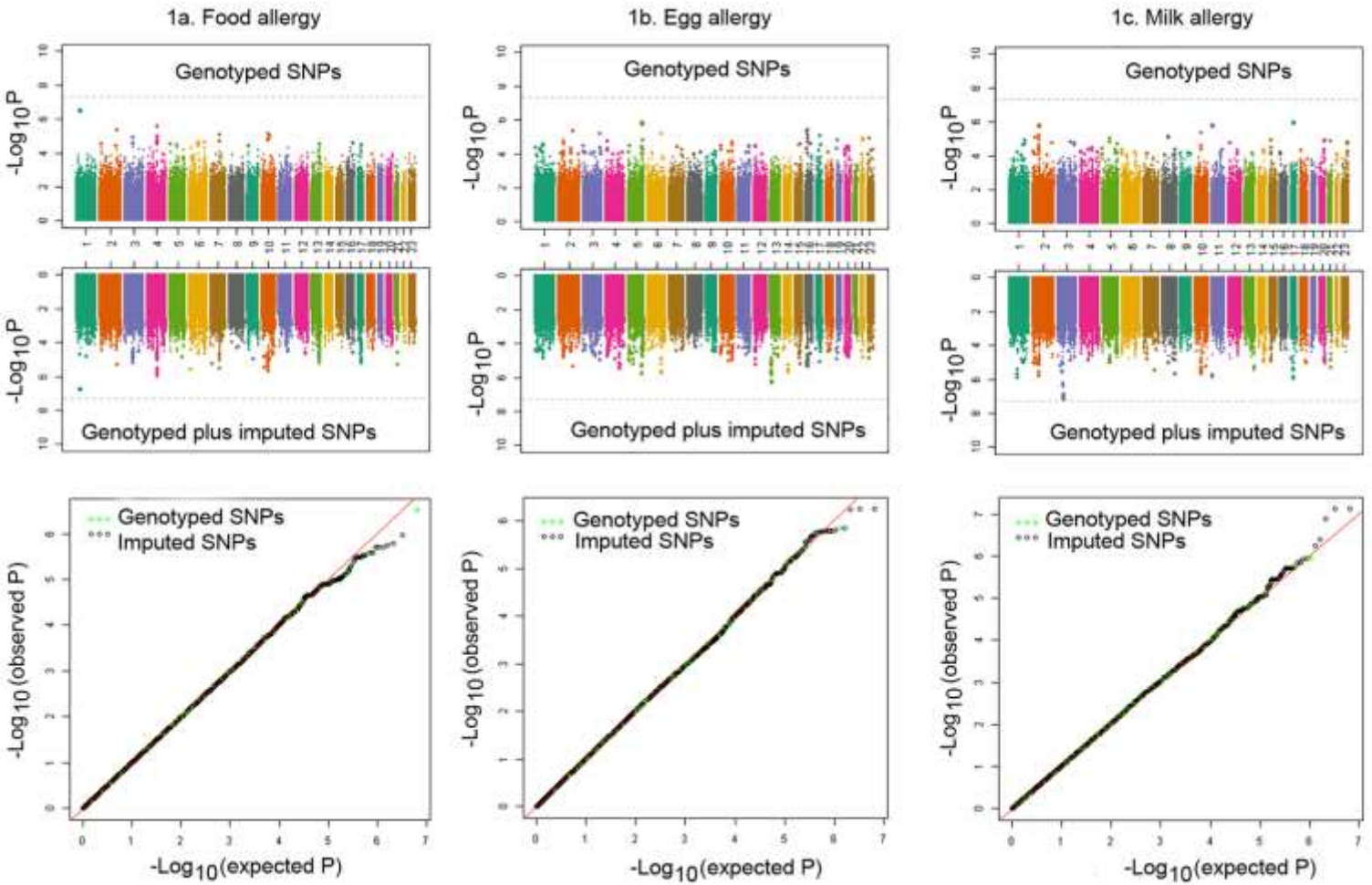
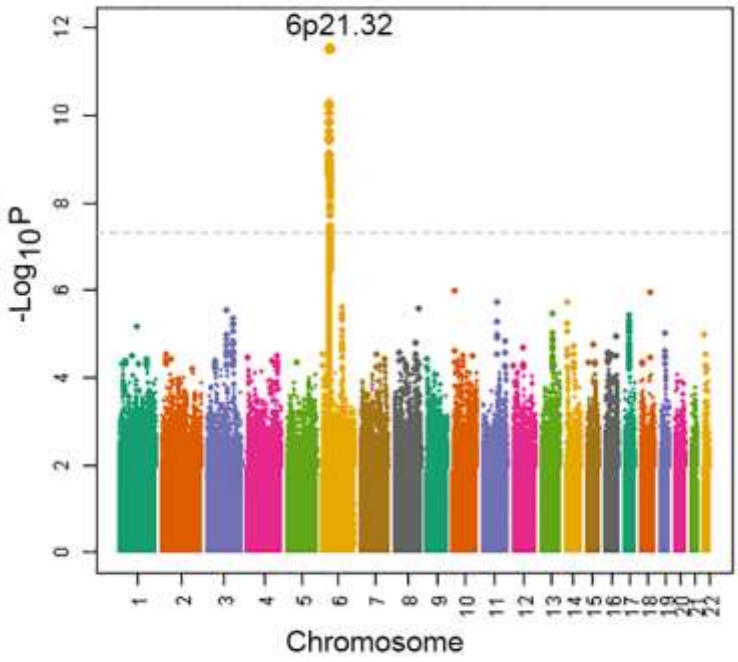
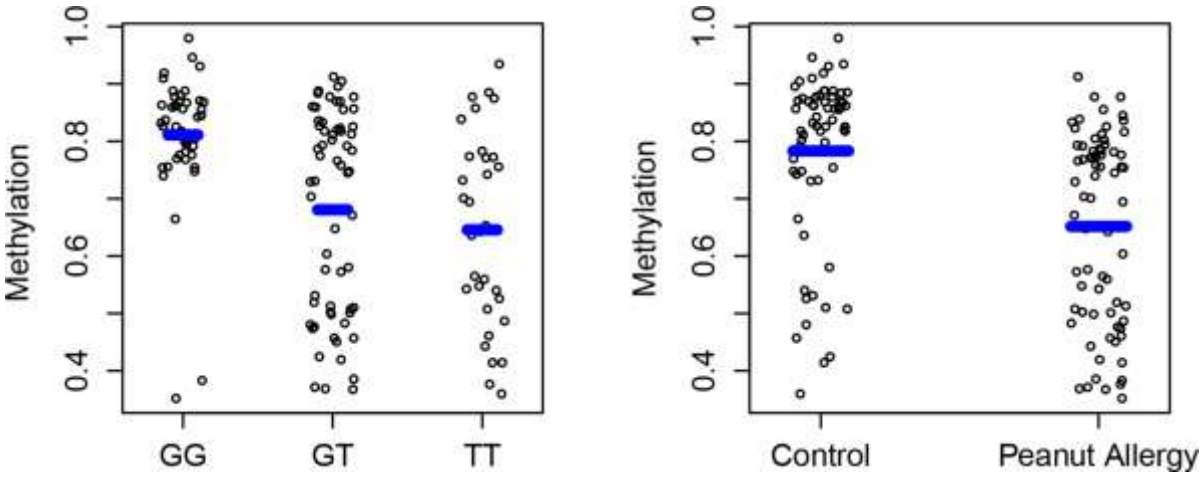
Supplementary Information



