Original article

A genome-wide association study of plasma total IgE concentrations in the Framingham Heart Study

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Background: Atopy and plasma IgE concentration are genetically complex traits, and the specific genetic risk factors that lead to IgE dysregulation and clinical atopy are an area of active investigation.
Objective: We sought to ascertain the genetic risk factors that lead to IgE dysregulation.
Methods: A genome-wide association study (GWAS) was performed in 6819 participants from the Framingham Heart Study (FHS). Seventy of the top single nucleotide polymorphisms (SNPs) were selected based on *P* values and linkage disequilibrium among neighboring SNPs and evaluated in a meta-analysis with 5 independent populations from the Cooperative Health Research in the Region of Augsburg cohort, the British 1958 Birth Cohort, and the Childhood Asthma Management Program cohort.
Results: Thirteen SNPs located in the region of 3 genes, *FCER1A*, signal transducer and activator of transcription 6 *(STAT6)*, and *IL13*, were found to have genome-wide significance in the FHS cohort GWAS. The most significant SNPs from the 3 regions were rs2251746 (*FCER1A*, $P = 2.11 \times 10^{-12}$), rs1059513 (*STAT6*, $P = 2.87 \times 10^{-8}$), and rs1295686 (*IL13*, $P = 3.55 \times 10^{-8}$). Four additional gene regions, *HLA-G*, *HLA-DQA2*, *HLA-A*, and Duffy blood group, chemokine receptor *(DARC)*, reached genome-wide statistical significance in a meta-analysis combining the FHS and replication cohorts, although the *DARC* association did not appear independent of SNPs in the nearby *FCER1A* gene.
Conclusion: This GWAS of the FHS cohort has identified genetic loci in *HLA* genes that might have a role in the pathogenesis of IgE dysregulation and atopy. It also confirmed the association of the known susceptibility loci *FCER1A*, *STAT6*, and *IL13* for the dysregulation of total IgE. (J Allergy Clin Immunol 2011;■■■:■■■-■■■.)

Key words: *Total IgE, atopy, asthma, genome-wide association study*

IgE-mediated allergy to environmental allergens plays a central role in the pathophysiology of asthma, allergic rhinoconjunctivitis, atopic dermatitis, and food allergy. Atopic persons have abnormally high concentrations of IgE reactive against 1 or more specific allergens and often have an increased plasma total IgE concentration.[1] Atopy and an increased IgE concentration are genetically complex traits, and the specific genetic risk factors that lead to IgE dysregulation and clinical atopy are an area of active investigation.

Genetic linkage studies of total IgE concentrations have been conducted in numerous samples ascertained for asthma and atopy, with associations reported for locations on multiple chromosomes. Fine mapping of genes at several of these locations and candidate gene studies have implicated a number of genetic variants as potentially important determinants of plasma IgE concentration, with *IL4*, *IL13*, and signal transducer and activator

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Abbreviations used

B58C:	British 1958 Birth Cohort
CAMP:	Childhood Asthma Management Program
CEU:	Western European
DARC:	Duffy blood group, chemokine receptor
FHS:	Framingham Heart Study
GWAS:	Genome-wide association study
KORA:	Cooperative Health Research in the Region of Augsburg
LD:	Linkage disequilibrium
MACH:	Markov Chain haplotyping
RAD50:	RAD50 homolog *(Saccharomyces cerevisiae)*
SNP:	Single nucleotide polymorphism
STAT6:	Signal transducer and activator of transcription 6

of transcription 6 *(STAT6)* among the most consistently replicated associations.[2,3]

To date, there have been 2 genome-wide association studies (GWASs) published investigating total IgE concentration. Weidinger et al,[4] in 2008, reported findings from a population-based German cohort of 1530 subjects, with replication analyses performed in 4 independent population-based study samples that included a total of 9769 subjects. The study found that functional variants of the α chain of the high-affinity receptor for IgE *(FCER1A)* were strongly associated with total IgE levels. The study also confirmed *STAT6* as a susceptibility locus, as well as identifying the RAD50 homolog *(Saccharomyces cerevisiae)* gene *(RAD50)*, which is located adjacent to the *IL13* gene, as a potential determinant of IgE dysregulation. More recently, the GABRIEL asthma genetics consortium found, among both asthmatic patients and nonasthmatic control subjects, a single nucleotide polymorphism (SNP) near *HLA-DRB1* to be associated with total IgE concentrations with genome-wide statistical significance, as well as evidence of association for *FCER1A*, *STAT6*, and *IL13*.[5]

In this study we report the results of a GWAS of plasma total IgE concentrations in the Framingham Heart Study (FHS) cohort. In addition to confirming *FCER1A*, *STAT6*, and *IL13* as susceptibility genes for IgE dysregulation, we identify genetic variants in *HLA* genes as potential determinants of atopy and IgE concentration.

