

Letter to the Editor

Peach allergy in China: A dominant role for mugwort pollen lipid transfer protein as a primary sensitizer

To the Editor:

Lipid transfer protein (LTP)–associated peach allergy has been described as an almost exclusively Mediterranean phenomenon in which peach consumption is at the base of sensitization.^{1,2} In areas with high exposure to mugwort or plane tree pollen, sensitization to pollen-derived LTPs has been implicated as modifying the epitope-recognition spectrum by primary sensitization to pollen LTPs.^{3–5} Overall, however, unlike birch pollen–induced cross-reactivity to Bet v 1 homologs in fruits, sensitization to LTPs is primarily seen as a fruit consumption–driven process.⁶

Peach allergy has been frequently reported in China, especially among patients with mugwort allergy in northern China, but the molecular sensitization patterns to individual peach and mugwort allergens have not yet been characterized. Here we report the results of component-resolved diagnosis for peach and mugwort (rPru p 1, rPru p 3, rPru p 4, nArt v 1, and nArt v 3) using the ImmunoCAP system (Thermo Fisher, Uppsala, Sweden) among 70 patients (65 from the north and 5 from the south) with a convincing history of peach allergy, mugwort allergy, or both. Of these patients, 24 were allergic to peach and mugwort, 15 were allergic to peach only, and 31 were allergic to mugwort only (see Table E1 in this article's Online Repository at www.jacionline.org). The most commonly reported peach-related symptoms were the oral allergy syndrome, followed by urticaria, gastrointestinal symptoms, and a few cases of conjunctivitis, dyspnea, and anaphylaxis. Diagnosis was performed by experienced allergy specialists and further supported by a positive ImmunoCAP result. Written consent was obtained from all participants or their legal representatives, and the study was approved by the local ethics committee.

All but 1 of the 24 patients allergic to both mugwort and peach (all from northern China) had higher IgE titers against mugwort than peach, all had IgE against Art v 3, and 23 of 24 had IgE against Pru p 3, with the responses to Pru p 3 being lower (with 1 exception). All but 1 of the patients had specific IgE against Art v 1, but these levels were always lower than those against Art v 3. Pru p 1 was recognized by only 2 of the 24 patients with mugwort/peach allergy, and Pru p 4 was recognized by 7 of these patients. Of the 15 patients with peach allergy but tolerant of mugwort, only 6 had low-titer IgE levels against mugwort and Art v 3. The 5 patients from southern China were within this peach-only group. All but 1 had specific IgE against Pru p 3, with the exception producing the highest response to Pru p 1. The 6 selective patients with peach allergy and mugwort sensitization had IgE against Art v 3 but none against Art v 1. In contrast to the group with mugwort/peach allergy, the IgE responses against Art v 3 were lower than those against Pru p 3 (with 1 exception).

The 31 patients with mugwort allergy only had specific IgE against mugwort but with significantly lower titers than those with accompanying peach allergy. Specific IgE against Art v 1 was detected in 25 of 31 patients, but only 12 of 31 had

specific IgE against Art v 3. Seventeen patients in this group had specific IgE against peach, of whom 9 were Pru p 3 sensitized, always together with Art v 3 sensitization. Four were sensitized to Pru p 4 but none to Pru p 1. As observed for the patients with mugwort/peach allergy, responses to mugwort and Art v 3 were much higher than to peach and Pru p 3 (with 2 exceptions). Table E1 lists individual clinical and serologic data of all 70 patients.

The specific IgE-recognition patterns to mugwort, peach, and their respective LTPs point to 2 types of patients. The first and by far largest group of patients (with mugwort allergy) showed high-level sensitization to mugwort pollen and Art v 3 accompanied by lower sensitization to Pru p 3, translating into clinical peach allergy in approximately 35% of the cases. This suggests a Pru p 3–associated peach allergy was induced by primary sensitization to Art v 3. A second smaller group of patients with peach allergy had non–pollen-related sensitization to Pru p 3 with little or no recognition of Art v 3. This group resembled the typical Mediterranean peach allergy phenotype, displaying primary sensitization to Pru p 3.

