Detection of clinical markers of sensitization to profilin in patients allergic to plant-derived foods

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Background: A proper classification of patients allergic to plant-derived foods is of pivotal importance because the clinical features of allergic reactions to fruits and vegetables depend on the nature and characteristics of proteins responsible for sensitization. However, in normal clinical settings this is presently impossible.
Objective: We sought to detect clinical markers of sensitization to profilin.
Methods: Seventy-one patients allergic to fruits and vegetables but not sensitized to lipid transfer protein or natural rubber latex were studied. Food allergy was ascertained on the basis of clinical history and positive skin prick test responses with fresh foods, commercial extracts, or both. Allergies to foods that had caused less than 2 adverse reactions were confirmed by means of open oral challenge. IgE reactivity to rBet v 1/rBet v 2 and to natural *Phleum* species profilin were detected. Moreover, IgE to the 30- to 40-kd and 60- to 90-kd birch pollen–enriched fractions, which also can be involved in cross-reactivity phenomena, were measured in sera from 52 patients by means of ELISA.
Results: On the basis of in vitro tests, 24, 18, and 25 patients turned out to be sensitized to Bet v 1, Bet v 2, or both, respectively. Four patients had negative test results for both allergens. Hypersensitivity to Bet v 2 was strongly associated with clinical allergy to citrus fruits (39% in patients monosensitized to Bet v 2 vs 4% in patients monosensitized to Bet v 1, $P < .025$), melon or watermelon (67% vs 0%, $P < .001$), banana (66% vs 8%, $P < .001$), and tomato (33% vs 0%, $P < .05$), whereas Bet v 1 sensitivity was associated with clinical allergy to apple (100% vs 39%, $P < .001$) and hazelnut (56% vs 0%, $P < .001$). The sensitivity of a history of allergy to gourd fruits, citrus fruits, tomato, banana, or a combination thereof as a means to detect profilin-hypersensitive patients was 85% (41/48). The specificity of an allergy to any of these fruits exceeded 85%, with positive predictive values ranging between 68% and 91%.
Conclusion: In clinical settings in which laboratory investigations are not easily accessible, allergy to melon, watermelon, citrus fruits, tomato, and banana can be used as a marker of profilin hypersensitivity once a sensitization to natural rubber latex and lipid transfer protein is ruled out. (J Allergy Clin Immunol 2003;112:427-32.)

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Profilin is a 12- to 15-kd monomeric actin-binding protein present in all eukaryotic cells. It was first reported as a minor allergen in birch pollen[1] but is presently considered an ubiquitous plant panallergen[2,3] and one of the main causes of cross-sensitization between pollen and plant-derived foods. Although sera from patients with pollen allergy sensitized to profilin invariably show both in vivo (on skin prick tests [SPTs] with fresh material) and in vitro IgE reactivity against virtually all fruits and vegetables, the clinical significance of such sensitization is still poorly defined. Profilin has been involved in the birch-mugwort-celery-spice syndrome,[4-8] and several studies concluded that this protein can also play a role in patients allergic to hazelnut,[9] celery, carrot,[3,10] peach, pear, apple,[3,11] potato,[3] lychee,[12] tomato,[13] and pumpkin seed.[14] However, recent studies suggested that profilin sensitization has little or no clinical relevance.[15,16] A possible reason for such discrepancies is that few subjects are monosensitized to profilin, with most patients being sensitized also to other cross-reacting structures in pollen and vegetable foods, such as Bet v 1 or Art v 1, or to primary food allergens, such as lipid transfer protein (LTP), a fact that has certainly hampered a clear assessment of the clinical relevance of profilin sensitization. Clearly, the only way to overcome this problem is to examine selected patients who are monosensitized to this protein. The present study aimed to detect food allergies specifically associated with profilin sensitization to be used as clinical markers of profilin allergy in the clinical practice.