METHODS

Subjects

FHS. In 1948, two thirds of the age-eligible men and women from the town of Framingham, Massachusetts, were recruited for the first round of physical examinations and lifestyle interviews to identify risk factors for cardiovascular disease. This FHS original cohort included 5209 men and women who were between the ages of 28 and 62 years. Beginning in 1971, the FHS offspring cohort was established, comprising 5124 men and women who were either the offspring of the original cohort or spouses of those offspring. In 2002, 4095 adult men and women who were the children of the offspring cohort were enrolled in the generation 3 cohort.

During each examination cycle, the participants undergo a detailed examination, including physical examination, medical history, laboratory testing, and electrocardiography. Over the years, other tests have included pulmonary function, lifestyle questionnaires, cognitive function questionnaires, and noninvasive cardiovascular tests, including echocardiograms.

Replication cohorts. *Cooperative health research in the region of Augsburg.* The Cooperative Health Research in the Region of Augsburg (KORA) cohorts KORA S3 and KORA S4 are independent population-based samples from the general population living in the region of Augsburg, Southern Germany, and were examined in 1994/1995 (KORA S3) and 1999/2001 (KORA S4).[6] The KORA S3 sample included 4856 subjects (participation rate, 75%), and the KORA S4 sample included 4261 subjects (participation rate, 67%). In the KORA S3 sample 1644 subjects were randomly selected for genotyping, including 1530 subjects with total IgE concentrations available. From KORA S4, 1814 subjects were randomly selected for genotyping, including 1764 subjects with measurements of total IgE. Total IgE concentrations were measured with the FEIA CAP system (Pharmacia, Freiburg, Germany). Genotyping was performed with the Affymetrix 500K Gene Chip for KORA S3 and Affymetrix 6.0 for KORA S4 (Affymetrix, Santa Clara, Calif). Imputation of SNP genotypes that were not directly measured was implemented with IMPUTE.[7] For the selected SNPs, additive genetic models were fitted on log-transformed IgE levels adjusting for sex and age by using SNPTEST (www.stats.ox.ac.uk/~marchini/software/gwas/snptest.html).

British 1958 Birth Cohort. The British 1958 Birth Cohort (B58C) is an ongoing follow-up of all persons born in Great Britain during 1 week in 1958, including a biomedical assessment during 2002-2004[8] at which blood samples and informed consent were obtained for creation of a genetic resource (http://www.b58cgene.sgul.ac.uk/). Through use of this resource as a nationally representative control sample, whole-genome typing was carried out on separate subsets of the cohort by the Wellcome Trust Case-Control Consortium (B58C-WTCCC)[9] and the Type 1 Diabetes Genetic Consortium (B58C-T1DGC).[10] For the B58C-WTCCC subset, Affymetrix 500K genotypes were imputed to the HapMap 2 western European (CEU) template by using IMPUTE, whereas for the B58C-T1DGC subset, genotyping was performed with an Illumina Infinium 550K array (Illumina, San Diego, Calif) and imputed to the HapMap 2 CEU template by using Markov Chain haplotyping (MACH). Total IgE concentrations were assayed by using the HYTEC automated enzyme immunoassay (Hycor Biomedical, Edinburgh, United Kingdom), and results of its association with both Affymetrix and Illumina SNPs and with *HLA* subtypes measured by Dynal[11] are displayed online (www.b58cgene.sgul.ac.uk/phenosearch.php?pheno=1).

Childhood Asthma Management Program. The Childhood Asthma Management Program (CAMP) was a multicenter, randomized, double-masked clinical trial initially designed to determine the effects of 3 inhaled treatments for mild-to-moderate childhood asthma.[12] One thousand forty-one children aged 5 to 12 years at screening were enrolled, of which 568 white children with available genotypic and IgE data were included in this analysis. Genome-wide SNP genotyping for CAMP subjects was performed on either Illumina's HumanHap550 or Human610-Quad BeadChip, and imputation was performed with MACH based on 1000 Genomes Project haplotypes. Serum total IgE concentrations were measured by using a radioimmunosorbent assay.