ImmunoCAP inhibition studies were carried out with serum pools and individual serum samples representing the 2 molecular recognition patterns to provide further support for the existence of a prevalent group of patients with peach allergy with primary sensitization to Art v 3 and a smaller group with primary sensitization to Pru p 3. IgE binding to Pru p 3 was inhibited to a similar extent by rPru p 3 and rArt v 3 when using the serum pool and 7 individual sera (see Fig E1 in this article's Online Repository at www.jacionline.org), with significantly higher IgE levels to mugwort/Art v 3 than to peach/Pru p 3 (Fig 1, A). IgE binding to Art v 3 in this group was not inhibited by Pru p 3 (Fig 1, B). Using the serum pool and 3 individual sera (see Fig E2 in this article's Online Repository at www.jacionline.org) with the “Mediterranean” serotype, almost a mirror image was observed: there was almost no inhibition of IgE binding to Pru p 3 by Art v 3 and almost complete inhibition by Pru p 3 (Fig 1, C), whereas IgE binding to Art v 3 was fully inhibited by both Pru p 3 and Art v 3 (Fig 1, D).

Overall, the present study provides convincing support for the existence in northern China of a group of patients with peach LTP allergy whose food allergy originates from primary sensitization to pollen LTP (Art v 3). Although some reports from southern Europe have provided evidence for the existence of a small group of similar patients,^{3–5} the dominant view is that Pru p 3–associated peach allergy is a food allergy driven by primary sensitization to peach.^{1,2} A likely explanation for the contrasting cause of peach allergy in northern China and southern Europe is the dominant role of mugwort pollen exposure in China,^{7–9} which is analogous to that of birch pollen exposure in northern Europe.⁶

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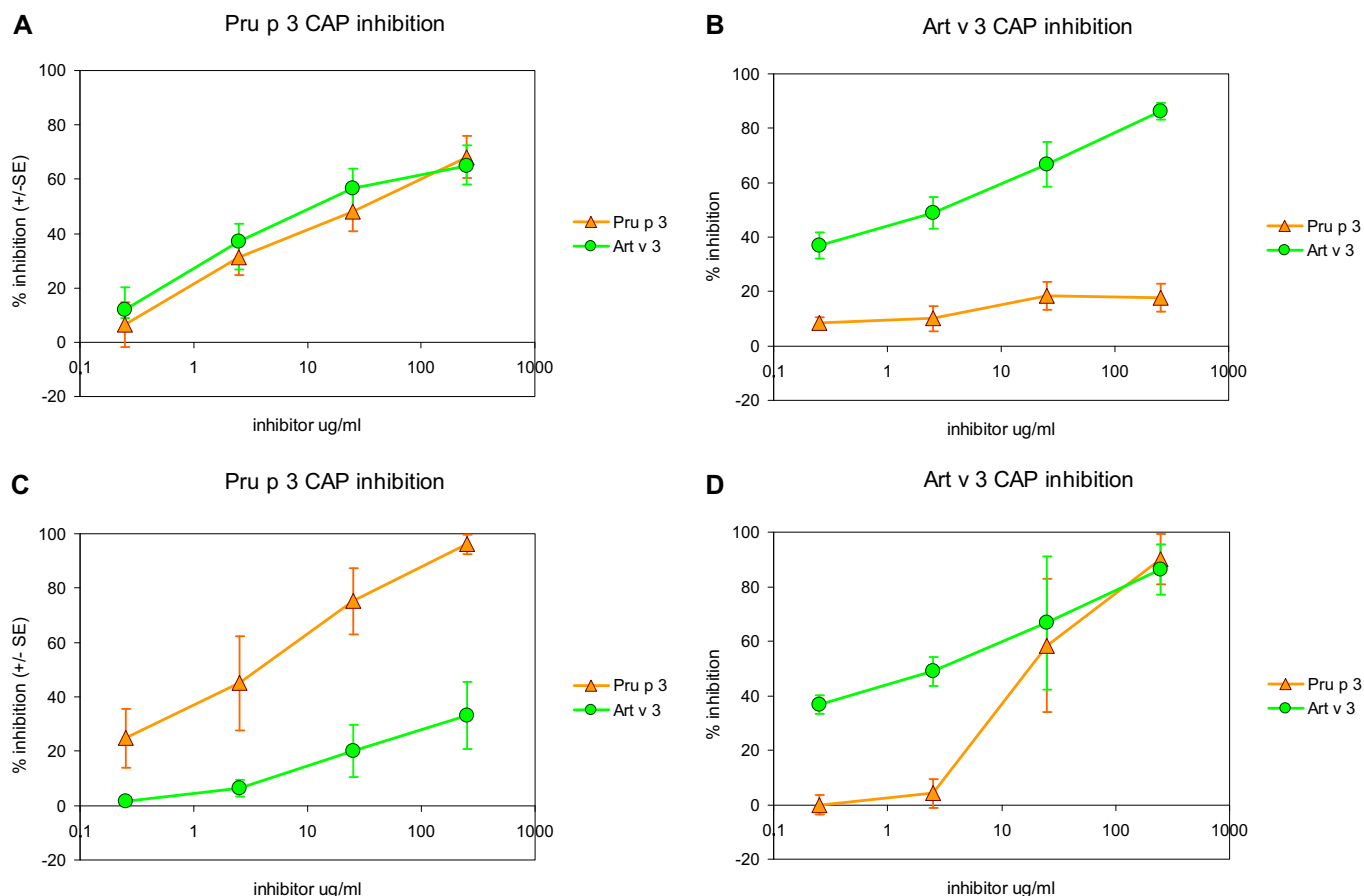


