Research Article

Pru p 7 predicts severe reactions after ingestion of peach in Japanese children and adolescents

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Short Title: Pru p 7 predicts severe peach allergy

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Abstract

Introduction: Component resolved diagnostics is used to diagnose food allergies. However, few reports have evaluated the severity of peach fruit allergy using peach allergen components, including Pru p 7.

Objective: This study aimed to predict peach fruit allergy severity based on the presence of specific IgE (sIgE) antibodies to peach allergenic components.

Methods: Twenty-seven patients with peach fruit allergy were enrolled and classified into two groups: the local reaction (LR) group, including 12 patients with only oral or throat mucosal symptoms, and the systemic reaction (SR) group, including 15 patients 10 of whom experienced anaphylaxis. Serum sIgE antibodies against crude peach extract; Pru p 1, 2, 3, 4, and 7; and tree pollen were measured.

Results: sIgE Ab titers of Pru p 1 and 4 and alder pollen in the LR group were significantly higher than those in the SR group. sIgE against Pru p 7 was significantly higher in the SR group than in the LR group. The frequencies of sIgE Abs against Pru p 1, 4, and 7 in the LR group were 91.7%, 66.7%, and 16.7%, respectively, while in the SR group, these were 80%, 20%, and 60%. Sensitization to Pru p 2 and 3 was detected but limited in all patients.

Conclusions: These findings suggest that sensitization to Pru p 1 and Pru p 4 is associated with local symptoms, and sensitization to Pru p 7 is associated with systemic reaction and anaphylaxis. To predict the severity of peach fruit allergy, it is useful to assess sIgE Ab reactions combining Pru p 1, 4, and 7.

Introduction

Peach (*Prunus persica*) fruit allergy is frequently encountered in pediatric outpatient clinics. Peaches are one of the common causes of fruit allergy in Japan and Western countries [1]. Component-resolved diagnostics (CRD) is a diagnostic approach that defines allergen sensitization of patients at the molecular level [2]. Moreover, reports using CRD to assess peach allergies are increasing [2]. In recent years, four types of peach allergies have been reported according to sensitizing allergen components. One well-known type of peach fruit allergy is pollen-food allergy syndrome (PFAS), which develops due to cross-reactivity and sensitization to Bet v 1, a major allergen from birch pollen. Bet v 1 is one of the pathogenesis-related protein-10 (PR-10) components with cross-reactivity to the peach homolog Pru p 1. PFAS can also develop due to another allergen, fruit profilin (Pru p 4), which has cross-reactivity to profilins from tree, grass, and weed pollen. The third type of reaction is non-pollen-related peach fruit allergy due to sensitization to lipid transfer protein (LTP). Pru p 3 is one LTP homolog found in peaches. This type is frequently reported in the Mediterranean area and is associated with severe clinical symptoms. The fourth type of reaction is a peach fruit allergy caused by the gibberellin-regulated protein (GRP) Pru p 7. Pru p 7 was first reported by Tuppo, et al. in 2013 and is related to severe allergic reactions, similar to those of LTP [1, 3]. Therefore, laboratory tests for Pru p 7-specific IgE (sIgE) are important for predicting severe allergic symptoms. Recently, it was reported that GRP from Cupressaceae pollen might be a primary sensitizer for peach fruit allergy [4]. Moreover, in Southern Europe, patients with a cypress pollen allergy frequently have a concomitant peach fruit allergy [4]. Additionally, Pru p 2, a thaumatin-like protein (TLP; PR-5), has been reported to be one of the allergens responsible in PFAS [5]. TLP is also present in Cupressaceae pollens. Pru p 9, PR-1, has recently been identified as an allergen component of peach pollen. Pru p 9 has been reported to exhibit symptoms such as bronchial asthma and rhinitis [6].

However, reports are limited regarding sIgE Ab development and reaction to these five peach allergen components in children and adolescents with peach fruit allergy. Our aim was to predict the severity of peach fruit allergy by measuring sIgE sensitivity to the peach-allergen components Pru p 1, Pru p 2, Pru p 3, Pru p 4, and Pru p 7 using standard and experimental ImmunoCAP tests and to investigate the relationship between these components and tree pollen sensitization.

