

Letter to the Editor

Specific IgE reactivity to Tri a 36 in children with wheat food allergy

To the Editor:

Wheat is an important part of our daily diet, but it can also elicit IgE-associated allergic reactions after ingestion in 0.5% to 1% of the population.¹ In patients with wheat allergy, intake of wheat-containing food can lead to immediate wheat food allergy, which occurs in children, or to wheat-dependent exercise-induced anaphylaxis, which has been reported to affect adults. The use of natural wheat allergen extracts for serological testing for wheat-induced food allergy may deliver specific IgE reactivities that are not associated with clinically relevant sensitization in patients with grass pollen allergy.²

Therefore, Tri a 19, an omega-5-gliadin, which has been described as a major allergen in immediate allergy in children³ and wheat-dependent exercise-induced anaphylaxis,⁴ is widely used for serological testing for wheat-induced food allergy. Tri a 19 has recently also been used to establish a murine model for wheat allergy in mice,⁵ and its utility for the diagnosis of wheat allergy was confirmed in a pediatric multicenter challenge study.⁶

We have recently identified a low molecular weight glutenin as new major wheat food allergen Tri a 36 and expressed and purified the recombinant allergen rTri a 36.⁷ Here, we compared its IgE-binding frequency in an IgE ELISA performed as described,⁸ with the routinely used wheat allergen extract and Tri a 19 ImmunoCAPs (Thermo Fisher Scientific Inc, Uppsala, Sweden). Fig 1 shows a comparison of purified rTri a 36 and rTri a 19. Specific IgE antibodies were measured in sera from selected groups of patients, that is, children with wheat food allergy (n = 37), patients with grass pollen allergy (n = 15), and patients with atopic dermatitis (AD) (n = 16) (see Table E1 in this article's Online Repository at www.jacionline.org). Children with wheat food allergy (w1-w37) had a clear clinical history (see the Online Repository at www.jacionline.org) of wheat food allergy with symptoms clearly attributable to wheat ingestion (Table E1). Patients with grass pollen allergy (g1-g15) suffered from grass pollen-induced respiratory allergy but regularly ate wheat products without any clinical symptoms. Patients with AD (AD1-AD16) suffered from various sensitizations but also regularly ate wheat products without symptoms (Table E1).

When we used wheat extract-based ImmunoCAP, all but 1 of the patients with wheat food allergy showed wheat-specific IgE but 12 (ie, 80%) of the 15 patients with grass pollen allergy and 13 (81%) of the 16 patients with AD without clinical symptoms to wheat showed IgE reactivity to the wheat extract (Fig 2, A, left panel; Table E1). The positive reactions to wheat in patients with grass pollen allergy and patients with AD could possibly be explained by IgE cross-reactivity with clinically irrelevant antigens in food allergy.² Two cross-reactive allergens in pollen and plant food without or with low clinical relevance in food allergy are Phl p 4-associated carbohydrates as well as profilins. In fact, 46% and 43% of the patients with grass pollen allergy and AD, respectively, showed IgE reactivity to natural Phl p 4 by ISAC chip analysis (Thermo Fisher Scientific).⁹ The other cross-reactive allergen, profilin, was recognized by 26% and 6% of the patients with grass pollen allergy and patients with AD, respectively. Nineteen of the 37 (ie, 51%) patients with wheat food allergy showed omega-5-gliadin-specific

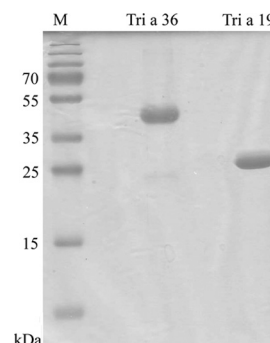


FIG 1. Coomassie-stained SDS-PAGE containing purified recombinant Tri a 36 and Tri a 19. A molecular weight marker (M) was used as standard.