FIG 1. Comparison of homologous and heterologous inhibition of IgE binding to Pru p 3 and Art v 3 using competitive ImmunoCAP analysis. **A** and **B**, The serum pool and individual samples used originated from patients with higher serum IgE levels against Art v 3 than Pru p 3. **C** and **D**, The serum pool and individual samples used originated from patients with lower IgE levels to Art v 3 than Pru p 3 (see Table E1). Inhibitor concentrations were as follows: 0.25, 2.5, 25, and 250 $\mu\text{g}/\text{mL}$.

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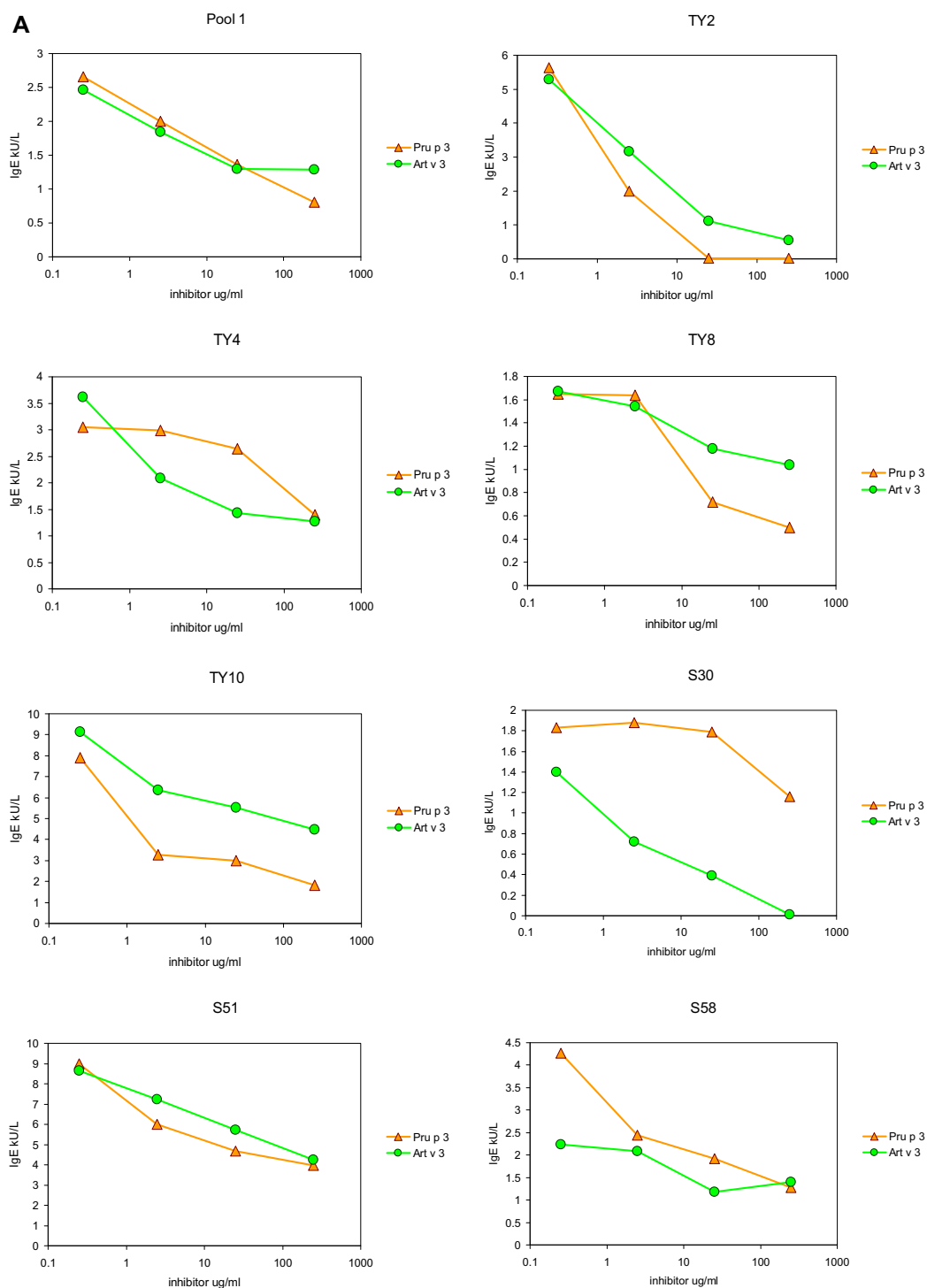


FIG E1. Comparison of homologous and heterologous inhibition of IgE binding to Pru p 3 (A) and Art v 3 (B) using competitive ImmunoCAP analysis with pool 1 and 7 individual sera originating from patients with higher serum IgE levels against Art v 3 than Pru p 3. Results are expressed in kilounits per liter. For serum codes, please see Table E1.