Materials and Methods

Patients

Twenty-seven consecutive patients diagnosed with a peach fruit allergy at the Department of Pediatrics, Dokkyo Medical University Hospital between October 2012 and September 2017 were enrolled in the present study. Diagnosis was made on the basis of a convincing history of allergic reactions within 2 h after ingesting peach and the presence of sIgE Abs to crude peach extract (>0.1 UA/mL) in the sera of patients. This study was approved by the Ethical Review Board of Dokkyo Medical University.

Patient groups and symptoms

The patients were classified into two groups according to their symptoms following the ingestion of peach: the local reaction (LR) only group, and the systemic reaction (SR) group. Local reactions consisted of only mucosal symptoms, which included oral itching, pharyngeal itching, and/or angioedema of the lips. Systemic reactions consisted of itching or urticaria, cough, dyspnea, and/or vomiting [7]. We defined anaphylaxis as two or more of the following symptoms that occurred rapidly after the ingestion of peach: involvement of the skin-mucosal tissue (e.g., generalized hives, itching and skin flushing, and angioedema of the lips), respiratory compromise (e.g., coughing,

dyspnea, wheezing and bronchospasm, stridor, and reduced peak expiratory flow or hypoxemia), reduced blood pressure or associated symptoms (e.g., hypotonia [collapse], syncope or incontinence), and persistent gastrointestinal symptoms (e.g., crampy abdominal pain or vomiting) [8].

Serum-specific IgE sensitivity measurements by ImmunoCAP

The specific IgE values to commercially available crude peach extract, Pru p 1, Pru p 3, Pru p 4, and Japanese cedar and alder pollen were measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). For measurement of the sensitivity of sIgE Abs to recombinant Pru p 2 produced by insect cells or native Pru p 7 purified from peach pulp according to the methods developed by Tuppo, et al. [3], the allergens were immobilized on an experimental ImmunoCAP. The cut-off value for sensitization was set at >0.35 UA/mL. Since Pru p 9 is an allergenic component of peach pollen, it was not measured because it was not related to this peach fruit allergy.

Statistical analysis

For the analysis, sIgE Ab levels below the lower limit of quantitation (<0.10 UA/mL) were assigned a value of 0.09 UA/mL for statistical calculations, while sIgE Ab levels over the higher limit of quantitation (>100 UA/mL) were assigned a value of 101 UA/mL. Statistical analysis was performed using SPSS version 25 (IBM Corp. in 2015 Armonk, NY, USA). Data were compared using Mann-Whitney U tests. Using a receiver operating characteristic (ROC) curve, the cutoff values that Pru p 1, Pru p 4, and Pru p 7 were classified into the LR and the SR group were calculated. $P < 0.05$ was considered statistically significant.

Results

Patient groups

Twenty-seven patients were enrolled in this study. The median age at the time of blood sampling was 13 years (range, 7-20 years). All patients had pollinosis. The LR group consisted of 12 patients (age range, 7-20; median age, 13.5; 8 were males). The SR group consisted of 15 patients (age range, 9-19; median age, 13.0; 8 were males). There were no differences in baseline characteristics between the LR and SR groups in terms of blood sampling, age, and sex (Table 1). However, the number of causative plant food allergens in the LR group was significantly higher than that in the SR group.

Allergy symptoms

Among the 27 patients, oropharyngeal symptoms were seen most frequently, appearing in 17 patients (17/27, 63%). Systemic urticaria and dyspnea were seen in eight patients (8/27, 30%), followed by facial edema, conjunctival injection, and systemic pruritus, which were each observed in 3 patients (3/27, 11%) (Table 1, Table 2).

All patients in the LR group experienced oropharyngeal symptoms. Angioedema of the lips was only reported in one patient. The symptoms seen in the SR group included systemic urticaria in eight cases (8/15, 53%), dyspnea in eight cases (8/15, 53%), and oropharyngeal symptoms in five cases (5/15, 33%). Overall, 10 patients (10/15, 67%) developed anaphylactic reactions (Table 2); for these patients, the most common symptom other than skin and mucosal symptoms was dyspnea (8/10, 80%), and two patients experienced a cough (2/10, 20%). Only one patient experienced vomiting. Exercise was a cofactor in the eight patients who experienced anaphylaxis (Table 1).