METHODS

Patient selection

The study was carried out with 71 adult patients (31 male and 40 female patients; age range, 14-66 years) seen at the allergy unit of the hospital of Bollate (Milan, Italy) with a history of oral allergy syndrome (OAS; defined as the onset of immediate oral itching with or without angioedema of the lips and oral mucosa) after the ingestion of vegetable foods. Offending foods were ascertained both by means of a thorough interview and a standardized questionnaire; specific IgE hypersensitivity was confirmed by means of positive SPT responses with fresh material, commercial extracts, or both. Clinical reactivity to foods that had caused less than 2 adverse reactions was confirmed by means of an open oral challenge. Exclusion criteria were as follows: clinical history of natural rubber latex aller-

Abbreviations used
LTP: Lipid transfer protein
NPV: Negative predictive value
OAS: Oral allergy syndrome
OD: Optical density
PPV: Positive predictive value
SPT: Skin prick test

gy and hypersensitivity to LTP, as shown by a positive SPT response with a commercial plum extract (Dome-Hollister/Stier 1:20 wt/vol). In a previous study[17] we demonstrated that reactivity to this extract is associated with LTP hypersensitivity.*

Skin tests and preliminary classification of the patients

Patients underwent SPTs with a large panel of commercial extracts (Allergopharma, Reinbeck, Germany) of both seasonal and perennial airborne allergens, including grass, mugwort, ragweed, pellitory, plantain, birch, hazel, olive, cypress, several molds, house dust mite, cat dander, and dog dander. Skin tests with a large panel of commercial vegetable food extracts, including rice, wheat, maize, peanut, pea, soybean, bean, walnut, hazelnut, carrot, celery, plum, melon, banana, and tomato (1:20 wt/vol; Dome-Hollister/Stier, Spokane, Wash) and peach peel (440 μg of protein/mL; Lofarma, Milan, Italy), were carried out as well. Finally, all patients underwent SPTs with the fresh offending foods by means of the prick-prick technique. All skin tests were carried out on the volar side of the forearm with sterile 1-mm-tip lancets (Dome-Hollister/Stier). Readings were taken after 15 minutes. Reactions were expressed as the mean wheal diameter (adding the longest diameter to the orthogonal diameter and dividing by 2). A wheal diameter of 3 mm or more was considered positive.[18] Histamine, 10 mg/mL, and saline were used as positive and negative controls, respectively. On the basis of positive SPT responses with birch pollen extract in the absence of any skin reactivity to other pollen extracts, 24 patients were preliminarily classified as probably Bet v 1 reactive/Bet v 2 nonreactive, whereas 47 patients with positive SPT responses with most of the pollen species tested[19] were classified as possibly Bet v 2 reactive, with or without Bet v 1 reactivity.

In vitro studies

Detection of IgE to rBet v 1/rBet v 2. IgE reactivity to rBet v 1 and rBet v 2 of sera from all 71 patients was measured by using the CAP system (Pharmacia, Uppsala, Sweden) according to the manufacturer's instructions. Levels of greater than 0.35 KU/L were considered positive.

Detection of IgE to natural profilin. In view of previous studies showing that the sensitivity of the rBet v 2 assay is not ideal in the detection of subjects hypersensitive to profilin,[20] sera from 52 patients (44 of those suspected as being profilin reactors and 8 subjects suspected as being Bet v 1 reactors only) underwent the detection of IgE to natural profilin purified from *Phleum pratense* pollen by means of ELISA. *P pratense* pollen was submitted to 5% aqueous extraction in PBS overnight at 4°C during stirring. The suspension was centrifuged at 20,000*g* for 30 minutes at 4°C, and the supernatant was filtered through a 0.22-mm filter. Protein content was measured according to the method of Bradford (Bio Rad, Milan, Italy).[21] Profilin was purified by means of affinity chromatography in a poly-(L-proline) cyanogen bromide–activated Sepharose column.[22] Briefly, the gel was prepared by coupling 30 mg of poly-(L-proline) (Sigma, Milan, Italy) to 2 g of cyanogen bromide–activated Sepharose 4B (Pharmacia Biotech). *P pratense* pollen extract (3.66 g) was applied to a column of poly-(L-proline) cyanogen bromide–activated Sepharose equilibrated in PBS. Profilin was eluted with 6 mol/L urea in PBS. Absorbance at 280 nm revealed one elution peak. The presence of profilin in the elution peak was checked by means of SDS-PAGE. Electrophoresis of samples was carried out in a 10% polyacrylamide precast Nupage Bis-Tris gel according to the manufacturer's instructions (Novex, Prodotti Gianni, Milan, Italy) at 180 mA for 1 hour. The resolved proteins were stained with Coomassie Brilliant Blue. Fractions containing exclusively profilin (Fig 1) were used in ELISA assays.