Supplementary Figure 1. Manhattan and quantile-quantile (Q-Q) plots for genome-wide associations of genotyped SNPs alone and genotyped plus imputed SNPs with any food allergy, egg allergy and milk allergy in 2,197 discovery samples of European ancestry. (1a) Manhattan and Q-Q plots for any food allergy. (1b) Manhattan and Q-Q plots for egg allergy. (1c) Manhattan and Q-Q plots for milk allergy. All analyses were performed using the modified quasi-likelihood score test. In the Manhattan plots, the top panels were for genotyped SNPs alone and the bottom panels were for the genotyped plus imputed SNPs. Dashed lines represent genome-wide significance level with $P=5\times10^{-8}$.



Supplementary Figure 2. Manhattan plot for the genome-wide meta-analysis on peanut allergy across the discovery and replication samples. Y axis is the log10-transformed *P*-value, which was generated using the Stouffer's weighted z-score method to combine the association results in the discovery sample and in the replication sample (*N*=2,328). Dashed lines represent genome-wide significance level with $P=5\times10^{-8}$.



Supplementary Figure 3. DNA methylation level at DMP cg15982117 in the *HLA-DRB1* gene that associated with the rs7192 genotype and with peanut allergy. The blue bars represent median methylation levels. These graphs were limited to 73 PA cases and 67 non-PA controls having both genome-wide SNP and DNA methylation data.

Supplementary Table 1. The demographic and clinical characteristics of the 2,694 subjects in the discovery GWAS from the Chicago Food Allergy Study.

Variables	European (*N*=2,197) [a]	Non-European (*N*=497) [a]
Family characteristics		
Number of fathers	554	122
Number of mothers	594	141
Number of children	1,049	234
Sibship size, mean (range)	1.5 (1-4)	1.6 (1-6)
Children's characteristics		
Number of children	1,049	234
Age (year), Mean±SD	5.8±3.8	6.0±3.8
Male, *N* (%)	626 (60.0)	122 (52.1) *
IgE ≥ 95% PPV, *N*(%)[b]		
Peanut	255 (25.3)	68 (30.2)
Egg	125 (12.4)	40 (17.8) **
Milk	88 (8.7)	29 (12.9)
SPT, mean wheal size ≥8mm, *N*(%)[c]		
Peanut	204 (27.8)	57 (33.7)
Egg	70 (9.5)	20 (11.8)
Milk	85 (11.6)	21 (12.4)
Food allergy (FA), *N*(%)		
Any	671 (64.3)	155 (66.2)
Peanut allergy	316 (30.1)	80 (34.2)
Egg allergy	217 (20.7)	47 (20.1)
Milk allergy	291 (27.7)	54 (23.1)
Number of FAs, *N*(%)		
0	378 (36.0)	79 (33.8)
1	389 (37.1)	88 (37.6)
2	160 (15.3)	43 (18.4)
3+	122 (11.6)	24 (10.3)
Other physician-diagnosed atopic disease, *N*(%)		
Eczema	608 (58.0)	143 (61.1)
Asthma	329 (31.4)	71 (30.3)
Hay fever	331(31.6)	82 (35.0)

GWAS: genome-wide association study; IgE: Immunoglobulin E; PPV: positive predictive value; SPT: skin prick test; FA: food allergy; SD: standard deviation.

[a]Ethnicity ancestry was defined based on principal component analyses using the genome-wide SNP genotyping data.

[b] A total of 41 children of European ancestry and 9 children of non-European ancestry had no available IgE measurement.

[c] A total of 314 children of European ancestry and 65 children of non-European ancestry had no available SPT measurement.

*P <0.05 and **P <0.01 based on t-tests and chi-square tests for the difference in continuous and categorical variables, respectively, between children of European ancestry and of non-European ancestry.

