ONLINE REPOSITORY

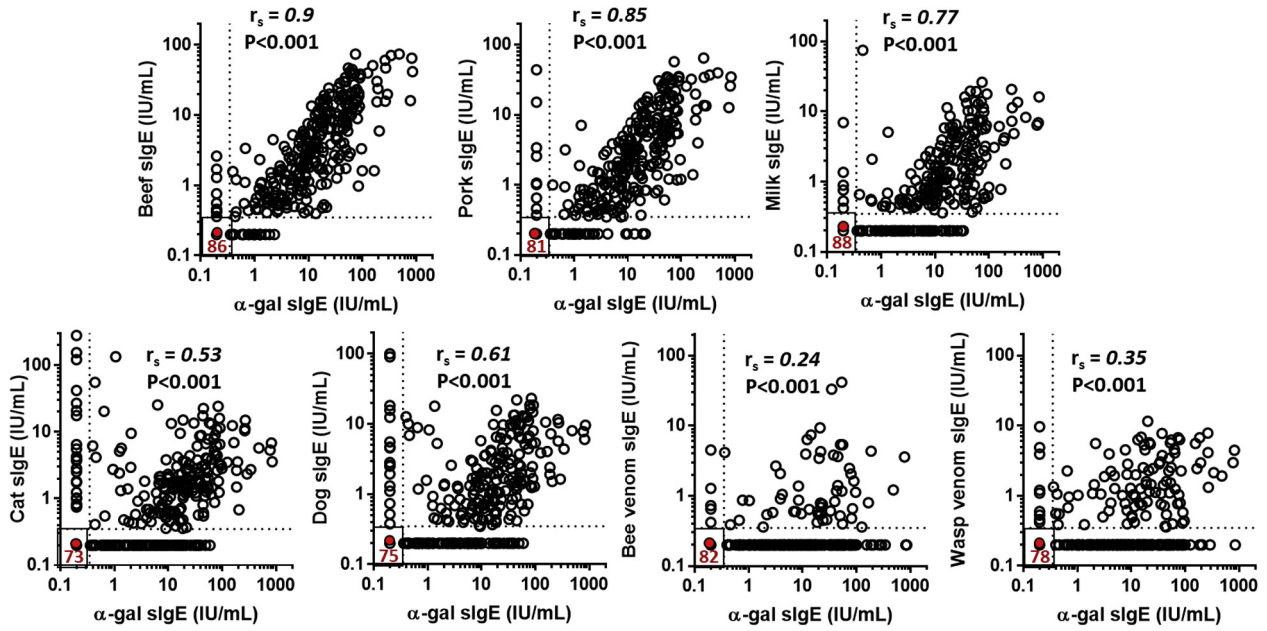

FIGURE E1. Correlation plots of galactose-α-1,3-galactose (α-Gal) specific IgE (sIgE) versus sIgE to mammalian and venom extracts from the whole cohort (n = 408). Shown are Spearman's rank values (r_s) with *P* value. The red circle and accompanying number (underneath) in red text represents the number of sera that had levels <0.35 IU/mL to both allergens.