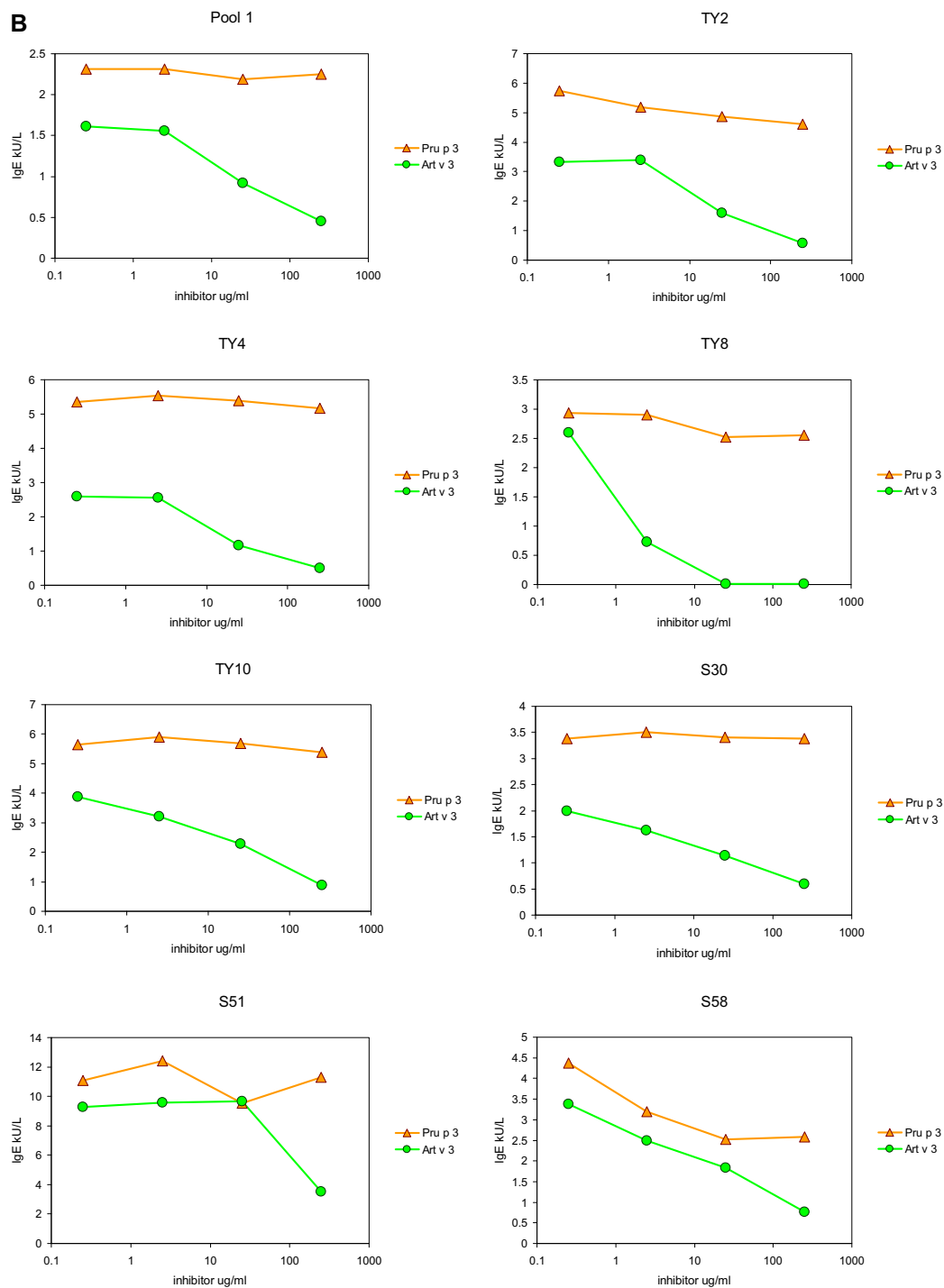


FIG E1. (Continued)