Sensitization rate to peach and tree pollen allergens

Sensitization rates to Pru p 1, Pru p 4, and Grey alder in the LR group were significantly higher than those in the SR group, while the sensitization rates to Pru p 7 in the SR group were significantly higher than those in the LR group. There were no differences noted in the sensitization rates of crude peach extract and Japanese cedar between the two groups (Figure 1, Figure 2). Pru p 3 was positive in 3 cases in the LR group and 1 case in the SR group. It was low in 14% (4/27) of all cases.

Analysis using ROC curve

Using a receiver operating characteristic (ROC) curve, the cut-off value for diagnosing the LR and the SR groups was calculated. Pru p 1 (Area under the curve; AUC 0.856) and Pru p 4 (AUC 0.794) were useful for diagnosis of the LR group (Figure 3-A). The cutoff value for Pru p 1 was 35.1 IU / ml, the sensitivity was 66.7%, and the specificity was 86.7%. The cutoff value of Pru p 4 was 1.92 IU / ml, the sensitivity was 58.3%, and the specificity was 93.3%. On the other hand, Pru p 7 (AUC 0.894) was useful for diagnosis of the SR group (Figure 3-B). The cutoff value of Pru p 7 was 0.102 IU / ml, the sensitivity was 86.7%, and the specificity was 83.3%.

Combination with multiple components

We examined whether allergy severity could be evaluated by combining the peach allergen components of Pru p 1, Pru p 4, and Pru p 7, which resulted in significant differences (Figure 1) between the LR and SR groups. When Pru p 7 was negative, and either Pru p 1 or Pru p 4 was positive (LR group, 10 patients; SR group, 2 patients), none of the 12 patients experienced anaphylaxis. When Pru p 7 was positive, and either Pru p 1 or Pru p 4 was negative (LR group, none; SR group, 12 patients), there were 9 cases of anaphylaxis out of 12.

Discussion/Conclusion

In the present study, sIgE Abs to the allergen components related to peach fruit allergy registered in the WHO/IUIS allergen nomenclature (available at http://allergen.org/) were measured in the sera of children and adolescents diagnosed with peach fruit allergy. Pru p 9, present in peach pollen has been reported. However, this was a study on peach fruit allergy and this component has not been measured previously. The results were compared to allergic symptoms after ingestion of peach and the sIgE Ab concentration to major tree pollen allergens in Japan. Sensitization to Pru p 1, Pru p 4, and alder pollen were associated with oral allergy symptoms (the LR group) as has been shown in previous reports [1]. In recent years, the number of children sensitized to alder pollen has been increasing, and we see many children with PFAS in our outpatient clinic. Alder pollen and birch pollen sIgE antibodies are highly correlated [9]. Patients with birch pollinosis have allergic symptoms due to the Rosaceae family of fruits such as apples and peaches [10]. Alder pollen might be the primary sensitizer to PR-10 and/or profilin in peach fruit allergy patients experiencing oral symptoms.

The cut-off value of Prup7-specific IgE was very low.If Prup7 is detected, it is thought that it can be diagnosed as an SR group, so we think that it is possible to distinguish between local and systemic responses by combining three components to improve diagnostic accuracy. In the SR group, 80% of patients were sensitized to Pru p 7; however, only two (17%) were sensitized to this component in the LR group, and these patients had low sIgE Ab titers. We, therefore, suggest that, when Pru p 7 is negative, and either Pru p 1 or Pru p 4 is positive, there is a high possibility for a local reaction. We also found that, when Pru p 7 was positive and either Pru p 1 or Pru p 4 were positive, there was a high possibility of anaphylaxis. Only one patient with Pru p 3 (LTP) developed sensitization in the anaphylaxis group. The reason that LTP was less sensitized as compared to sensitization of Pru p 7 may have been due to a difference in eating habits and the distribution of allergens in peaches rather than differences in peach cultivars [1]. It has been observed that Pru p 7 is distributed in both peach peel and pulp; however, Pru p 3 is localized in the peach peel [1,3]. Most Japanese individuals eat

peeled peaches and, therefore, they do not ingest the LTP that is found in the peel. However, in Western countries it has been suggested that there is LTP sensitization when peaches are eaten unpeeled [1]. Ebisawa et al. reported the sensitization of Ara h 9, as peanut LTP, which was also less common in Japan [11]. Meanwhile, in China, Ma et al. reported that the sensitization component of peanut allergy patients was mainly Ara h 9 [12]. Most of these patients were sensitized to mugwort pollen, and many suffered from peach allergies. This fact is very similar to Mediterranean sensitization [13]. There are mugworts in Japan, but there are many types of mugworts; and it is possible that there are different types of mugworts.