Detection of IgE reactivity to other cross-reacting birch pollen allergens. The IgE reactivity of the same 52 sera to the 30- to 40-kd and 60- to 90-kd enriched fractions from birch pollen was also assessed by means of ELISA to exclude the possible influence of sensitization to other recently described cross-reacting birch pollen allergens, such as Bet v 5,[23-25] Bet v 6,[26] and Bet v 8.[27] Birch pollen was extracted as previously described. Lyophilized extract was resuspended in one tenth of the original volume and submitted to gel permeation chromatography on a Superdex 75 column (Pharmacia, Milan, Italy) equilibrated in PBS-0.05% NaN_3 (bed volume, 150 mL). Fractions were analyzed by means of SDS-PAGE stained with Coomassie Brilliant Blue. Fractions exclusively containing the regions 30 to 40 kd or 60 to 90 kd (Fig 1) were used.

*ELISA.*ELISA was carried out by using 0.5 μg per well of protein diluted in coating buffer (15 mmol/L Na_2CO_3 and 35 mmol/L $NaHCO_3$, pH 9.6) and coated onto the wells of 96-microwell ELISA plates (Maxisorp Nunc, Roskilde, Denmark). Bound specific IgE was detected by adding a peroxidase-conjugated anti-human IgE serum and developing colorimetric reaction by using tetramethyl benzidine/H_2O_2 as the substrate. Results were expressed as optical density (OD) units. On the basis of the mean value of 4 normal sera (<400 OD units), OD values of greater than 800 were considered positive.

Statistical methods

Proportions were compared by using the χ^2 test with the Yates' correction. Probability levels of less than 5% were considered statistically significant. The usefulness of a clinical history of OAS (confirmed by positive SPT responses) as a marker of profilin sensitization was assessed by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) by using established methods[28]:

$$\text{Sensitivity} = TP/TP + FN$$
$$\text{Specificity} = TN/TN + FP$$
$$PPV = TP \times P/TP \times P + FP\ (1 - P)$$
$$NPV = TN\ (1 - P)/TN\ (1 - P) + FN \times P,$$

where P represents prevalence, TP represents true-positive results, TN represents true-negative results, FP represents false-positive results, and FN represents false-negative results.

RESULTS

By using the CAP system, 25 patients turned out to have positive rBet v 1/negative rBet v 2 results; this group included all 24 subjects preliminarily considered as probably monosensitized to Bet v 1 and 1 putative Bet v 2 reactor. Eighteen sera were from patients with negative rBet v 1/positive rBet v 2 results, 24 sera were from patients with positive rBet v 1/positive rBet v 2 results, and 4 sera were from patients with negative rBet v 1/negative rBet v 2 results. In patients with negative rBet v

*This commercial extract is presently not available on the market. Recent studies (unpublished) carried out by Dr Asero found that the commercial peach extract by ALK-Abello (1:20 wt/vol) shows the same properties.