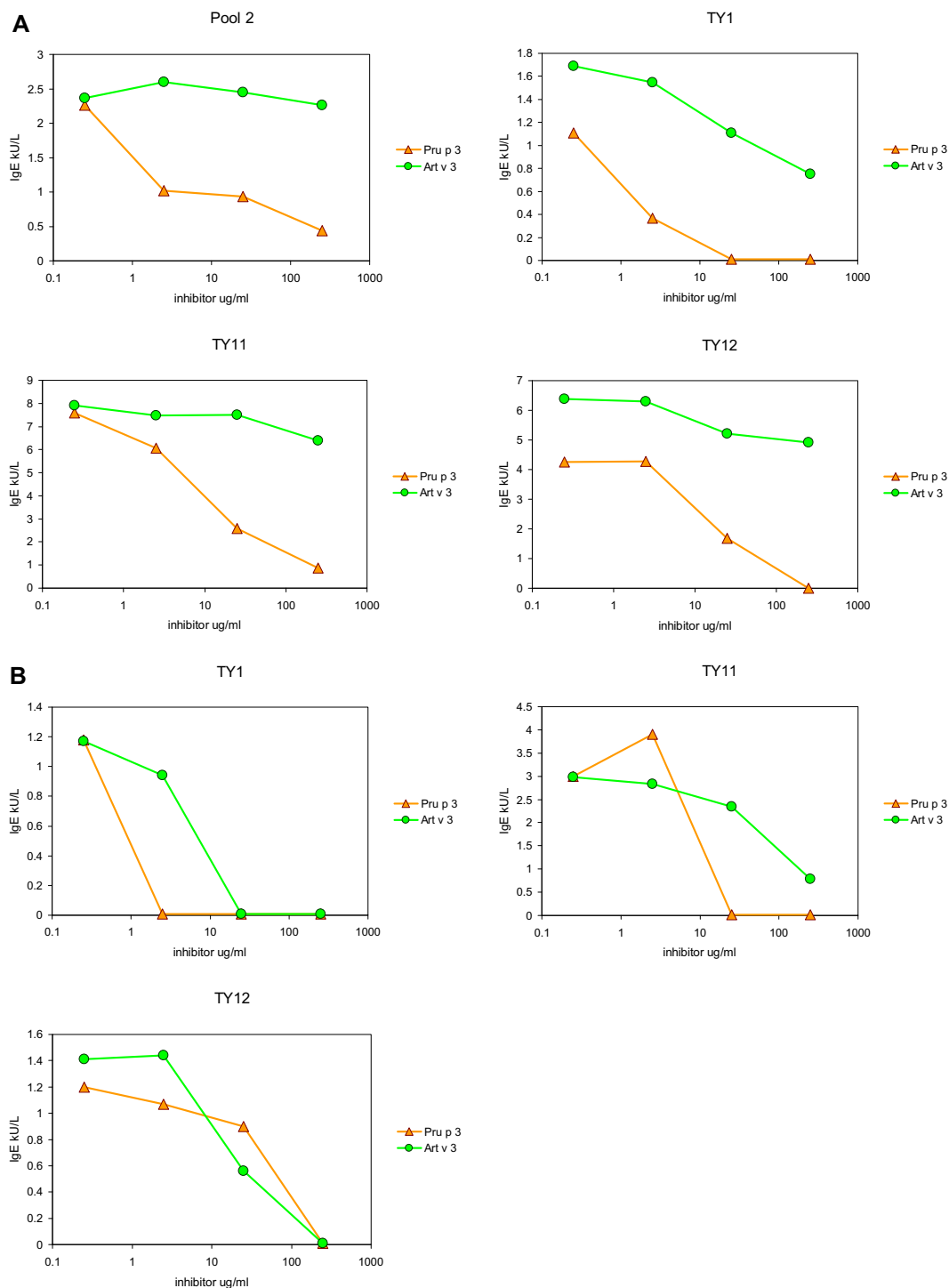


FIG E2. Comparison of homologous and heterologous inhibition of IgE binding using competitive ImmunoCAP. **A**, Binding to Pru p 3 with pool 2 and 3 individual sera originating from patients with lower serum IgE levels against Art v 3 than Pru p 3. **B**, Binding to Art v 3 with 3 individual sera originating from patients with lower serum IgE levels against Art v 3 than Pru p 3. Results are expressed in kilounits per liter. For serum codes, please see [Table E1](#).

Table E1 Patient information, allergy symptoms, and specific IgE values (n = 70)