Tuppo, et al. reported that peamaclein (Pru p 7) was a new marker in 2013 [3]. Next year, Inomata et al. reported that Pru p 7 was related to systemic reactions [1]. In a reported by Tuppo, et al., 14 patients (mean age, 26.0 years; range: 5-45 years) showed a positive response to purified Pru p 7 by skin prick tests (SPTs). Of the 14 patients, two (14.3%) presented with anaphylaxis. One of these had positive sIgE Abs only to Pru p 7, while the other was positive to both Pru p 3 and Pru p 7 [3]. Inomata, et al. reported that 64.3% of 14 patients with systemic reactions to peach (mean age, 32.0 years; range: 7-55 years) had sIgE to purified Pru p 7, and that GRP sensitization was frequently seen in patients with facial edema, laryngeal tightness, and food-dependent exercise-induced anaphylaxis (FDEIA) [1,14]. In our study, laryngeal symptoms (4/15, 27%), FDEIA (8/15, 53%), and anaphylaxis (10/15, 67%) were seen in Pru p 7-sensitized patients.

In southern Europe, patients with a cypress allergy frequently had peach fruit allergy [4]. Recently, it was reported that Cupressaceae (Cupressus sempervirens) pollen might be a primary sensitizer of peach and citrus allergies [15]. All patients in our study were strongly sensitized to Japanese cedar pollen. Furthermore, there was no significant difference in the sensitization rate and sIgE Ab titers to Japanese cedar pollen between the LR and SR groups. Therefore, we could not confirm that

189 sensitization to Pru p 7 was caused by Cupressaceae pollen. Studies regarding other types of
190 Cupressaceae pollen (Chamaecyparis obtuse, Juniperus chinensis) would help supplement the
191 findings of the current research. As Pru p 7 is resistant to heat and digestion, sensitization of Pru p 7
192 might be via the gastrointestinal tract [16].

193

194 Sensitization to Pru p 2 and Pru p 3 was low in both the LR and SR groups. Several reports from Japan
195 have shown a low frequency of LTP sensitization in patients with plant food allergy, and our results
196 confirm this [1]. There is currently limited research on TLP sensitization in Japan. However, TLP from
197 Japanese cedar pollen (Cry j 3) has been characterized, and it was found that 27% of patients with
198 Japanese cedar pollinosis were sensitized to Cry j 3 [17]. Furthermore, the cross-reactivity between
199 Cry j 3 and Pru p 2 might be low, because patients in both the LR and SR groups were strongly
200 sensitized to Japanese cedar pollen. However, further studies on the role of Pru p 2 in peach allergies
201 are needed.

202

203 We also found that sIgE Ab levels to Pru p 1, Pru p 4, and Pru p 7 were relatively higher than those to
204 crude peach extract. Two patients had sIgE Abs <0.35 UA/ml to crude extract; however, their sIgE Abs
205 to allergen components were positive with respect to the cut-off for sensitization (Pru p 4, 1.06
206 UA/mL; Pru p 7, 0.45 UA/mL). Thus, using peach allergen components for measuring sIgE Abs can be
207 more sensitive than using crude peach extract alone.

208

209 There is a limitation to this study. Ideally, diagnoses should be confirmed by oral food challenge.
210 However, we performed oral food challenge tests only in some cases. Although it is a verification tool
211 used to assess adult patients, according to the diagnostic algorithm developed by Skypala, et al., it is
212 possible to diagnose PFAS using a diagnostic questionnaire [18]. Our patients were children and

adolescents; however, it is possible that this algorithm could be applied to the LR group. In the SR group, if the peach-allergic patients were experiencing severe symptoms such as anaphylaxis, it was difficult to perform oral food challenge tests. Roberts reported that, if a patient has a history of adverse reactions to a particular food, the possibility that the food is the allergen is approximately 50%, and, if a patient has a history of three similar adverse reactions to a particular food, the possibility that the food is the allergen rises to approximately 100% [19]. The number of inductions in the SR group was 1.9 on average, and most patients had a history of two or more allergic symptoms. The number of our cases is small, and we plan to expand this number and re-examine the current cases.