1/positive rBet v 2 results, IgE to rBet v 2 ranged from 0.58 to 12.6 KU/L; in patients with positive rBet v 1/positive rBet v 2 results, IgE to rBet v 2 ranged from 0.46 to 62.8 KU/L. ELISA with profilin from *P pratense* confirmed the results of the CAP system in 51 of 52 cases; one patient with positive rBet v 1/negative rBet v 2 results (notably the only patient preliminarily considered as a possible Bet v 2 reactor in this subgroup) had IgE reactivity to natural *P pratense* profilin (963 OD units) and was therefore included in the subgroup with positive Bet v 1/positive Bet v 2 results. On the basis of the findings of both the CAP system with rBet v 2 and ELISA with natural grass profilin, the sensitivity of the preliminary clinical classification as a means to detect profilin-hypersensitive patients turned out to be 91% (43/47).

A comparison between the prevalence of OAS induced by various foods in the different subgroups of patients is shown in Table I. Bet v 1 hypersensitivity was typically associated with apple allergy (24/24 [100%] in patients with positive Bet v 1/negative Bet v 2 results vs 7/18 [39%] in patients with negative Bet v 1/positive Bet v 2 results, $P < .001$) and with hazelnut allergy (14/24 [58%] vs 0/18 [0%], $P < .001$). Bet v 2 hypersensitivity was typically associated with clinical allergy to citrus fruits (7/18 [39%] in patients with negative Bet v 1/positive Bet v 2 results vs 1/24 [4%] in patients with positive Bet v 1/negative Bet v 2 results, $P < .025$); melon, watermelon, or both (12/18 [67%] vs 0/24 [0%], $P < .001$); banana (12/18 [66%] vs 2/24 [8%], $P < .001$); and tomato (6/18 [33%] vs 0/24 [4%], $P < .01$). The prevalence of adverse reactions to all other relevant offending foods, including several Rosaceae foods, walnut, Apiaceae foods, and kiwi, was nearly identical in patients sensitized to Bet v 1 or Bet v 2. The spectrum of offending foods in patients sensitized both to Bet v 1 and Bet v 2 included fruits and vegetables that were specific for the 2 monosensitized subgroups, such as apple and hazelnut (Bet v 1 associated), as well as citrus fruits, melon-watermelon, tomato, and banana (Bet v 2 associated). Offending foods in the 4 patients with negative Bet v 1/negative Bet v 2 results included peach (n = 3), apricot (n = 1), melon (n = 3), watermelon (n = 2), tomato (n = 2), kiwi (n = 2), and banana (n = 2). Altogether, if patients with negative Bet v 1/negative Bet v 2 results were included, the sensitivity of a clinical history (confirmed by positive SPT responses) of OAS induced by any fruit among gourd fruits (watermelon, melon, or both), citrus fruits (orange, tangerine, or both), tomato, and banana as a means to detect profilin-hypersensitive patients was 85% (41/48). The sensitivity, specificity, PPV, and NPV of OAS induced by each of these fruits as a marker of profilin sensitization are shown in Table II. Notably, specificity exceeded 85% in all cases, and PPVs ranged between 68% and 91%.

On ELISA, sera from 15 of 52 patients showed IgE reactivity to the 30- to 40-kd enriched birch pollen fraction; 12 patients belonged to the subgroup with positive Bet v 1/positive Bet v 2 results, whereas 3 patients were distributed in the remaining 3 subgroups. The comparative analysis did not show any difference in the prevalence of OAS caused by particular foods between patients with positive and negative results for this fraction (data not shown). Sera from 13 of 54 patients showed IgE reactivity to the 60- to 90-kd enriched birch pollen fraction; 9 patients belonged to the subgroup with positive Bet v 1/positive Bet v 2 results, and 4 patients belonged to the subgroup with negative Bet v 1/positive Bet v 2 results. Again, no difference in the prevalence of OAS caused by particular foods between patients with positive and negative results for this fraction was found (data not shown). Nine patients had IgE reactivity to both the 30- to 40-kd and 60- to 90-kd enriched birch pollen fractions.