Serum group	Inhibition	Serum code	Serum dilution Pru p 3 CAP-inhibition	Serum dilution Art v 3 CAP-inhibition	Age/Sex	Geographical location	Peach symptoms	Mugwort symptoms	ImmunoCAP (kU _A /L)						
									Peach	rPru p 1	rPru p 3	rPru p 4	Mugwort	nArt v 1	nArt v 3
Serum IgE against mugwort higher than against peach	Pool 1 for CAP-inhibition	S31	undiluted	1:10	42/M	N	OAS, D, U	R	5.6	0.1	2.7	0.1	7.5	0.9	12.4
		S36			21/F	N	OAS, R	R	16.5	0.1	6.7	7.5	67.1	40.9	100.0
		S37			33/M	N	OAS, C	R	12.7	0.1	9.7	0.1	68.9	36.7	68.9
		S47			40/F	N	G	R, As	2.6	0.1	4.1	0.1	15.4	5.4	21.3
		S48			16/M	N	OAS	R, As	1.6	0.1	2.2	0.1	5.3	1.2	6.1
		S53			30/F	N	U	R	4.6	0.1	6.3	0.1	39.0	2.9	56.2
		S69			46/M	N	OAS	R	1.9	0.1	2.4	0.1	5.2	0.2	9.1
		S49			29/F	N	Ns	R, As	4.0	0.1	6.2	2.2	82.5	41.0	82.6
		S54			47/M	N	Ns	R	2.8	0.1	2.2	0.9	17.6	7.4	15.4
	individual sera for CAP-inhibition	TY2	1:3	1:10	22/F	N	OAS, G, U	As	28.4	0.1	32.9	0.1	97.5	27.9	90.1
		TY4	undiluted	1:5	42/F	N	G	R, As	4.9	0.1	4.4	0.9	38.8	3.1	36.9
		TY8	undiluted	undiluted	18/M	N	OAS, U	As	1.5	0.1	2.3	0.2	5.5	0.5	4.3
		TY10	undiluted	1:10	18/M	N	OAS, U	R, As	11.9	0.1	12.4	0.1	104.1	69.6	101.1
		S30	undiluted	1:5	43/F	N	OAS, D	R	3.3	0.1	2.7	0.1	26.0	6.4	30.5
		S51	1:2	1:10	26/F	N	OAS, G	R	21.5	0.1	24.8	0.1	125.7	70.3	130.0
		S58	1:5	1:5	5/M	N	OAS	R, As	22.9	0.1	29.6	5.0	25.5	0.9	37.6
	sera not used for CAP inhibition	S32			27/F	N	OAS, An	R, As	2.3	0.1	1.6	0.1	10.2	4.3	9.7
		S35			53/F	N	G, OAS	R	2.9	0.1	0.2	0.1	7.5	0.4	13.0
		S46			37/F	N	OAS, U	R	1.0	0.1	1.5	0.1	10.5	2.2	14.2
		S60			24/M	N	OAS	R, As	10.8	0.1	10.0	4.7	106.1	39.8	127.3
		S63			16/M	N	OAS, U	R, As	4.9	0.1	3.4	3.4	29.2	0.6	22.0
		S64			7/M	N	OAS	R	2.7	0.1	0.5	3.8	33.7	22.5	26.4
		S66			13/M	N	OAS, U	R	37.3	0.1	11.6	41.8	106.5	106.5	109.0
		S86			26/F	N	U	U	1.7	0.1	1.5	0.1	8.1	2.8	12.7
		TY14			26/M	N	OAS	As	5.1	1.6	0.6	0.1	44.7	19.4	30.9
		S61			11/M	N	Ns	R	2.9	0.1	3.2	0.1	22.6	4.5	25.3
		S67			40/F	N	Ns	R	0.2	ND	ND	ND	41.8	0.4	1.0
		S70			22/F	N	Ns	R	1.3	0.1	0.1	1.7	11.2	0.1	0.1
		S73			13/F	N	Ns	R, U	0.2	ND	ND	ND	44.7	83.5	0.2
		S74			12/F	N	Ns	R, As	1.8	0.1	0.7	0.2	85.2	50.5	0.5
		S75			61/M	N	Ns	R, U	0.1	ND	ND	ND	6.4	7.4	0.1
		S76			53/F	N	Ns	R, As, C, OAS	0.1	ND	ND	ND	10.7	16.1	0.1
		S77			8/M	N	Ns	R, C	10.1	0.1	8.7	0.1	77.9	53.9	58.7
		S78			21/M	N	Ns	R, As	2.0	0.1	0.1	0.1	6.6	0.8	6.6