Supplementary Table 2. Genome-wide significant loci associated with peanut allergy in 2,197 discovery samples of European ancestry

SNP[a]	Nearest gene	Info Score[b]	Allele[c]	MAF[d]	LD[d,e]	$P_{discovery}$[f]	$P_{replication}$[g]	P_{meta}[h]
The top significant SNPs[a]								
rs33980016*	*HLA-DQB1*	0.98	TG/T	0.23	0.54	3.2×10^{-11}	0.024	2.9×10^{-12}
rs9275596	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.36	1.00	6.8×10^{-10}	0.022	6.3×10^{-11}
Other genome-wide significant SNPs[a]								
rs35759989	*HLA-DRB1* | *HLA-DQA1*	-	T/C	0.05	0.10	2.3×10^{-8}	0.934	1.1×10^{-7}
rs113025416*	*HLA-DRB1* | *HLA-DQA1*	1.00	A/G	0.21	0.23	3.1×10^{-8}	0.021	3.2×10^{-9}
rs144565552*	*HLA-DRB1* | *HLA-DQA1*	1.00	G/A	0.05	0.10	3.1×10^{-8}	0.934	6.7×10^{-8}
rs114576492*	*HLA-DQA1*	1.00	T/C	0.05	0.10	4.7×10^{-8}	0.781	7.7×10^{-8}
rs34130005*	*HLA-DQA1*	1.00	T/G	0.05	0.10	4.7×10^{-8}	0.781	7.7×10^{-8}
rs34857804*	*HLA-DQA1*	1.00	C/T	0.05	0.10	4.7×10^{-8}	0.781	7.7×10^{-8}
rs28633411*	*HLA-DQA1* | *HLA-DQB1*	0.99	G/A	0.05	0.10	4.8×10^{-8}	0.781	7.9×10^{-8}
rs17612852*	*HLA-DQA1* | *HLA-DQB1*	1.00	A/G	0.28	0.42	2.9×10^{-8}	0.008	1.8×10^{-9}
rs28819191*	*HLA-DQA1* | *HLA-DQB1*	0.96	G/A	0.05	0.10	4.8×10^{-8}	NA	NA
rs12055445*	*HLA-DQA1* | *HLA-DQB1*	1.00	A/G	0.50	0.52	4.1×10^{-9}	0.068	7.9×10^{-10}
rs9273442*	*HLA-DQA1* | *HLA-DQB1*	1.00	G/T	0.24	0.57	9.0×10^{-9}	0.016	7.6×10^{-10}
rs9273448	*HLA-DQB1*	-	G/A	0.24	0.57	8.2×10^{-9}	0.024	8.5×10^{-10}
rs1049213*	*HLA-DQB1*	0.99	G/A	0.27	0.47	1.6×10^{-9}	NA	NA
rs1063347*	*HLA-DQB1*	0.99	G/C	0.26	0.51	4.4×10^{-10}	NA	NA
rs28703037*	*HLA-DQB1*	0.99	G/C	0.05	0.11	2.1×10^{-8}	0.853	4.0×10^{-8}
rs9273498*	*HLA-DQB1*	0.99	A/T	0.25	0.56	5.9×10^{-9}	NA	NA
rs73729446*	*HLA-DQB1*	0.96	C/G	0.05	0.11	2.1×10^{-8}	0.747	3.4×10^{-8}
rs9273713*	*HLA-DQB1*	0.99	G/A	0.24	0.56	3.8×10^{-9}	0.024	3.8×10^{-10}
rs9273817*	*HLA-DQB1*	0.99	C/T	0.24	0.56	3.7×10^{-9}	0.019	3.3×10^{-10}
rs79603908*	*HLA-DQB1*	0.99	T/C	0.05	0.11	2.3×10^{-8}	0.853	4.5×10^{-8}
rs9273841*	*HLA-DQB1*	0.99	T/C	0.23	0.55	5.4×10^{-10}	0.024	5.2×10^{-11}
rs1049133*	*HLA-DQB1*	0.98	G/A	0.23	0.55	1.6×10^{-9}	0.024	1.6×10^{-10}
rs9274468*	*HLA-DQB1*	0.99	T/G	0.24	0.56	2.8×10^{-8}	0.022	2.9×10^{-9}
rs9274469*	*HLA-DQB1*	0.98	G/A	0.25	0.53	1.1×10^{-8}	0.032	1.4×10^{-9}
rs9274485*	*HLA-DQB1*	0.98	C/G	0.25	0.56	1.9×10^{-8}	NA	NA
rs9274489*	*HLA-DQB1*	0.98	T/C	0.25	0.56	1.2×10^{-8}	NA	NA
rs3830058	*HLA-DQB1*	-	A/G	0.24	0.57	1.1×10^{-8}	0.044	1.2×10^{-9}
rs1049055*	*HLA-DQB1*	0.98	T/C	0.23	0.54	1.5×10^{-8}	0.024	1.6×10^{-9}
rs1049053	*HLA-DQB1*	-	T/C	0.24	0.57	8.2×10^{-9}	NA	NA
rs3134994	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.24	0.57	1.8×10^{-8}	0.029	2.2×10^{-9}
rs3134976	*HLA-DQB1* | *HLA-DQA2*	-	C/A	0.24	0.57	8.7×10^{-9}	0.024	2.0×10^{-9}
rs116561850*	*HLA-DQB1* | *HLA-DQA2*	0.98	C/T	0.25	0.65	4.4×10^{-8}	NA	NA
rs114061112*	*HLA-DQB1* | *HLA-DQA2*	0.99	C/T	0.25	0.57	3.1×10^{-8}	NA	NA