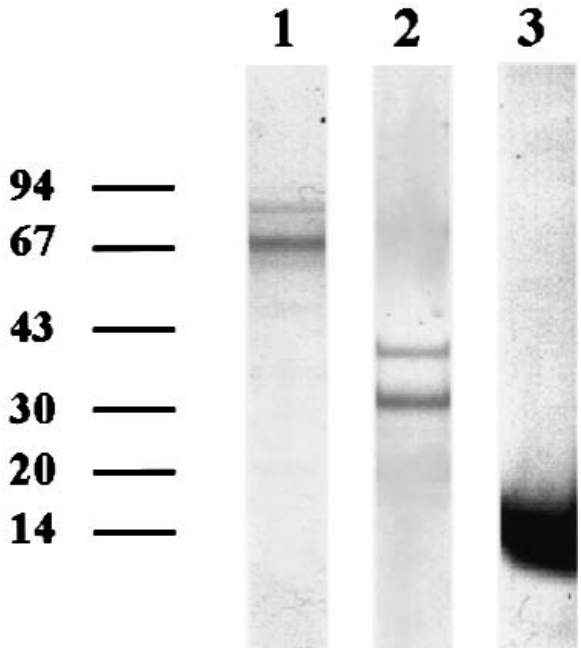

FIG 1. SDS-PAGE electrophoresis of protein fractions purified from birch and grass pollen: *lane 1,* 60- to 90-kd enriched fraction from birch pollen extract; *lane 2,* 30- to 40-kd enriched fraction from birch pollen extract; *lane 3,* profilin purified from *P pratense*.

DISCUSSION

In patients allergic to fruits and vegetables, the nature of proteins responsible for sensitization might profoundly influence both the spectrum of offending foods and the clinical features of allergic reactions. The risk of experiencing severe and potentially life-threatening reactions is relevant if the sensitizing allergen is heat stable, pepsin resistant, or both, such as LTP[29,30] or celery proteins cross-reactive with mugwort pollen.[5,31,32] In contrast, in patients sensitized to labile vegetable food proteins, such as patients with birch pollen allergy, the consequences of the ingestion of allergenic foods are generally less dramatic and limited to OAS, although severe local reactions (eg, laryngeal edema, asthma, or both caused by direct contact with or inhalation of food particles) have been sometimes reported. Therefore a proper classification of patients with a history of allergy to plant-derived foods is of pivotal importance for the allergologist

TABLE I. Offending foods in different subgroups allergic to fruits and vegetables