To conclude, we demonstrated that CRD with Pru p 1, Pru p 4, and Pru p 7 in combination can be useful for predicting the severity of peach fruit allergy in children and adolescents. Sensitization to Pru p 7 might predict severe allergic reactions after ingestion of peach, especially anaphylaxis, when exercise is a cofactor. There is cross-reactivity within the GRP family among fruits (Rosaceae, Rutaceae) and vegetables. Therefore, patients who are sensitized to Pru p 7 should also consider other fruits and vegetables as potential causative allergens and be aware that exercise and other cofactors may cause anaphylaxis after peach consumption. We suggest, therefore, that this awareness in patients/guardians and medical personal, as well as the extended testing described above, may help to prevent allergic reactions, especially severe reactions such as anaphylaxis.

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Statement of Ethics

This study was approved by the Ethical Review Board of Dokkyo Medical University(R-7-22). This study design and risks were fully explained to patients and their guardians, informed consent was obtained from all participants prior to their enrollment.

Disclosure Statement

We have no conflicts of interest directly relevant to the content of this article.

Author Contributions

Authors' contributions: Y.A. and S.Y. designed this study; Y.A. performed statistical analyses and drafted the manuscript; S.Y. supervised the project; all authors collected cases, contributed to, and approved the final draft for publication.

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Figure Legends

Fig. 1. Comparison of sIgE between the LR and SR groups.

These figures show Box plots of sIgE levels. The LR and SR groups were compared for sIgE concentrations to peach and peach-allergen components. All sIgE Ab sensitivities were measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). Pru p 1 (B) showed significantly higher values in the LR group than in the SR group. Pru p 4 (E) showed significantly higher values in the LR group than in the SR group. Pru p 7 (F) showed significantly higher values in the SR group than in the LR group.

**: $p<0.01$; n.s.: not significant

Abbreviations: LR, local reaction; SR, systematic reaction; sIgE, specific IgE antibodies.

Fig. 2. Comparison of pollen sIgE between the LR and SR groups.

These figures show Box plots of sIgE levels. The LR and SR groups were compared for Japanese cedar (A) and Grey alder (B) pollen sIgE. All sIgE Ab sensitivities were measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). Grey alder (B) showed significantly higher sIgE values in the LR group than in the SR group.

*: $p<0.05$; n.s.: not significant

Abbreviations: LR, local reaction; SR, systematic reaction; sIgE, specific IgE antibodies.

Fig.3. Receiver operating characteristic (ROC) curve for Pru p 1, Pru p 4 and Pru p 7- sIgE.

(A) Only LR group patients

(B) Only SR group patients

Abbreviations: LR, local reaction; SR, systematic reaction; sIgE, specific IgE antibodies.

Table 1. Characteristics of the local reaction and systemic reaction groups

	All patients		Local reaction group		Systemic reaction group		p-value
Patients, n	27		12		15		
Age (yrs), mean (range)	13	(7-20)	13.5	(7-20)	13	(9-19)	0.492
Sex, female, n (%)	16	(59)	8	(67)	8	(53)	0.641
Pollinosis, n(%)	27	(100)	12	(100)	15	(100)	
Peach allergy reactions, n (%)							
Oropharyngeal symptoms	18	(63)	12	(100)	6	(40)	
Lip edema	2	(7)	1	(8)	1	(7)	
Facial edema	3	(11)			3	(20)	
Conjunctival injection	3	(11)			3	(20)	
Ear pruritus	1	(4)			1	(7)	
Facial urticaria	1	(4)			1	(7)	
Systemic pruritus	3	(11)			3	(20)	
Systemic urticaria	8	(30)			8	(53)	
Coughing	2	(7)			2	(13)	
Dyspnea	8	(30)			8	(53)	
Vomiting	1	(4)			1	(7)	
Co-factor, n (%)							
Exercise					8	(53)	

Table 2. All patient characteristics and serum-specific IgE sensitization outcomes