rs116322182*	*HLA-DQB1* | *HLA-DQA2*	0.99	C/T	0.39	0.90	4.8×10^{-8}	0.083	1.1×10^{-8}
rs9275212	*HLA-DQB1* | *HLA-DQA2*	-	T/G	0.38	0.91	3.9×10^{-8}	0.049	6.6×10^{-9}
rs144851421*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.49	0.56	1.1×10^{-8}	0.096	2.8×10^{-9}
rs148197467*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.38	0.91	3.3×10^{-8}	0.049	5.4×10^{-9}
rs116428867*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.49	0.55	1.2×10^{-8}	0.142	4.1×10^{-9}
rs151034841*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/T	0.48	0.49	1.2×10^{-8}	0.094	2.9×10^{-9}
rs116489784*	*HLA-DQB1* | *HLA-DQA2*	0.99	T/G	0.50	0.54	6.0×10^{-9}	0.151	2.1×10^{-9}
rs4248168	*HLA-DQB1* | *HLA-DQA2*	-	C/G	0.48	0.56	5.0×10^{-8}	0.181	3.0×10^{-9}
rs9275224	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.48	0.56	8.0×10^{-9}	0.181	3.0×10^{-9}
rs115206134*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs116560215*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs4713582	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.49	0.55	1.9×10^{-8}	0.142	3.3×10^{-9}
rs115499889*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/T	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114215692*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.49	0.55	1.2×10^{-8}	0.142	4.1×10^{-9}
rs143165005*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114800859*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs35608544*	*HLA-DQB1* | *HLA-DQA2*	0.99	AAC/A	0.47	0.48	2.0×10^{-8}	0.093	5.0×10^{-9}
rs116405302*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/C	0.49	0.56	3.4×10^{-10}	0.181	1.4×10^{-10}
rs115246142*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.49	0.56	3.4×10^{-10}	0.181	1.4×10^{-10}
rs9282186*	*HLA-DQB1* | *HLA-DQA2*	1.00	AT/A	0.49	0.56	5.7×10^{-10}	0.181	2.3×10^{-10}
rs2858324	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.38	0.91	4.0×10^{-8}	0.049	6.6×10^{-9}
rs114112561*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.49	0.55	1.2×10^{-8}	0.142	4.1×10^{-9}
rs115262919*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/G	0.49	0.56	2.8×10^{-9}	0.181	1.1×10^{-9}
rs9275245	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs116499960*	*HLA-DQB1* | *HLA-DQA2*	0.99	A/C	0.49	0.55	6.2×10^{-9}	0.101	1.6×10^{-9}
rs116372656*	*HLA-DQB1* | *HLA-DQA2*	0.99	C/T	0.49	0.55	4.3×10^{-9}	0.101	1.1×10^{-9}
rs114151447*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114730661*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/T	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114350602*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/T	0.48	0.56	1.4×10^{-8}	0.181	5.6×10^{-9}
rs116566905*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.41	0.79	4.1×10^{-8}	0.034	5.5×10^{-9}
rs2858319	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.38	0.91	1.5×10^{-8}	0.051	4.3×10^{-9}
rs116271293*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/T	0.38	0.91	4.0×10^{-8}	0.049	6.6×10^{-9}
rs116785116*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114740792*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs115092484*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/T	0.24	0.57	1.8×10^{-8}	0.029	2.2×10^{-9}
rs116443869*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.49	0.56	5.4×10^{-9}	0.100	1.4×10^{-9}
rs115682962*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.49	0.56	5.4×10^{-9}	0.100	1.4×10^{-9}
rs142702370*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.49	0.56	5.0×10^{-9}	0.187	2.1×10^{-9}
rs114452579*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/G	0.38	0.91	3.5×10^{-8}	0.069	7.2×10^{-9}
rs114992233*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.48	0.56	6.4×10^{-9}	0.284	3.7×10^{-9}
rs9275282	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.48	0.57	6.1×10^{-9}	0.284	3.6×10^{-9}
rs114512308*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.38	0.91	3.5×10^{-8}	0.069	7.2×10^{-9}

rs116728620*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.48	0.56	6.4×10^{-9}	0.282	3.7×10^{-9}
rs114225975*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.48	0.56	6.4×10^{-9}	0.296	3.8×10^{-9}
rs150178207*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.48	0.56	7.6×10^{-9}	0.187	3.1×10^{-9}
rs150315370*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.38	0.91	4.0×10^{-8}	0.056	7.1×10^{-9}
rs9275288	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs114109635*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/C	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs116458476*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.48	0.56	7.6×10^{-9}	0.181	3.0×10^{-9}
rs115324884*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/G	0.38	0.91	4.0×10^{-8}	0.053	6.9×10^{-9}
rs116105807*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/C	0.48	0.56	7.6×10^{-9}	0.182	3.0×10^{-9}
rs3129720	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.24	0.57	1.2×10^{-8}	0.035	2.4×10^{-9}
rs6457617	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.49	0.55	1.2×10^{-8}	0.142	4.1×10^{-9}
rs115961701*	*HLA-DQB1* | *HLA-DQA2*	0.99	C/G	0.50	0.55	3.9×10^{-8}	0.142	1.3×10^{-8}
rs114327385*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/C	0.38	0.91	4.0×10^{-8}	0.049	6.6×10^{-9}
rs2647012	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.38	0.91	4.4×10^{-8}	0.049	6.6×10^{-9}
rs2395522	*HLA-DQB1* | *HLA-DQA2*	-	A/T	0.49	0.56	3.2×10^{-9}	0.181	3.3×10^{-9}
rs2647003	*HLA-DQB1* | *HLA-DQA2*	-	G/T	0.38	0.91	4.0×10^{-8}	0.049	6.6×10^{-9}
rs2647001	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.38	0.91	2.8×10^{-8}	0.049	6.6×10^{-9}
rs2646998	*HLA-DQB1* | *HLA-DQA2*	-	G/T	0.38	0.91	3.3×10^{-8}	0.049	7.0×10^{-9}
rs2856725	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.38	0.91	4.0×10^{-8}	0.049	6.6×10^{-9}
rs3135006	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.24	0.57	2.3×10^{-8}	0.030	2.2×10^{-9}
rs114847720*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.38	0.91	3.1×10^{-8}	NA	NA
rs3135190	*HLA-DQB1* | *HLA-DQA2*	-	G/T	0.24	0.58	1.3×10^{-8}	0.023	1.3×10^{-9}
rs114179331*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.38	0.91	3.1×10^{-8}	0.061	6.0×10^{-9}
rs9282195*	*HLA-DQB1* | *HLA-DQA2*	1.00	TA/T	0.24	0.58	1.3×10^{-8}	0.030	1.5×10^{-9}
rs116417913*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.38	0.91	3.1×10^{-8}	0.053	5.4×10^{-9}
rs115782258*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/A	0.38	0.91	3.1×10^{-8}	0.053	5.4×10^{-9}
rs2858309	*HLA-DQB1* | *HLA-DQA2*	-	C/G	0.38	0.91	2.7×10^{-8}	0.049	5.1×10^{-9}
rs1612904	*HLA-DQB1* | *HLA-DQA2*	-	A/C	0.36	1.00	3.3×10^{-9}	0.022	8.9×10^{-11}
rs28993540*	*HLA-DQB1* | *HLA-DQA2*	1.00	AT/A	0.40	0.36	5.9×10^{-9}	0.811	1.1×10^{-8}
rs3135001	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.24	0.58	3.4×10^{-8}	0.030	1.5×10^{-9}
rs2856717	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.38	0.91	3.1×10^{-8}	0.049	5.1×10^{-9}
rs2858305	*HLA-DQB1* | *HLA-DQA2*	-	T/G	0.38	0.91	3.1×10^{-8}	0.049	5.1×10^{-9}
rs2647051	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.38	0.91	3.1×10^{-8}	0.049	5.1×10^{-9}
rs116647890*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.38	0.91	3.1×10^{-8}	0.049	5.1×10^{-9}
rs3134995	*HLA-DQB1* | *HLA-DQA2*	-	C/T	0.24	0.58	1.3×10^{-8}	0.030	1.5×10^{-9}
rs28986245*	*HLA-DQB1* | *HLA-DQA2*	0.98	C/CA	0.50	0.54	8.1×10^{-9}	NA	NA
rs11390203*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/CA	0.24	0.58	1.3×10^{-8}	0.030	1.5×10^{-9}
rs116386028*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.24	0.58	1.3×10^{-8}	0.029	1.6×10^{-9}
rs9275511	*HLA-DQB1* | *HLA-DQA2*	-	G/A	0.48	0.50	1.0×10^{-8}	0.146	2.8×10^{-9}
rs115924299*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/A	0.41	0.79	3.5×10^{-8}	0.063	6.7×10^{-9}
rs114141545*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/T	0.41	0.79	3.5×10^{-8}	0.063	6.7×10^{-9}
rs115002150*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.41	0.79	3.5×10^{-8}	0.063	6.7×10^{-9}