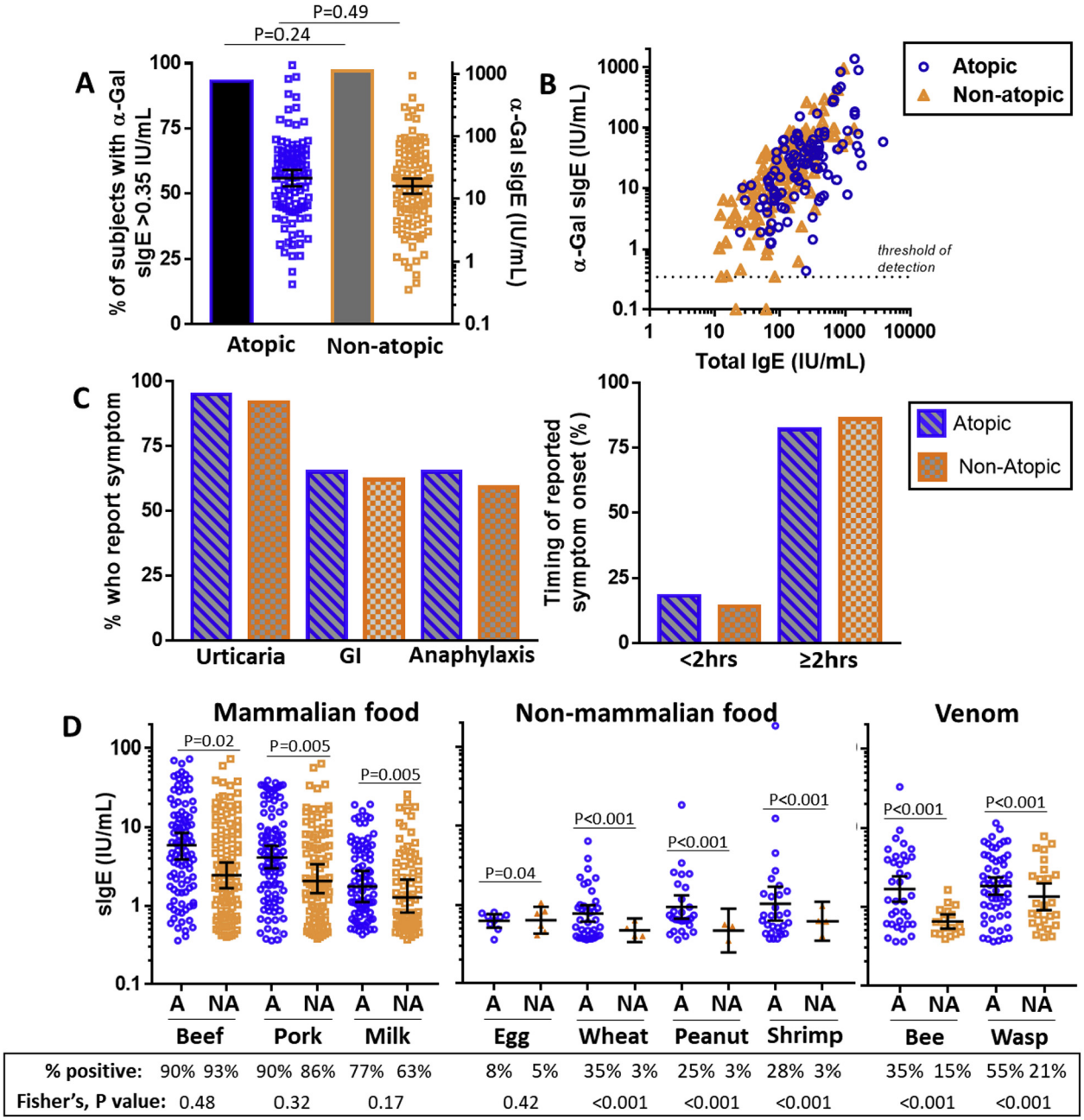

FIGURE E2. Relationship between characteristics of galactose-α-1,3-galactose (α-Gal) syndrome and atopy among subjects reporting reactions to red meat. **A**, Prevalence (bar graph, left *y*-axis) and titers (scatter plot, right *y*-axis) of specific IgE (sIgE) to α-Gal in atopics and nonatopics (atopy defined as sIgE ≥ 0.35 IU/mL to dust mite, Timothy grass ragweed, birch, cockroach, and/or *Alternaria*) where A denotes atopic and NA denotes nonatopic. **B**, Correlation of α-Gal sIgE and total IgE in atopic (n = 111) and nonatopic subjects (n = 118) who reported allergic reactions to mammalian meat. **C**, Symptoms reported by red meat allergic subjects in relation to atopy status. **D**, Prevalence (shown in table format under the graph) and titers of sIgE to mammalian and nonmammalian foods, and venom, among atopic and nonatopic subjects reporting reactions to red meat. Data expressed as geometric mean with 95% confidence interval; levels of detected sIgE compared by the Mann-Whitney *U* test and prevalence compared by Fisher's exact test. *GI*, Gastrointestinal.

TABLE E1. Characteristics of subjects who reported mammalian meat allergy stratified according to timing of symptom onset

Demographics, clinical, and immunologic characteristics	Self-reported allergy to mammalian meat*		
	Symptom onset 0 to <2 h	Symptom onset ≥2 h	*P* value
n	41	217	na
Age at enrollment, y, mean (range)	47.2 (10-81)	45.7 (5-82)	.62**
Age at onset of urticaria or anaphylaxis†			
Mean	41.9 (35.7-48.2)	41.0 (38.6-43.5)	.78**
≤21, n (%)	8 (20%)	41 (19%)	.93††
22-40, n (%)	10 (24%)	52 (24%)	.95††
>40, n (%)	23 (56%)	124 (57%)	.90††
Sex, male	13 (32%)	106 (48%)	.04††
Race			
Caucasian	40 (98%)	204 (94%)	.36††
African American	1 (2%)	4 (2%)	.62††
Other	0	9 (4%)	.18††
Physician diagnosis of asthma	8/41 (20%)	35/215 (16%)	.61††
Seasonal or perennial rhinitis	28/41 (68%)	142/214 (66%)	.81††
Urgent care for hives or anaphylaxis?	29 (71%)	135 (62%)	.30††
Total IgE, GM, IU/mL (95% CI)	128 (91-182)	147 (126-171)	.58
α-Gal sIgE			
Prevalence, n (%)	35 (85%)	207 (95%)	.02††
GM, IU/mL (95% CI)‡	15.9 (10-25)	18.2 (15-23)	.69‡‡
Beef sIgE			
Prevalence, n (%)	31/35 (89%)	181/192 (94%)	.21††
GM, IU/mL (95% CI)‡	3.8 (2.2-6.4)	5.0 (4.1-6.1)	.28‡‡
§Inhalant sIgE, prevalence, n (%)	18/35 (51%)	80/191 (42%)	.29††
¶Food sIgE, prevalence, n (%)	10/33 (30%)	56/187 (30%)	.97††
#Venom sIgE, prevalence, n (%)	12/33 (36%)	80/186 (43%)	.48††