Patient no.	Group	Age (year)	sex	†Symptoms (peach)	Anaphylaxis	Cofactor	Pollinosis	sIgE (UA/ml)								Reported food allergens to other plant food
								Peach	Pru p 1	Pru p 2	Pru p 3	Pru p 4	Pru p 7	Japanese cedar	Grey alder	
1	LR	20	M	Os,El	-	none	+	0.82	3.53	<0.1	0.85	2.79	<0.1	18.4	6.71	cherries, grapefruit, dekopon, watermelon, melon, wheat
2	LR	7	M	Os	-	none	+	21.2	45.9	<0.1	<0.1	<0.1	<0.1	75.8	43.3	apple
3	LR	14	F	Os	-	none	+	2.52	20.1	<0.1	0.30	<0.1	<0.1	100≦	24.6	orange, kiwi, pineapple, watermelon, melon, corn
4	LR	15	F	Os	-	none	+	18.8	65.8	<0.1	<0.1	<0.1	<0.1	100≦	100≦	apple, pear, cherries, strawberry, melon, bean sprouts, soy
5	LR	13	M	Os	-	none	+	4.10	42.6	<0.1	<0.1	7.31	<0.1	100≦	49.4	melon
6	LR	10	M	Os	-	none	+	18.7	44.6	0.87	<0.1	18.8	<0.1	100≦	NT	pear, banana, melon, bean sprouts, cucumber, nuts, buckwheat
7	LR	9	M	Os	-	none	+	46.1	>100	<0.1	<0.1	15.5	<0.1	100≦	100≦	apple, orange, strawberry, banana, kiwi, pineapple, melon, persimmon
8	LR	15	F	Os	-	none	+	1.44	8.19	<0.1	0.13	<0.1	<0.1	100≦	11.9	apple, kiwi, pineapple
9	LR	16	F	Os	-	none	+	0.33	0.14	0.31	<0.1	1.06	<0.1	100≦	2.69	apple, orange, grapefruit, strawberry, kiwi, pineapple, watermelon, papaya, tomato, bamboo shoots
10	LR	8	M	Os	-	none	+	71.8	>100	0.85	0.60	7.81	0.92	100≦	100≦	strawberry, pineapple
11	LR	16	M	Os	-	none	+	19.7	87.4	0.26	6.99	3.34	0.48	100≦	100≦	avocado, nuts, buckwheat
12	LR	13	M	Os	-	none	+	21.6	>100	0.17	0.28	4.00	<0.1	95	100≦	apple, strawberry, banana, kiwi, watermelon, melon, tomato
13	SR	14	M	Os,El,Uf	-	none	+	24.8	27.9	0.32	0.16	7.79	<0.1	NT	98.1	apple, kiwi, watermelon, peanuts, nuts
14	SR	12	F	Pe,Os	-	none	+	10.9	42.39	<0.1	0.55	<0.1	<0.1	100≦	40.2	eggplant
15	SR	14	M	Os,Ps,Ci	-	none	+	5.62	7.88	<0.1	<0.1	<0.1	2.71	88.7	NT	none
16	SR	13	M	Os,Ps	-	none	+	5.81	16.54	<0.1	<0.1	<0.1	1.79	100≦	60.9	apple, pear, kiwi