				P value		
	A (n = 24)	B (n = 18)	C (n = 25)	A vs B	B vs C	A vs C
Apple	24 (100%)	7 (39%)	14 (56%)	<.001	NS	<.001
Pear	7 (29%)	4 (22%)	6 (24%)	NS	NS	NS
Peach	14 (58%)	8 (44%)	15 (60%)	NS	NS	NS
Cherry	14 (58%)	2 (11%)	7 (28%)	<.005	NS	NS
Plum	4 (17%)	2 (11%)	5 (20%)	NS	NS	NS
Apricot	7 (29%)	6 (33%)	7 (28%)	NS	NS	NS
Strawberry	2 (8%)	4 (22%)	5 (20%)	NS	NS	NS
Loquat	1 (4%)	1 (6%)	0 (0%)	NS	NS	NS
Almond	5 (21%)	1 (6%)	3 (12%)	NS	NS	NS
Any Rosaceae fruit	24 (100%)	12 (66%)	22 (88%)	<.01	NS	NS
Peanut	2 (8%)	0 (0%)	4 (16%)	NS	NS	NS
Hazelnut	14 (58%)	0 (0%)	7 (28%)	<.001	<.05	NS
Walnut	6 (25%)	5 (28%)	5 (20%)	NS	NS	NS
Chestnut	1 (4%)	0 (0%)	0 (0%)	NS	NS	NS
Pistachio	1 (4%)	0 (0%)	0 (0%)	NS	NS	NS
Celery	1 (4%)	1 (6%)	2 (8%)	NS	NS	NS
Carrot	4 (17%)	3 (17%)	3 (12%)	NS	NS	NS
Fennel	8 (33%)	4 (22%)	3 (12%)	NS	NS	NS
Orange	1 (4%)	6 (33%)	5 (20%)	<.05	NS	NS
Tangerine	0 (0%)	3 (17%)	1 (4%)	NS	NS	NS
Any citrus fruit	1 (4%)	7 (39%)	6 (24%)	<.025	NS	NS
Melon	0 (0%)	10 (56%)	16 (64%)	<.001	NS	<.001
Watermelon	0 (0%)	6 (33%)	8 (32%)	<.01	NS	<.01
Any gourd fruit	0 (0%)	12 (67%)	19 (76%)	<.001	NS	<.001
Banana	2 (8%)	12 (66%)	9 (36%)	<.001	NS	NS
Tomato	0 (0%)	6 (33%)	8 (32%)	<.01	NS	<.01
Kiwi	11 (46%)	8 (44%)	13 (52%)	NS	NS	NS
Fig	1 (4%)	1 (6%)	1 (4%)	NS	NS	NS
Onion	0 (0%)	0 (0%)	1 (4%)	NS	NS	NS
Coconut	0 (0%)	1 (6%)	0 (0%)	NS	NS	NS
Persimmon	0 (0%)	2 (11%)	0 (0%)	NS	NS	NS
Salad	1 (4%)	2 (11%)	1 (4%)	NS	NS	NS
Eggplant	1 (4%)	0 (0%)	2 (8%)	NS	NS	NS
Pineapple	0 (0%)	2 (11%)	2 (8%)	NS	NS	NS
Grapes	1 (4%)	1 (6%)	5 (20%)	NS	NS	NS

A, Positive Bet v 1/negative Bet v 2 results; *B,* negative Bet v 1/positive Bet v 2 results; *C,* positive Bet v 1/positive Bet v 2 results; *NS,* not significant.

TABLE II. Usefulness of clinical history of allergy to several plant-derived foods as a means to detect profilin sensitization

History	Sensitivity	Specificity	PPV	NPV
Gourd fruits	72%	89%	91%	69%
Citrus fruits	30%	96%	76%	78%
Tomato	33%	93%	68%	75%
Banana	49%	86%	74%	67%

because his or her advice to patients might change on the basis of allergens involved in adverse reactions. Unfortunately, the identification of the vegetable food allergens responsible for clinical symptoms is not an easy task in normal clinical settings. Purified food proteins (either natural or recombinant) for in vivo testing are presently not available, and because of their high cost, it seems unlikely they will come into routine use in the future. Immunoblot analysis is not used in routine practice, and IgE specific for rBet v 1 and rBet v 2 are measured only by a minority of laboratories. The aim of the present study was to detect some markers of sensitization to profilin that could be easily used during the daily practice. To this purpose, we selected a population of patients sensitized only to labile vegetable food allergens and excluded patients allergic to natural rubber latex or LTP on the basis of clinical history and SPTs,[17] respectively. As in most clinical settings, offending foods were identified by using careful interviews of patients and by using a standardized questionnaire, and sensitizations were subsequently confirmed by means of SPTs with fresh foodstuff, with commercial extracts, or with both. Open confirmative challenges with suspected foods were carried out only in a minority of patients reporting single episodes of OAS with particular foods. A preliminary classification of patients as possibly sensitized to profilin on the basis of vegetable food allergy associated with multiple skin reactivity to seasonal airborne allergens