rs9275518	*HLA-DQB1* | *HLA-DQA2*	-	A/G	0.41	0.80	1.5×10^{-8}	0.035	3.2×10^{-9}
rs116183619*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.38	0.91	3.1×10^{-8}	0.049	5.1×10^{-9}
rs115670275*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.41	0.79	4.2×10^{-8}	0.031	5.4×10^{-9}
rs115168371*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.41	0.79	4.2×10^{-8}	0.031	5.4×10^{-9}
rs114095685*	*HLA-DQB1* | *HLA-DQA2*	0.99	G/T	0.36	1.00	3.4×10^{-9}	0.024	3.6×10^{-9}
rs116453192*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.41	0.79	4.1×10^{-8}	0.037	5.8×10^{-9}
rs116763127*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/T	0.41	0.79	3.4×10^{-8}	0.031	4.3×10^{-9}
rs116556846*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/C	0.36	1.00	9.9×10^{-9}	0.022	9.3×10^{-11}
rs9275556	*HLA-DQB1* | *HLA-DQA2*	-	T/C	0.41	0.79	3.6×10^{-8}	0.032	5.2×10^{-9}
rs113036356*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.41	0.79	3.3×10^{-8}	0.025	3.8×10^{-9}
rs116836218*	*HLA-DQB1* | *HLA-DQA2*	1.00	C/T	0.41	0.79	3.5×10^{-8}	0.018	3.3×10^{-9}
rs115640523*	*HLA-DQB1* | *HLA-DQA2*	1.00	G/A	0.41	0.79	3.3×10^{-8}	0.032	4.2×10^{-9}
rs115194195*	*HLA-DQB1* | *HLA-DQA2*	1.00	T/C	0.41	0.79	3.3×10^{-8}	0.024	3.6×10^{-9}
rs6932517	*HLA-DQB1* | *HLA-DQA2*	-	G/C	0.41	0.79	4.1×10^{-8}	0.032	4.2×10^{-9}
rs9275570	*HLA-DQB1* | *HLA-DQA2*	-	A/G	0.41	0.79	3.7×10^{-8}	0.032	4.2×10^{-9}
rs115353421*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/G	0.24	0.58	1.8×10^{-8}	0.030	2.1×10^{-9}
rs115970015*	*HLA-DQB1* | *HLA-DQA2*	1.00	A/T	0.38	0.91	2.6×10^{-8}	0.049	4.2×10^{-9}
rs3998157	*HLA-DQB1* | *HLA-DQA2*	-	A/C	0.41	0.79	4.8×10^{-8}	0.032	6.6×10^{-9}
rs4273729	*HLA-DQB1* | *HLA-DQA2*	-	G/C	0.41	0.79	3.5×10^{-8}	0.032	6.6×10^{-9}
rs9282209*	*HLA-DQB1* | *HLA-DQA2*	1.00	GA/G	0.42	0.77	3.1×10^{-8}	NA	NA

[a] All SNPs are located at chromosome 6p21.32, and are ordered according to their relative genomic position.

* Imputed SNPs.

[b] IMPUTE2 info column score (reflects imputation quality).

[c] The major/minor allele. The major allele is the reference allele.

[d] Calculated based on genotyping data from parents of European ancestry.

[e] Linkage disequilibrium (r^2) with rs9275596.

[f] *P*-value from the modified quasi-likelihood score (MQLS) test in the discovery sample of European ancestry (*N*=2,197), assuming a population prevalence of peanut allergy of 1%.

[g] *P*-value from the generalized estimating equation (GEE) model in the replication sample of European ancestry (*N*=131), with adjustment for age and gender.

[h] *P*-value from the meta-analysis using the Stouffer's weighted z-score method to combine the association results from the MQLS tests in the discovery sample and from the GEE analyses in the replication sample.

NA: Analyses not available.