α-Gal, Galactose-α-1,3-galactose; *CI*, confidence interval; *na*, not applicable; *sIgE*, specific IgE.
*3 subjects who did not report a specific time of symptom onset were excluded from this analysis.
†Of those who had urticaria or anaphylaxis and identified a distinct time of onset.
‡Geometric mean (GM) calculated for positive values.
§IgE to dust mite, timothy, or ragweed ≥0.35 IU/mL.
¶IgE to egg, wheat, peanut, or shrimp ≥0.35 IU/mL.
#IgE to bee or wasp venom ≥0.35 IU/mL.
**Unpaired Student's *t*-test.
††χ^2 test.
‡‡Mann-Whitney *U* test.

TABLE E2. Clinical characteristics of a cohort of 408 subjects, based on α-Gal sIgE status

Demographics and clinical characteristics	α-Gal < 0.35	α-Gal ≥ 0.35	*P* value
N	97	311	–
Age at enrollment, y, mean (range)	46.7 (12-78)	45.9 (5-82)	.74†
Age at onset of urticaria or anaphylaxis*			
mean (range)	32.0 (1-61)	41.0 (1-81)	**.003**†
≤21, n (%)	14/44 (32%)	61/302 (20%)	.12‡
22-40, n (%)	15/44 (34%)	68/302 (23%)	.13‡
>40, n (%)	15/44 (34%)	173/302 (57%)	**.006**‡
Gender, male	27 (28%)	145 (47%)	**.001**‡
Race			
Caucasian	84 (87%)	291 (94%)	**.04**‡
African American	7 (7%)	10 (3%)	.09‡
Other	6 (6%)	10 (3%)	.23‡
Physician diagnosis of asthma	50/96 (52%)	62/307 (20%)	**<.001**‡
Seasonal or perennial rhinitis	74/97 (76%)	210/308 (68%)	.16‡
Hives ever	64/97 (66%)	293/311 (94%)	**<.001**‡
Anaphylaxis ever	36/97 (37%)	213/311 (68%)	**<.001**†
Hives or anaphylaxis requiring urgent care	33/97 (34%)	191/310 (62%)	**<.001**‡
Presentation to ED related to hives or anaphylaxis	28/97 (29%)	168/310 (54%)	**<.001**‡

α-Gal, Galactose-α-1,3-galactose; *ED*, emergency department; *sIgE*, specific IgE.
Bold indicates statistical significance ($P < .05$).
*For those who reported urticaria or anaphylaxis.
†Unpaired Student's *t* test.
‡Fisher's exact test.

TABLE E3. (A) ABO prevalence in current cohort as compared to the USA.* (B) ABO blood group distribution as relates to the presence or absence of detectable α-Gal sIgE, or to subjects with mammalian meat allergy† as determined by reverse typing and self-report, or (C) reverse typing alone

(A) ABO prevalence in current cohort

	Total		White		Black	
ABO	USA	UVA cohort	USA	UVA cohort	USA	UVA cohort
A, %	37.1%	41.5%	39.7%	42.6%	25.8%	33.3%
B, %	12.2%	7.0%	10.9%	6.5%	19.7%	16.7%
O, %	46.6%	48.2%	45.2%	47.3%	50.2%	50%
AB, %	4.1%	3.3%	4.1%	3.6%	4.3%	0%
B or AB, %	16.3%	10.3%	16.3%	10.1%	24.0%	16.7%

(B) ABO blood group distribution

ABO group	USA average	α-Gal sIgE negative (n = 77)	α-Gal sIgE positive (n = 222)	Mammalian meat allergy (n = 174)
A	37.1%	30 (39.0%)	94 (42.3%)	76 (43.7%)
O	46.6%	36 (46.8%)	108 (48.6%)	84 (48.3%)
B or AB	16.3%	11 (14.3%)	20 (9.0%)	14 (8.0%)

(C) Reverse typing alone

ABO group	USA average	α-Gal sIgE negative (n = 59)	α-Gal sIgE positive (n = 133)	Mammalian meat allergy (n = 96)
A	37.1%	21 (35.6%)	53 (39.8%)	39 (40.6%)
O	46.6%	29 (49.2%)	65 (48.9%)	48 (50.0%)
B or AB	16.3%	9 (15.3%)	15 (11.3%)	9 (9.4%)

α-Gal, Galactose-α-1,3-galactose; *sIgE*, specific IgE.
*Data on USA prevalence from Garratty G, Glynn SA, McEntire R; Retrovirus Epidemiology Donor Study. ABO and Rh(D) phenotype frequencies of different racial/ethnic groups in the United States. Transfusion 2004;44:703-6
†As defined by history of reactions to mammalian meat and positive α-Gal sIgE.