proved very sensitive. We also confirmed that the sensitivity of the CAP assay to rBet v 2 as a means to detect profilin-hypersensitive patients is not always ideal[20] because it failed in 1 (2%) of 43 cases. The possible cosensitization to other minor allergens involved in the cross-reactivity phenomena was taken into account. In particular, we studied the IgE response against Bet v 5, a 35-kd birch allergen belonging to a family of isoflavone reductase proteins involved in cross-sensitization to allergens from lychee, mango, banana, orange, apple, pear, and carrot[23-25]; Bet v 6, another minor birch pollen allergen causing cross-sensitization to homologous allergens in apple, pear, peach, orange, lychee, strawberry, persimmon, zucchini, and carrot[26]; and/or the pectin esterase Bet v 8, which was recently identified as a further cross-sensitizing allergen in birch, grass, and mugwort pollen, as well as in peanut, celery, and apple.[27] Patients sensitized and not sensitized to the 30- to 40-kd and 60- to 90-kd enriched fractions of birch pollen did not show any difference in offending foods, thus suggesting that sensitization to these novel cross-reacting allergens did not influence the results of the present study. The clinical relevance of sensitization to these proteins remains undefined.

Analysis of offending foods in different groups of patients sensitized to Bet v 1, Bet v 2, or both showed a strong association between profilin hypersensitivity and clinical allergy to melon, watermelon, citrus fruits, tomato, and banana. A history of allergy to these fruits showed both a high specificity and a high PPV for profilin sensitization. As far as we know, these plant-derived foods have been rarely reported to cause allergic reactions in patients other than those sensitized to profilin or those with the latex fruit syndrome. Clinical allergy to melon, watermelon, and banana was first reported in subjects hypersensitive to ragweed pollen.[33,34] Unfortunately, no further details about skin reactivity of allergic patients to other pollens, such as birch, grass, or mugwort, were given in those studies, and cross-reacting allergens were not characterized. More recent observations that watermelon allergens cross-react with cucumber and Apiaceae foods[35] and that most patients with melon allergy have clinical pollinosis and are allergic to watermelon, avocado, kiwi, banana, chestnut, and peach,[36] represent an indirect evidence of a possible role of profilin in allergic reactions to these foods. Furthermore, a recent study reported a case of allergy to melon that healed after subcutaneous administration of grass pollen and ragweed-mugwort pollen extracts.[37] An association between profilin sensitization and banana allergy has been recently reported,[38] and tomato allergy was first reported in children with grass pollinosis.[39] Subsequent studies demonstrated that profilin is the relevant cross-reacting allergen in patients with tomato allergy.[13] Few data exist about allergies to citrus fruits. Ortolani et al[40,41] reported that positive SPT responses with orange is frequent among patients allergic to pollen, particularly grass. Subsequently, the same group observed that approximately 70% of patients with orange allergy showed IgE reactivity to a 14-kd protein, most probably profilin, on immunoblot analysis.[42] Several other fruits and vegetables have been reported to trigger allergic symptoms in patients sensitized to profilin. However, some of them, such as Apiaceae,[8,38,43] hazelnut,[9] and Rosaceae,[3,11] are not sufficiently specific to be used as clinical markers of profilin sensitivity, whereas others, including pumpkin seeds,[14] zucchini,[44] lychee,[12] pineapple,[38] and persimmon,[45] are more rarely eaten or cause symptoms only in a minority of patients with profilin allergy. Nonetheless, all patients with a clinical history of pineapple and persimmon intolerance in this study were profilin reactors. We are not able to confirm or confute the conclusions of previous studies suggesting that profilin has limited clinical relevance[15,16] because this work was not designed to detect the prevalence of food allergies among subjects sensitized to this protein. We showed that sensitization to profilin is very likely in the presence of OAS to citrus fruit, the gourd family, banana, and/or tomato. Although some variability in dietary habits might exist between different countries, our findings suggest that, at least in patients sensitized to labile vegetable food allergens, allergy to these fruits might be used by clinical allergologists as a marker of profilin hypersensitivity in all settings in which laboratory investigations are not easily accessible.

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