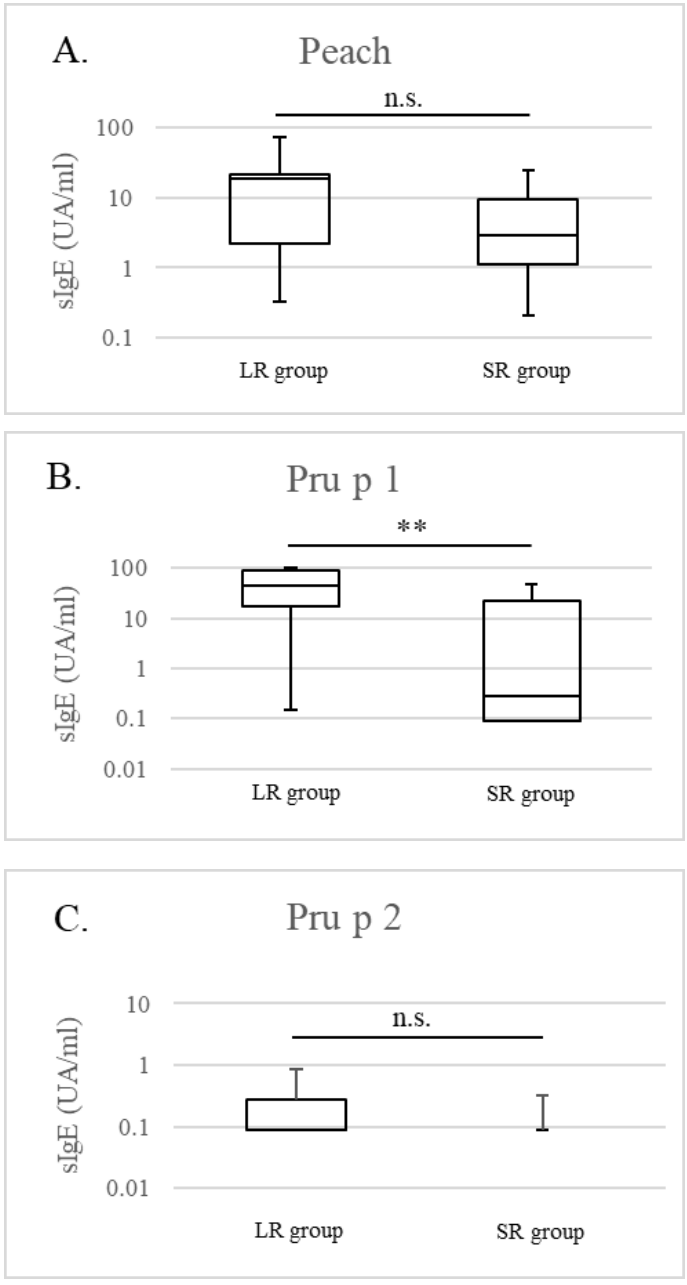
17	SR	13	F	Us,Ef	-	none	+	0.43	<0.1	<0.1	0.22	<0.1	1.13	100≦	0.41	apple, orange, kiwi
18	SR	13	F	Os,Dy	+	none	+	1.31	1.14	<0.1	<0.1	<0.1	6.72	31.9	1.74	cherries, strawberry, Japanese apricot
19	SR	14	F	Os,Us,Co,Dy	+	none	+	2.95	<0.1	0.10	0.65	<0.1	0.12	100≦	4.30	sweet potato
20	SR	9	M	Ci,Ef,Dy	+	exercise	+	0.96	<0.1	<0.1	NT	<0.1	8.20	100≦	0.34	orange, grapefruit, melon
21	SR	9	F	Ps,Dy	+	exercise	+	2.02	0.29	0.15	0.13	<0.1	6.44	100≦	1.25	grapefruit
22	SR	11	M	Us,Ef,Co	+	exercise	+	2.34	<0.1	<0.1	<0.1	<0.1	12.2	100≦	0.13	none
23	SR	12	F	Us,Ci,Vo	+	exercise	+	17	48.5	<0.1	<0.1	<0.1	19.8	NT	100≦	pear, cherries, strawberry, banana, kiwi, tomato, soy, spinach
24	SR	12	M	Us,Dy	+	exercise	+	8.02	<0.1	<0.1	<0.1	<0.1	12.1	100≦	2.98	none
25	SR	16	F	Us,Dy	+	exercise	+	0.42	<0.1	<0.1	<0.1	<0.1	0.76	30.2	<0.1	apple, cherries, orange, grapefruit, strawberry
26	SR	19	M	Us,Dy	+	exercise	+	0.21	<0.1	<0.1	<0.1	<0.1	0.45	15.4	0.19	orange, grapefruit, watermelon, eggplant
27	SR	11	M	Us,Dy	+	exercise	+	20.4	27.2	<0.1	<0.1	<0.1	24.5	100≦	100≦	loquat, Japanese apricot

†Symptoms are patient-reported.

Abbreviations: Os, Oropharyngeal symptoms; El, Lip edema; Ef, Facial edema; Ci, Conjunctival injection; Pe, ears pruritus; Pf, facial pruritus; Uf, facial urticaria; Ps, systemic pruritus; Us, systemic urticaria; Co, Coughing; Dy, Dyspnea; Vo, Vomiting;

NT: not tested.

