

IgE component-resolved allergen profile and clinical symptoms in soy and peanut allergic patients

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Component-resolved diagnostics (CRD), evaluating the IgE profile of individual allergens, provides deepened insight into diagnosis of food allergy, as recently

described for peanut allergy in children (1). In soy-allergic patients, the soy seed storage allergens Gly m 5 and Gly m 6 have been associated with severe allergic reactions (2), while the clinical importance of the major soy allergen Gly m 4 is debated (3, 4). Although individual soy and peanut allergens share sequence homology and serological cross-reactivity, few studies exist on soy 2S albumins even though related 2S albumins from peanut (Ara h 2/6/7) are implicated as clinically important allergens.

The goal of this study was to determine if CRD could better predict the clinical relevance of specific allergens

inducing IgE sensitization to soy, in peanut and/or soy allergic patients.

The medical records of patients seen at an allergy clinic (APA, Arnhem, the Netherlands) over the past 4 years were digitally screened for a clear medical history of anaphylactic reactions to peanut and/or soy. Of these, all adult patients with a positive skin prick test to commercial peanut and/or soy extract (ALK-Abelló, Nieuwegein, the Netherlands) and a positive specific IgE test to peanut and/or soy (Phadia ImmunoCAP, Uppsala, Sweden) and/or a positive allergen provocation test were selected for inclusion ($n = 60$). After informed consent, 20 patients volunteered to participate in this study. IgE levels to peanut, soy and pea extract, rAra h 1, 2, 3 and 8 from peanut, rGly m 4, nGly m 5, nGly m 6 and 2S from soy (kind gifts of Sigrid Sjölander, Phadia, Uppsala, Sweden), rBet v 1 from birch and cross-reactive carbohydrate determinants (CCD) were determined by ImmunoCAP (Table 1).

Most (6/8) soy allergic patients had no specific IgE to soy extract or nGly m 5 and 6, but all patients showed IgE to rGly m 4 and four to soy 2S. Most (7/11) peanut, but clinically non-soy allergic patients, tested serologically positive for soy extract and for nGly m 5 and 6. IgE levels to peanut and soy extract were strongly correlated (Pearson $r = 0.924$, $P < 0.001$); and similar results were obtained for pea ($r = 0.821$, $P < 0.001$, data not shown). rGly m 4 was positive in four of the peanut allergic patients and its levels correlated in both soy and peanut allergic patients with IgE levels to rAra h 8 ($r = 0.917$, $P < 0.001$) and rBet v 1 ($r = 0.940$, $P < 0.001$). Cross-reactive carbohydrate determinants sensitization was negative for all patients

except one (data not shown), which excludes the presence of cross-reactive IgE to legumes and grass pollen CCD.

Only rGly m 4 IgE levels were positive in all included soy allergic patients, which suggests rGly m 4 sensitization to be a valid indicator of severe soy allergy probably mediated by IgE cross-reactivity with Bet v 1 (5). Thus Gly m 4 seems to be more relevant in detecting clinical soy allergy than nGly m 5, m 6, soy 2S or total soy extract. However, we cannot exclude a different soy sensitization profile in other countries. In our peanut allergic patients IgE sensitization to soy and pea extract was found to have low diagnostic specificity probably because of clinically non-relevant cross-reactivity between peanut specific IgE and homologous soy or pea components. Even a positive rGly m 4 test in peanut allergic patients could be clinically non-relevant as seen in 4 of 12 peanut allergic patients.

In conclusion, soy CRD seems to discriminate between solely soy allergic patients and soy and/or peanut allergic patients. However, especially in peanut allergic patients with IgE to Gly m 4, a soy challenge test is still indicated to confirm a clinically relevant soy allergy.

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Table 1 Clinical features and immunological findings of the peanut and/or soy allergic patients