Supplementary Table 3. **Associations of the two top peanut allergy-associated SNPs with other allergic phenotypes in 2,197 discovery samples of European ancestry.**

Phenotype [a]	Case/control [b]	rs7192 [c]				rs9275596 [d]			
		OR[e]	95%CI	P_{GEE}	P_{MQLS}[f]	OR[e]	95%CI	P_{GEE}	P_{MQLS}[f]
Food sensitization	1,430/747	1.0	0.9-1.2	0.746	0.479	1.0	0.9-1.2	0.785	0.166
Aero sensitization	1,509/668	1.1	0.9-1.2	0.398	0.500	1.1	1.0-1.3	0.082	0.023
Any sensitization	1,738/439	1.0	0.9-1.2	0.760	0.723	1.1	0.9-1.3	0.288	0.057
Asthma	564/1,622	1.0	0.8-1.1	0.607	0.587	1.0	0.9-1.2	0.918	0.806
Eczema	803/1,376	1.0	0.9-1.1	0.740	0.724	1.0	0.9-1.2	0.988	0.428
Allergic rhinitis	775/1,406	0.9	0.8-1.0	0.058	0.088	0.9	0.8-1.0	0.028	0.072

SNP: single nucleotide polymorphism; OR: odds ratio; CI: confidence interval; PA: peanut allergy; GEE generalized estimating equation ; MQLS: modified quasi-likelihood score.

[a] Phenotype definition*: Food sensitization* is defined as a subject having detectable specific IgE ($\geq$ 0.1kU L^{-1}) or having positive skin prick test (mean wheal size $\geq$ 3mm) to any of the nine foods allergens (egg white, sesame, peanut, soy, milk, shrimp, walnut, cod fish and wheat); *Aero sensitization* is defined as a subject having detectable specific IgE ($\geq$ 0.1kU L^{-1}) or having a positive skin prick test (mean wheal size $\geq$ 3mm) to any of the six aeroallergens (Dermatophagoides pteronyssinus, dermatophagoides farinae, cat dander, dog dander, German cockroach and Alternaria alternata). *Any sensitization* is defined as a subject having either food or aero sensitization as defined above. *Eczema, Asthma and Allergic Rhinitis* was defined based on self-reported physician diagnosis, respectively.

[b] Number of cases/controls.

[c] Using the minor allele (T allele) as the effective allele.

[d] Using the minor allele (C allele) as the effective allele.

[e] The GEE model was applied to estimate the effect size of each SNP (additive genetic model) on the risk of each phenotype with adjustment for age and gender, and controlling for within-family relationship.

[f] The MQLS test was applied to estimate the *P*-value for each phenotype.

Supplementary Table 4. Demographic characteristics of the replication sample from the Chicago Food Allergy Study.

	Normal controls	Children with PA
Children with European Ancestry[a]		
N	69	62
Age, years	6.6±4.7	7.0±4.1
Male, *N* (%)	33 (47.8)	41 (66.1)
Children with non-European Ancestry		
N	58	24
Age, years	7.5±4.6	6.3±3.5
Male, *N* (%)	36 (62.1)	17 (70.8)

PA: Peanut allergy

[a] Estimated based on principal component analyses using the genome-wide SNP genotyping data.

Supplementary Table 5. Associations of imputed classical HLA alleles and amino acid polymorphisms with peanut allergy in the discovery and replication samples of European ancestry.

Gene	Variation[a]	Allele	Discovery				Replication				
			Case[b] (*N*=316)	Control[b] (*N*=144)	Uncertain[b,c] (*N*=1737)	P_{MQLS}[d]	Case[b] (*N*=62)	Control[b] (*N*=69)	OR(95%CI)[e]	P_{GEE}[e]	P_{Meta}[f]
HLA-classical allele imputed by HLA*IMP											
HLA-DQA1	0102	Present	0.28	0.20	0.20	4.5×10^{-8}	0.27	0.16	1.9 (1.1-3.3)	0.025	5.0×10^{-9}
HLA-classical allele imputed by SNP2HLA											
HLA-DQA1	0102	Present	0.28	0.20	0.19	2.7×10^{-8}	0.25	0.15	1.9(1.0-3.4)	0.045	4.2×10^{-9}
HLA-DQB1	06	Present	0.35	0.25	0.25	5.4×10^{-9}	0.30	0.20	1.9(1.1-3.3)	0.029	6.2×10^{-10}
Polymorphic amino acids imputed by SNP2HLA											
HLA-DRB1	71	Arg	0.38	0.45	0.50	2.3×10^{-10}	0.40	0.49	0.7(0.4-1.2)	0.189	9.8×10^{-11}
HLA-DQA1	207	Met	0.28	0.20	0.20	2.7×10^{-8}	0.25	0.15	1.9(1.0-3.4)	0.045	4.2×10^{-9}
HLA-DQB1	-5	No Ser or Pro	0.33	0.25	0.24	3.7×10^{-8}	0.30	0.18	2.0 (1.1-3.6)	0.017	3.3×10^{-9}
HLA-DQB1	26	Leu	0.71	0.63	0.60	1.1×10^{-8}	0.73	0.62	1.5(0.7-2.9)	0.266	6.1×10^{-9}
HLA-DQB1	86	Gly	0.10	0.06	0.05	1.6×10^{-8}	0.06	0.06	1.0(0.4-2.6)	0.965	3.8×10^{-8}
HLA-DQB1	125	Gly	0.35	0.25	0.25	5.4×10^{-9}	0.30	0.20	1.9(1.1-3.3)	0.029	6.2×10^{-10}
HLA-DQB1	130	Gln	0.10	0.06	0.05	1.6×10^{-8}	0.06	0.06	1.0(0.4-2.6)	0.965	3.8×10^{-8}

OR: odds ratio; CI: confidence interval. MQLS: modified quasi-likelihood score.

[a] The imputed classical HLA alleles and polymorphic amino acids that were significantly associated with peanut allergy ($p < 5\times10^{-8}$) in the discovery sample are shown.

[b] The frequencies of each variant in each group.

[c] Controls of uncertain phenotypes, which included 1,148 parents and 589 children.