IgE reactivity. Two (13%) of the patients with grass pollen allergy and none of the patients with AD showed IgE reactivity to omega-5-gliadin (Fig 2, A, right panel; Table E1). Twenty-one of the 37 (ie, 57%) patients with wheat food allergy and only 1 patient with grass pollen allergy (7%) showed IgE reactivity to Tri a 36 (Fig 2, B; Table E1). Seventeen of 19 omega-5-gliadin-positive patients and 18 of 21 Tri a 36-positive patients suffered from anaphylaxis, respectively.

Our results indicate that rTri a 36 can be used for specific *in vitro* testing for IgE-associated wheat allergy in children. The frequent and specific IgE recognition of rTri a 36 by the children with wheat food allergy may also reflect their broad sensitization, and so further studies are needed to assess the predictive value. In the populations tested, rTri a 36 detected more patients with wheat food allergy than did the routinely used omega-5-gliadin ImmunoCAP. However, rTri a 36 performed similarly as Tri a 19 in detecting patients with wheat food allergy ($P = .641$). Our results also demonstrate that rTri a 19 and rTri a 36 together will not diagnose all patients with wheat food allergy, which is in agreement with other studies,¹⁰ emphasizing that there is a need to define additional wheat allergens for sensitive and specific diagnosis of wheat allergy.

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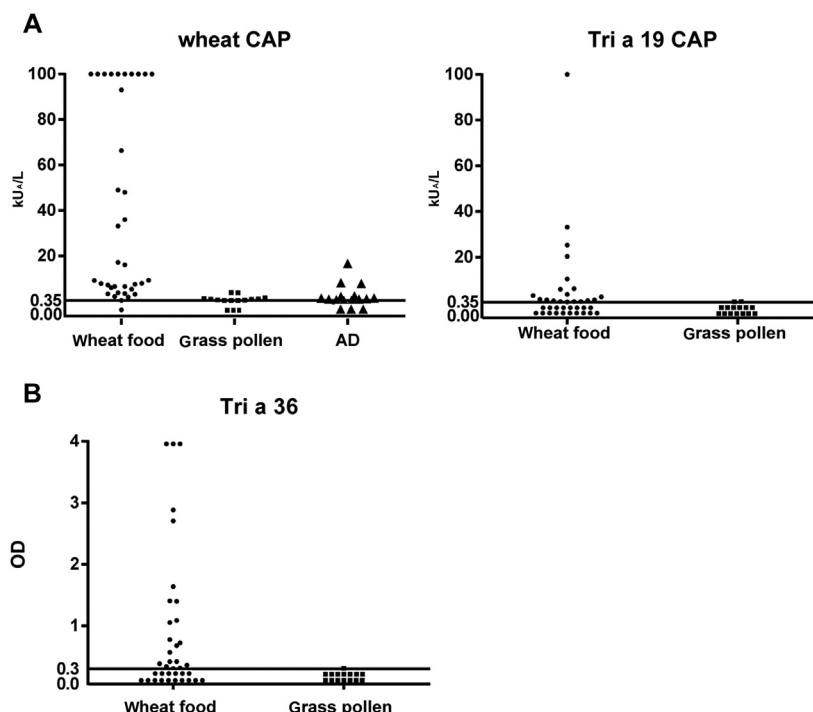


FIG 2. Specific IgE of patients suffering from wheat food allergy, grass pollen allergy, or AD without wheat food allergy to wheat extract and Tri a 19 (A) measured by ImmunoCAP (y-axes: IgE levels in kU_A/L) and Tri a 36 (B) measured by ELISA (y-axes: OD values). The horizontal lines mark the cutoffs.

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Table E1: Demographic, clinical and serological characterization of patients suffering from wheat food allergy (w), grass pollen allergy (g) or atopic dermatitis (AD) without wheat food allergy.

