the groups for *P pratense* symptoms (Mann-Whitney test,  $P=.1602$ ), rPhl p 1 IgE levels ( $P=.1116$ , Mann-Whitney test), and rPhl p 12 IgE levels ( $P=.0732$ , Mann-Whitney test).

*Association between *Phleum pratense* and tomato-specific IgE values.* We found an acceptable and significant correlation between *P pratense* and tomato-specific IgE (Spearman's  $\rho = 0.458$ ;  $P=.0008$ ); this result was also confirmed using a robust exploratory regression in which *Phleum* IgE was set as the dependent variable and tomato IgE as the regressor ( $P<.0001$ , Wald test).

*Association between peach and tomato-specific IgE levels.* No differences were found between mild symptoms and severe symptoms as regards peach-specific IgE ( $P=.3669$ , Mann-Whitney test) or tomato-specific IgE levels ( $P=.7037$ , Mann-Whitney test).

## Discussion

In the present study, 50 Italian patients with peach allergy were selected because of symptoms of tomato allergy of varying severity. The patients were classified according to the severity of their tomato symptoms using an OAS severity score [14] as having mild or severe symptoms [14]. We found statistically higher levels of anti-rPru p 1 IgE in patients with mild symptoms and anti-rPru p 3 IgE in patients with severe



symptoms. Clinically, a patient presenting severe symptoms to peach is at higher risk of developing severe symptoms to tomato, as previously shown for peach [14], whereas anti-rPrup 1 IgE levels could be a marker for milder tomato symptoms [14]. This clinical association between severe symptoms to peach and tomato occurs even if the amino acid identity of peach and tomato LTP is limited (39% by sequence alignment in the UniProt Knowledgebase, [www.uniprot.org](http://www.uniprot.org); and 49% using NCBI BLAST software, <http://blast.ncbi.nlm.nih.gov/Blast.cgi>) [8], probably because all the patients in the present study had peach allergy and peach LTP is believed to contain all of the cross-reactive tomato LTP epitopes. Prup 3 may play the role of a precursor in sensitization to other LTPs, even if they are not botanically related, as demonstrated for nuts [17]. In Italian patients with allergic reactions to both hazelnut and peach, Prup 3 was a stronger stimulus for cross-reacting T-cell lines than Cor a 8, thus indicating that peach LTP is the primary sensitizer in patients with hazelnut and peach allergy [17]. Moreover, preincubation of sera with Prup 3 completely abolished IgE reactivity to Cor a 8, but not contrariwise, thus confirming that the primary sensitizer is Prup 3. As for peanut, ELISA cross-inhibition experiments showed that Prup 3 was the predominant allergen and primary sensitizer in Spanish patients, thus confirming that Prup 3 acted as the main sensitizer in patients with peanut allergy [18].

A recent study on Spanish fruit-allergic patients [19] showed that peach LTP was the most frequently recognized allergen (75% of patients), whereas Lye 3 (tomato LTP) was recognized in about 30-40% of patients. Given that marked cosensitization was found between Prup 3 and other LTPs, fruit-allergic patients were highly likely to be polysensitized. Inhibition studies performed with serum from a patient with tomato anaphylaxis showed that peach LTP completely inhibited IgE reactivity to tomato, thus confirming that peach LTP contains all of the determinants of this allergen [20]. It was recently demonstrated that Prup 3 can cross the gastrointestinal epithelium intact, with transport kinetics that are similar to those of the vesicle transport system of proteins and induce an immune response with the production of  $T_H2$  cytokines, unlike other LTPs [21]. In the present study, we found 34% prevalence of tomato-allergic patients in a cohort of 148 peach-allergic patients. In a recent study by Asero [8], 33% of a cohort of 96 patients with plant food allergy were allergic to tomato. In the same study, no significant correlation was found between peach IgE levels and tomato allergy, but a significant correlation was detected between peach- and tomato-specific IgE levels in the subgroup of LTP-sensitized patients. These differences could be due to the fact that in the present study, the patients were selected on the basis of their clinical symptoms, which were confirmed by food challenge, whereas Asero stratified patients on the basis of their sensitization pattern (ie, pure PR-10, pure profilin, PR-10 and profilin, pure LTP, mixed group, and genuine tomato).

In the present study, we confirm our previous findings for peach allergy, ie, that sensitization to rPrup 3 is a marker of possible severe reactions to other plant foods. In fact, we recently demonstrated that severe peach allergy is significantly related to severe fennel allergy, since LTP is a major fennel allergen. However, no significant correlations were detected between the severity of fennel-induced symptoms and anti-

rPrup 3 IgE levels or anti-rBet v 1, anti-rPrup 1, and anti-rBet v 2 IgE levels [22]. As for other plant foods and peach allergy, we also showed that allergic reactions to rice can occur in patients with peach allergy, even if these are rarer than with fennel and tomato, and that anti-rPrup 3 IgE levels are significantly higher in patients with rice allergy than in patients who are sensitized but rice-tolerant [23]. Also relevant is the correlation between mild reactions to tomato and grass pollen sensitization. This result correlates well with data in the literature [1-3], as grass pollen-allergic patients frequently present OAS to tomato. It is interesting to note that rPhlp 1 and rPhlp 12 have no protective role in the development of allergic symptoms to tomato, unlike rBet v 1, which has a protective role in inducing severe symptoms in Prup 3-sensitized patients [14]. Therefore, the possible involvement of other allergens in relieving tomato allergy symptoms needs to be investigated.

### 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 February 11, 2014; accepted for publication July 14, 2014.*

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