Figure 1. Comparison of specific IgE between the LR and SR groups



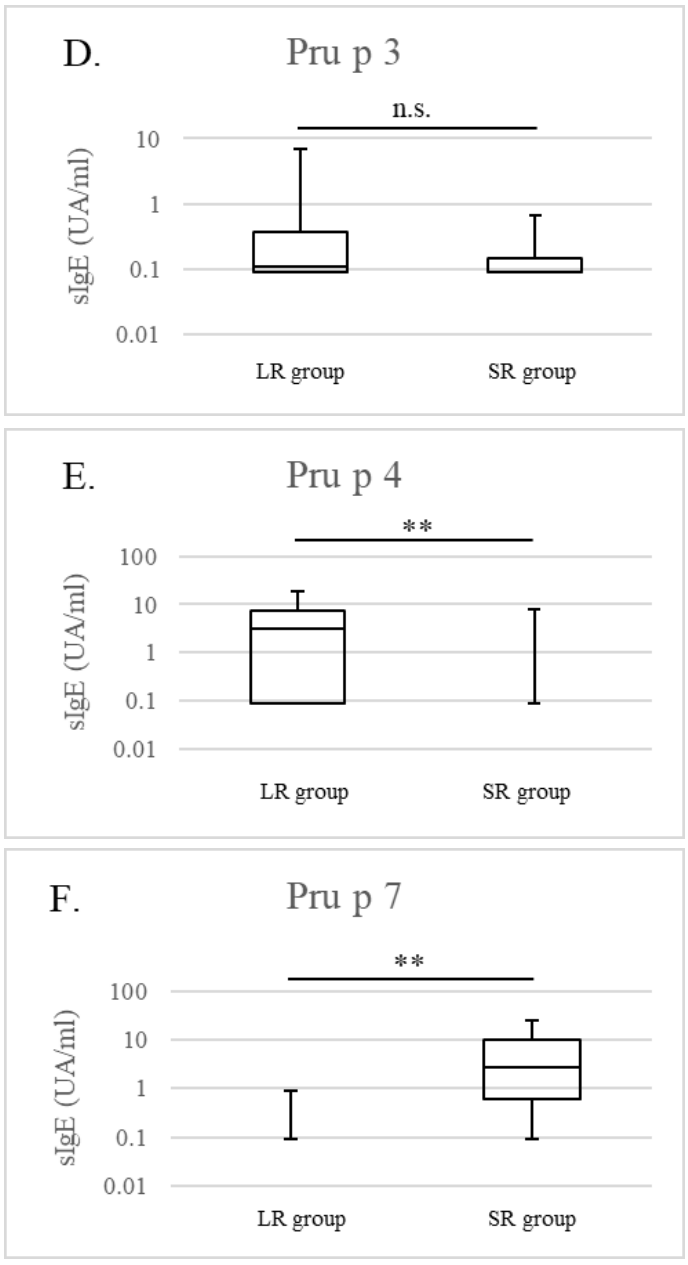

D.
Pru p 3
n.s.
sIgE (UA/ml)
10
1
0.1
0.01
LR group
SR group
E.
Pru p 4
**
sIgE (UA/ml)
100
10
1
0.1
0.01
LR group
SR group
F.
Pru p 7
**
sIgE (UA/ml)
100
10
1
0.1
0.01
LR group
SR group

Figure 2. Comparison of pollen-specific IgE between the LR and SR groups

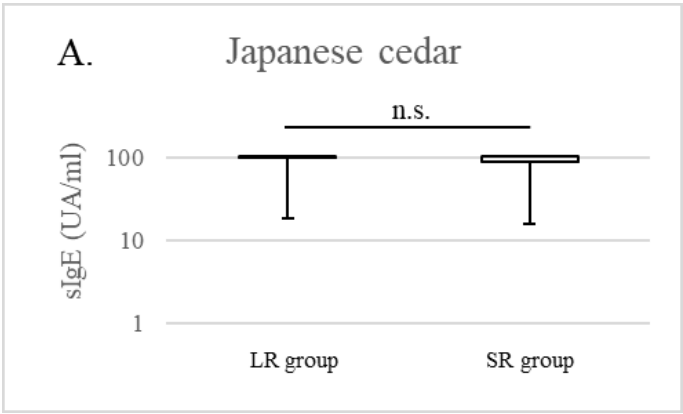


Figure 3. Receiver operating characteristic (ROC) curve for Pru p 1, Pru p 4 and Pru p 7-specific IgE.