ID	age	symptoms	wheat	Tri a 19	Tri a 36
			kUA/l	kUA/l	ELISA (OD)
w1	3	ad, ana	66.3	1.56	1.4052
w2	4	ad, ana	7.57	-	-
w3	4	a, ad, ana	9.2	0.94	0.36155
w4	1	a, ad, ana, u	6.5	2.63	0.4172
w5	1	ad, u	6.04	3.23	1.05525
w6	6	a, ad, ana	>100	0.53	0.5713
w7	1	ad, ana	-	0.52	0.41885
w8	6	a, ad, ana, gi, u,	49	1.32	0.67795
w9	1	ana, u	3.77	-	0.337
w10	4	ad, ana, u	>100	3.73	2.70695
w11	2	ad, u	3.1	-	-
w12	3	ad, ana	7.95	-	0.7767
w13	10	ad, u	0.36	-	-
w14	5	ad, u	7.24	-	-
w15	10	ad, ana	>100	20.3	1.6409
w16	2	ad, u	3.27	-	-
w17	4	ad,	17.2	-	-
w18	7	ad, u	16.1	-	-
w19	8	a, ad, ana	>100	6.18	3.95945
w20	10	ad, u	7.84	-	-
w21	3	ad, u	3.47	-	-
w22	8	a, ad, aw, u	35.9	-	0.30385
w23	6	a, ad, ana	93.1	0.36	0.7253
w24	14	a, ad, ana	>100	1.32	1.08825
w25	1	a, ad, ana, u	6.5	0.54	0.3851
w26	3	a, ad, u	>100	10.4	1.39835
w27	2	ad, ana	>100	25.2	2.8845
w28	5	a, ad, ana	>100	33.1	3.95765
w29	3	ad, u	33.1	-	-
W30	5	a, ad	48	-	-
W31	14	a, ad, ana, u	>100	>100	3.9586
W32	3	a, ad, ana	9.29	-	-
W33	4	ad, u	1.89	-	-
W34	6	ad, ana	5.39	-	-
W35	5	a, ad, ana, u	>100	5.94	-
W36	1	ad, ana	n.d.	-	0.3138
W37	1	ad, ana	2.1	0.9	-
g1	11	r	0.41	-	0.3077
g2	8	a, r	0.37	-	-
g3	13	r	1.15	-	-
g4	10	r	1.58	-	-
g5	19	rc	3.92	0.45	-
g6	14	r	1.07	-	-
g7	15	rc	0.68	-	-
g8	24	a, r	0.96	-	-
g9	9	a, r	0.55	0.58	-
g10	15	c, r	-	-	-
g11	8	a, r	0.38	-	-
g12	11	r	-	-	-
g13	11	r, u	-	-	-
g14	16	r	3.76	-	-

ID	age	symptoms	wheat	Tri a 19	Tri a 36
			kUA/l	kUA/l	ELISA (OD)
g15	no info	r	0.92	-	-
AD1	14	ad, r	1.41	-	-
AD2	4	a, ad, r	0.38	-	-
AD3	14	ad, r	-	-	-
AD4	9	a, ad, rc	0.96	-	-
AD5	9	a, ad, r	2.15	-	-
AD6	5	ad, r	8.16	-	-
AD7	11	a, ad, r	2.36	-	-
AD8	10	a, ad, r	0.74	-	-
AD9	9	a, ad, r	7.9	-	-
AD10	14	ad, r, a	1	-	-
AD11	10	a, ad	-	-	-
AD12	5	a, ad, r	1.43	-	-
AD13	10	a, ad, r	0.36	-	-
AD14	2	ad	1.13	-	-
AD15	0.5	ad	-	-	-
AD16	9	ad, r	16.7	-	-

Abbreviations used: a: asthma, ad: atopic dermatitis, ana: anaphylaxis, aw: upper airway symptoms, c: conjunctivitis, g: grass pollen allergic, gi: gastrointestinal symptoms, n.d.: not done, no info.: no information available, r: rhinitis, rc: rhinoconjunctivitis, u: urticaria, w: wheat food allergic, dashes indicate values below the cut off 0.3 in ELISA and 0.35 in CAP