[d] The MQLS test was applied to explore the association between each variant (additive genetic model) and the risk of PA in the discovery samples of European ancestry (*N*=2,197).

[e] The generalized estimating equation (GEE) model was applied to explore the association between each variant (additive genetic model) and the risk of PA, with adjustment for age and gender, in the replication samples of European ancestry (*N*=131).

[f] *P*-value from the meta-analysis using the Stouffer's weighted z-score method to combine the association results from the MQLS tests in the discovery sample and from the GEE analyses in the replication sample (*N*=2,328).

Supplementary Table 6. Associations between the top peanut allergy-associated SNPs and expression of genes in multiple tissues from existing expression quantitative trait loci databases.

SNP	Allele[a]	Gene	Omental adipose[b]		Subcutaneous adipose[b]		Liver[b]		Lympho-Blastoid[d]
			effect	P[c]	effect	P[c]	effect	P[c]	
rs7192	G/T	*HLA-DRA*	↓	3.8×10^{-12}	↓	4.0×10^{-11}	↓	1.9×10^{-16}	+
		HLA-DRB5	↑	2.0×10^{-22}	↑	4.6×10^{-18}	↑	2.4×10^{-16}	+
		HLA-DRB1	↑	8.1×10^{-30}	↑	4.5×10^{-23}	↑	1.1×10^{-29}	+
		HLA-DQA1	↑	4.0×10^{-17}	↑	1.4×10^{-20}	↑	1.4×10^{-27}	+
		HLA-DQB1	↑	1.2×10^{-18}	↑	5.1×10^{-25}	NS	NS	+
		HLA-DQA2	↓	5.0×10^{-18}	↓	3.0×10^{-13}	↓	2.6×10^{-10}	
rs9275596	T/C	*HLA-DRA*	↓	2.3×10^{-8}	↓	2.5×10^{-9}	↓	4.3×10^{-12}	
		HLA-DRB5	↑	1.9×10^{-19}	↑	1.8×10^{-13}	↑	8.8×10^{-11}	+
		HLA-DRB1	↑	2.8×10^{-27}	↑	6.9×10^{-18}	↑	4.9×10^{-21}	
		HLA-DQA1	↑	1.7×10^{-27}	↑	2.7×10^{-27}	↑	2.8×10^{-34}	+
		HLA-DQB1	↑	1.0×10^{-20}	↑	8.0×10^{-30}	↑	NS	+
		HLA-DQA2	↓	3.0×10^{-14}	↓	1.2×10^{-10}	NS	NS	

[a]Non-effective/effective allele. The effective allele is the risk allele for peanut allergy in this study.
[b]Associations ($P<5\times10^{-8}$) between the two SNPs and expression of genes located within +/- 1 mb distance were explored in omental adipose (N=744), subcutaneous adipose (N=612) and liver (N=569), respectively, using the existing eQTL database as published previously[1].
[c] The linear regression model was applied to explore the associations, with adjustment of age and gender.
[d, +] Significant associations between the SNP and gene expression level in lymphoblastoid cell lines, according to a RegulomeDB search (http://regulome.stanford.edu/), although detailed information on effect direction and/or P-value is lacking. Please refer to the Results section for references.
NS: no significant association.

Supplementary Table 7. The most significant cis-eQTLs for the HLA-DR and -DQ genes in the adipose and liver tissues.

Tissue	Gene[a]	cis-eQTL[b]	Position[c]	Allele	*P*-value[d]	LD	
						rs9275596[e]	rs7192[f]
Omental adipose (*N*=744)							
	HLA-DRA	rs61117681	32411035	C/A	5.0×10^{-14}	0.38	0.82
	HLA-DRB5	rs3129750	32581515	A/G	4.4×10^{-84}	0.25	0.28
	HLA-DRB1	rs9271182	32578230	G/A	9.9×10^{-131}	<0.10	<0.10
	HLA-DQA1	rs66832686	32581732	GA/G	4.5×10^{-100}	0.16	0.21
	HLA-DQB1	rs4947344	32677846	C/T	3.5×10^{-70}	0.37	0.44
	HLA-DQA2	rs510205	32584693	C/G	7.1×10^{-82}	0.13	<0.10
Subcutaneous adipose (*N*=612)							
	HLA-DRA	rs9268659	32410941	C/T	1.7×10^{-13}	0.38	0.82
	HLA-DRB5	rs9271347	32583543	G/A	4.2×10^{-99}	0.30	0.30
	HLA-DRB1	rs9271182	32578230	G/A	2.5×10^{-155}	<0.10	<0.10
	HLA-DQA1	rs66832686	32581732	GA/G	1.6×10^{-111}	0.16	0.21
	HLA-DQB1	rs4947344	32677846	C/T	5.1×10^{-76}	0.37	0.44
	HLA-DQA2	rs9268926	32433067	A/G	4.7×10^{-93}	0.12	0.16
Liver (*N*=569)							
	HLA-DRA	rs3763327	32413830	G/C	1.8×10^{-16}	0.48	0.99
	HLA-DRB5	rs9271347	32583543	A/G	5.8×10^{-78}	0.30	0.30
	HLA-DRB1	rs9271554	32590317	G /A	1.9×10^{-114}	0.19	0.27
	HLA-DQA1	rs3134979	32650178	A/T	3.2×10^{-69}	0.61	0.33
	HLA-DQB1	rs3104361	32652278	T/C	2.0×10^{-29}	0.14	<0.10
	HLA-DQA2	rs9268926	32433067	G/A	9.2×10^{-25}	0.12	0.16

cis-eQTL: expression quantitative trait loci in cis fashion; LD: linkage disequilibrium.

[a] Only genes whose expression levels were significantly associated with rs7192 and/or rs927559 (see Supplementary Table 6) are shown.

[b] The most significant cis-eQTL for each combination of gene and tissue type.

[c] The location of the corresponding cis-eQTL at chromosome 6.

[d] The associations were tested based on the linear regression model, with adjustment of age and gender.

[e] LD between the most significant cis-eQTL and rs9275596.