Serum IgE against peach higher than mugwort		S79			49/M	N	Ns	R, As	7.3	0.1	0.2	0.1	53.7	59.8	0.2				
		S80			46/M	N	Ns	G, As	1.2	0.1	0.1	0.1	9.5	2.6	0.1				
		S81			50/M	N	Ns	R, As	3.0	0.1	6.1	0.1	69.1	92.0	76.6				
		S82			39/F	N	Ns	R, As	0.1	ND	ND	ND	1.2	0.1	0.1				
		S83			22/F	N	Ns	R, C, U	5.0	0.1	2.5	0.1	42.0	3.1	49.5				
		S84			11/F	N	Ns	R, U	0.1	ND	ND	ND	17.3	0.2	0.1				
		S85			31/M	N	Ns	R, As	0.1	ND	ND	ND	6.5	0.2	11.9				
		S41			51/F	N	Ns	R, As	0.1	ND	ND	ND	14.4	13.2	0.1				
		S42			47/M	N	Ns	R	0.1	ND	ND	ND	1.9	2.5	0.1				
		S44			51/M	N	Ns	R, C, D	4.7	0.1	0.1	13.4	11.8	0.4	0.1				
		S45			7/M	N	Ns	R, C	0.7	0.1	0.1	0.1	82.0	63.2	0.3				
		S57			40/M	N	Ns	R	0.1	ND	ND	ND	4.9	5.6	0.1				
		S59			10/M	N	Ns	R, As	0.3	ND	ND	ND	4.4	4.5	0.1				
		S62			11/M	N	Ns	R, As	1.2	0.1	0.1	0.1	11.6	0.2	0.1				
		S65			13/M	N	Ns	R	0.1	ND	ND	ND	56.5	40.1	0.1				
		TY3			26/F	N	Ns	U, As	0.1	ND	ND	ND	21.3	21.4	0.1				
		TY7			42/F	N	Ns	R, As	0.1	ND	ND	ND	18.4	17.3	0.1				
		TY9			18/F	N	Ns	R, C	0.6	0.1	0.1	0.1	1.9	0.2	0.1				
					Pool 2 for CAP-inhibition	S18	undiluted		21/F	S	U, G	Ns	3.8	0.1	4.9	0.1	0.1	ND	ND
						S21			22/M	S	OAS	Ns	3.7	0.1	3.7	0.1	0.1	ND	ND
S24	40/F		S	OAS, C, U		Ns			4.3	0.1	4.3	0.1	1.2	0.2	0.4				
S39	14/M		N	U		Ns			2.7	0.1	3.4	0.1	2.7	0.1	0.3				
S56	4/M		N	OAS, U		Ns			3.8	0.1	4.0	0.1	0.4	0.1	0.6				
TY11	18/F		N	U		Ns			8.6	0.1	11.6	0.1	2.2	0.1	4.9				
individual sera for CAP-inhibition	TY12		undiluted	50/M	N	OAS, U	Ns	9.1	0.1	10.6	0.1	1.9	0.1	2.5					
	TY1			18/M	N	OAS, U	R, As, C	3.3	1.3	3.2	0.1	2.1	0.1	2.1					
sera not used for CAP-inhibition	S1				21/M	N	OAS, U	Ns	2.9	5.1	0.1	0.1	0.2	ND	ND				
	S16				22/M	N	OAS, U	Ns	3.2	0.1	1.4	0.1	0.1	ND	ND				
	S17				20/M	N	U, C	Ns	1.5	0.1	0.9	0.1	1.0	0.1	2.7				
	S19	22/F			N	OAS	Ns	1.3	0.1	1.4	0.1	0.2	ND	ND					
	S22	23/M			S	U, G	Ns	1.9	0.1	1.1	0.1	0.1	ND	ND					
	S27	24/M			S	U	Ns	2.0	0.1	1.7	0.1	0.2	ND	ND					
	S33	32/M			N	OAS, U	Ns	1.0	0.1	1.4	0.1	0.3	ND	0.2					
	S34	15/M			N	OAS, C	Ns	0.5	0.1	0.6	0.1	0.1	ND	0.1					
	S71	51/F			N	Ns	R, C, OAS	3.4	0.1	5.5	0.1	3.0	0.4	4.7					
	S72	11/M			N	Ns	R, As	37.6	0.1	34.7	0.1	23.0	1.7	38.1					

Symptom abbreviations: An, anaphylaxis; As, asthma; C, conjunctivitis; D, dyspnea; G, gastrointestinal symptoms; OAS, oral allergy syndrome; R, rhinitis; U, urticaria; Ns, no symptoms.

ND in the ImmunoCAP value column means not determined because the extract CAP result was negative (below 0.35kU_A/L).