Age/ sex	Sympt. (grade); SPT (-/+/+)		Specific IgE to extracts (kU/l)		Specific IgE to recombinant peanut allergens (kU/l (Percentage of total))				Specific IgE to soy allergens (kU/l)					Severity hay fever (-/+/+)		
	Peanut	Soy	Peanut (f13)	Soy (f14)	rAra h 1 (f422)*	rAra h 2 (f423)†	rAra h 3 (f424)‡	rAra h 8 (f352)\$	rGly m 4 (f353)\$	nGly m 5 (f431)*	nGly m 6 (f432)‡	Soy 2S (f2s)†	rBet v 1 (t215)\$	Tree pollen	Grass pollen	
Peanut allergic patients																
1	20/f	1; ++	0; nd	17.6	0.74	7.26 (43)	8.19 (48)	1.44 (9)	<0.35 (0)	<0.35	0.98	0.4	<0.35	<0.35	-	-
2	18/f	1/2; +	0; -	4.75	<0.35	2.32 (36)	4.21 (64)	<0.35 (0)	<0.35 (0)	nd	nd	nd	<0.35	0.72	+	+
3	25/m	2; ++	0; nd	33.2	0.61	6.34 (27)	11.5 (49)	5.65 (24)	<0.35 (0)	0.47	0.85	<0.35	<0.35	1.77	++	++
4	22/f	2/3; ++	0; nd	33.6	1.13	9.42 (34)	16.3 (58)	2.17 (8)	<0.35 (0)	0.73	1.63	<0.35	0.58	0.59	++	-
5	23/m	3; ++	0; -	8.59	<0.35	5.09 (76)	1.57 (24)	<0.35 (0)	<0.35 (0)	<0.35	<0.35	<0.35	<0.35	2.77	+	-
6	24/f	3; ++	0; nd	79.6	7.32	43.8 (60)	20.4 (28)	9.38 (13)	<0.35 (0)	6.42	5.32	<0.35	0.59	<0.35	+	++
7	27/m	3; ++	0; +	16	<0.35	5.45 (44)	5.13 (41)	1.92 (15)	<0.35 (0)	<0.35	0.36	<0.35	<0.35	<0.35	-	#
8	19/f	3/4; ++	0; nd	>100	7.29	98.5 (41)	>100 (42)	40.4 (17)	0.46 (0)	3.06	6.95	0.41	7.87	1.31	++	++
9	18/m	4; ++	0; nd	>100	10.1	35.9 (27)	70.9 (53)	24.4 (18)	2.98 (2)	10.1	12.4	<0.35	0.43	12.30	#	#
10	46/f	3; nd	0; nd	54.4	0.76	6.94 (9)	50.7 (69)	<0.35 (0)	16.1 (22)	<0.35	0.46	<0.35	0.43	25.70	-	+
11	21/m	3/4; ++	0; nd	6.98	<0.35	5.04 (48)	2.57 (25)	<0.35 (0)	2.84 (27)	4.72	<0.35	<0.35	<0.35	13.00	+	+
Soy allergic patients																
1	28/f	0; +	3; +	<0.35	<0.35	<0.35	<0.35	<0.35	1.05 (100)	2.85	<0.35	<0.35	0.94	4.43	++	++
2	51/f	0; +	3; -	<0.35	<0.35	<0.35	<0.35	<0.35	1.59 (100)	1.17	<0.35	<0.35	<0.35	8.00	++	#
3	58/f	0; +	3; ++	<0.35	<0.35	<0.35	<0.35	<0.35	8.5 (100)	10.7	<0.35	<0.35	<0.35	41.20	+	+
4	53/f	0; +	4; +	<0.35	<0.35	<0.35	<0.35	<0.35	1.81 (100)	0.93	<0.35	<0.35	<0.35	4.21	+	-
5	54/f	0; +	4; +	<0.35	<0.35	<0.35	<0.35	<0.35	3.34 (100)	7.05	<0.35	<0.35	1.07	17.70	+	-
6	60/f	0; +	4; ++	0.46	<0.35	<0.35	<0.35	<0.35	5.32 (100)	2.71	<0.35	<0.35	0.39	15.70	++	++
7	22/f	OAS; +	3; +	4.04	0.36	<0.35	<0.35	<0.35	6.15 (100)	6.45	<0.35	<0.35	<0.35	25.70	++	++
8	23/f	OAS; +	2/3; -	1.97	0.51	<0.35	<0.35	<0.35	19.1 (100)	14.4	<0.35	<0.35	0.76	60.50	-	-
Peanut and soy allergic patient																
1	21/f	3/4; ++	3; +	>100	6	35.8 (22)	>100 (63)	12.7 (8)	10.7 (7)	14	5.02	5.88	1.97	35.50	-	++

Pt, patient; m, male; f, female; nd, not determined; Symp., symptoms; OAS, oral allergy syndrome; r, recombinant; n, native; Severity SPT: -, negative; +, mild positive; ++, highly positive; Severity grass and tree pollen allergy: -, negative; +, mild hay fever; ++, severe hay fever; #, positive SPT with unknown clinical relevance.

Symptoms grading is based on Brockow and Ring (6). Grade 1 = dermal symptoms; grade 2 = gastro-intestinal problems like nausea and or cramping; grade 3 = any of the former grades plus vomiting/diarrhoea and respiratory tract problems like throat pruritus or tightness; grade 4 = any of the former grades and respiratory arrest plus cardiovascular problems like hypotension.

*7S globulin.

†2S albumin.

‡11S globulin.

\$PR-10 protein.

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