[f] LD between the most significant cis-eQTL and rs7192.

Supplementary Methods

Skin prick test (SPT) measurement

SPT to 9 food allergens [cow milk, egg white, soybean, wheat, peanut, English walnut, sesame seed, fish mix (cod, flounder, halibut, mackerel, tuna), and shellfish mix (clam, crab, oyster, scallops, shrimp)] and six aeroallergens (two dust mites [Dermatohagoides teronyssinus, Dermatophagoides farina], cat hair, dog epithelia, cockroach mix, and Alternaria tenius), plus negative (50% glycerinated saline) and positive (histamine, 1.0 mg mL^{-1}) controls (Greer, Lenoir,NC, USA) was performed using a Multi-Test II device (Lincoln Diagnostics). The results were measured 15 min after application. The Multi-test II device is easy to administer and has greater potential than other devices to be consistent among multiple operators across various locations; however, it has been reported to produce larger wheal sizes than the Hollilster-Stier and ALK Laboratories lancets[2], and may have the potential to increase the rate of falsely positive results[3] . To minimize such false positive results, readings were always made against parallel positive and negative controls. Data were excluded if the mean wheal size (MWD) for the negative control was ≥ 3 mm, for the positive control was < 3 mm or if the difference of the positive minus negative control was < 3 mm. A positive SPT was defined as a MWD ≥ 3 mm for a specific allergen.

Specific IgE measurement

Specific IgE (sIgE) for nine food allergens (egg white, sesame, peanut, soy, milk, shrimp, walnut, cod fish and wheat) and six aeroallergens (Dermatophagoides pteronyssinus and Dermatophagoides farinae, cat dander, dog dander, German cockroach and Alternaria alternata) were measured using the Phadia ImmunoCAP system (Phadia US Inc., Portage, MI, USA), by the Clinical Immunology Laboratory at Lurie Children's, a CLIA-certified laboratory for the ImmunoCAP assay. The detection limit was <0.1 $kU_A\ L^{-1}$ and the reported range for specific IgE was from 0.1 to 100 $kU_A\ L^{-1}$.

Genome-wide genotyping in the discovery GWAS

Before submission for genotyping, all DNA samples were quantified using a Quant-iT Broad-range dsDNA Assay Kit (Invitrogen), normalized with 1×TE and aliquoted into barcoded 96-well DNA plates at a concentration of 50 ng uL^{-1}. Samples with an original DNA concentration between 35 and 49 ng uL^{-1} were air dried to 50 ng uL^{-1}. DNA samples from each family were placed on the same plate in order to minimize batch effects within a family. All samples were frozen and shipped on dry ice to the Genome Technology Access Center, Washington University in St. Louis for genotyping. Genotyping was performed using the Illumina HumanOmni1-Quad BeadChip, according to the specifications listed in Illumina's protocol (Illumina, Inc.). After scanning on an Illumina iScan scanner, raw image data were then exported for genotype calling using Illumina's Genomestudio (version 2009.1) software. Genotypes were not called if the quality score from Genomestudio (GenCall score) was <0.25. Among the 2,759 subjects, 12 subjects failed to yield high quality genotyping calls, resulting in an overall genotyping success rate of 99.6% in the discovery GWAS samples. Finally, genotypes for 2,747 subjects were exported, with a total of 1,011,859 SNPs.

Genome-wide DNA methylation data preprocessing

These genome-wide DNA methylation data were cleaned and preprocessed according to the following steps: first, we examined the control probes included in the array to assess bisulfite conversion, extension, hybridization, staining, specificity, negative control and others; second, we looked for poorly performing arrays by plotting the median $\log_2$ (Unmeth) vs. median $\log_2$ (Meth) value for each sample, where Unmeth and Meth represent Unmethylated and Methylated signal intensity, respectively (no samples were removed at this step); and third, we annotated CpG probes that may be affected by genetic variations. With the comprehensive SNP annotation (dbSNP137, MAF > 1%) in the 'minfi' framework[3], we identified whether SNPs were at the single base extension sites, at the CpG sites on the probe, or within the probe body. A total of 17,541 probes with SNPs at position 0 and/or position 1 were removed from downstream analyses. We then checked for sex discrepancies by comparing self-reported genders

against data-derived sex values and found no sex discrepancies. Using the preprocessQuantile function in 'minfi'[3], a stratified quartile normalization procedure (involving both within- and between-sample normalization) was applied to the raw data, which were then converted to methylation values (Beta-values) on the 0-1 scale (Meth/Meth + Unmeth). The M values, or logit transformed Beta values (representing the methylation ratio), were then computed for downstream analyses, which have been reported to be better than Beta-values for identification of differential methylation.

Genetic ancestry

Genetic ancestry was carefully computed by PCA using Eigenstrat[4] and all European, American, African, and Asian individuals in the 1000 Genomes Project were used as a reference (1000GP, phase I, release_v3.20101123). Clean genotyping data from the 2,694 discovery samples in the Chicago Food Allergy Study were converted to HG19 forward strand orientation and further split into two datasets: one containing founders and a second comprised of non-founders. Both Chicago datasets were then restricted to the set of loci that overlapped with the 1000GP data (n=651,846), after which each was merged with the 1000GP data. We then utilized SmartPCA, within Eigenstrat[4], for the Chicago founders-1000GP and non-founders-1000GP datasets to compute eigenvectors. We visually examined the relationships among the discovery sample and the 1000GP anchor populations (European, African, American, and Asian) by plotting the first six principal components (PCs) against each other. To define the children with European ancestry for inclusion in our MQLS analyses, we used five PCs: 1, 2, 3, 5, and 6. We did not use PC4 because it primarily teases apart European sub-populations. It should be noted that no correlations between case/control status and European sub-populations were observed (data not shown). For each of the 5 PCs used to define European ancestry, we computed the mean value for the 1000GP European samples and 4 standard deviations (SD). Any study samples that were more than 4SD from the mean of any of the 5 PCs were classified as non-European (*N*=497).

Supplementary References

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