Measurement of total IgE concentrations

The plasma samples used in the FHS were collected and frozen at −80°C at examination 24 for the original cohort, examination 7 for the offspring cohort, and examination 1 for the generation 3 cohort. Total IgE measurements were performed with the Phadia ImmunoCAP 100 system (Phadia, Uppsala, Sweden) in which an anti-IgE antibody is bound to a solid-phase carrier followed by flouroenzyme-based quantitative measurement of total IgE concentrations with high precision and reproducibility.[13]

Genome-wide genotyping and imputation procedures

FHS participants were genotyped with the Affymetrix GeneChip Human Mapping 500K Array Set, which was comprised of 2 arrays generating approximately 262,000 SNPs with Nsp arrays and 238,000 SNPs with Sty arrays. An additional Affymetrix 50K Array (HuGeneFocused50K) with gene-centric and coding SNPs was also genotyped for a total of approximately 550,000 SNPs. Imputation of SNP genotypes that were not directly measured was performed with the CEU reference panel in HapMap release 22, build 26 and MACH software (http://www.sph.umich.edu/csg/abecasis/MACH/) to increase genome coverage to 2,540,223 SNPs. This procedure also filled in missing data for the genotyped SNPs.

TABLE I. Descriptive characteristics of the FHS participants

	Original cohort (n = 860)	Offspring cohort (n = 2377)	Generation 3 cohort (n = 3681)
Age (y)	73 (11)	60 (9)	40 (9)
Female sex	56%	55%	53%
Current smoker	34%	11%	16%
Pack years	30 (22)	27 (23)	13 (13)
Asthma	NA	8%	16%
Hay fever	NA	29%*	47%
Log IgE	1.59 (0.64)	1.55 (0.59)	1.51 (0.56)

For continuous variables, mean (SD) are shown.
NA, Not applicable.
*Prevalence of hay fever for the FHS offspring cohort was ascertained 5 years after plasma collection for IgE measurement.

These genotypic and comprehensive phenotypic data have been made publicly available through the National Heart, Lung, and Blood Institute's SNP Health Association Resource initiative (http://public.nhlbi.nih.gov/GeneticsGenomics/home/share.aspx).

Statistical analysis

Total IgE measurements were log transformed (base 10) to attain a normal distribution and, in the FHS family sample, were examined by using linear-mixed effects models with fixed effects for SNP genotypes and random effects for subjects correlated within families because of polygenic/familial shared effects. Population stratification in the Framingham sample was assessed by using principal component analysis with Eigenstrat (http://genepath.med.harvard.edu/~reich/Sortware.htm).[14] Association of IgE concentration with allele dose for each of the imputed genotypes was analyzed by using an additive model. Age, sex, current smoking, pack years of smoking, cohort membership, and principal component 1 were included as covariates in the linear mixed-effects model.

For identification of SNPs for replication, a nominal *P* value threshold of less than 10^{-4} resulted in 527 eligible SNPs. For each gene within this group, the highest associated SNP based on *P* value was chosen for replication (n = 33). SNPs within ±500 kb of the original SNP were also selected if minor allele frequencies differed by more than 0.05 (n = 15). Of the remaining regions that lay outside of reference genes, the same strategy was used to select an additional 22 SNPs, with a total of 70 SNPs selected for replication.

Association of total IgE concentrations with SNPs in the Framingham dataset (discovery sample) was assessed in the replication datasets by using meta-analysis based on $\log_{10}$ transformation of the total IgE concentration. For cohorts in which the original analysis was performed with natural log transformation of IgE concentration, the coefficients were converted to $\log_{10}$ for the meta-analysis. Meta-analysis was performed with Metal software, with weights based on the SEs of the β estimates (inverse variance method; http://www.sph.umich.edu/csg/abecasis/metal/index.html). We performed a meta-analysis of the 70 SNPs selected for replication among the replication cohorts only and among the replication cohorts plus the FHS cohort. SNAP (version 2.0; http://broad.mit.edu/mpg/snap) was used to generate regional association plots.

RESULTS

Characteristics of the FHS participants included in the IgE GWAS are provided in Table I, and characteristics of replication cohorts along with FHS participants are provided in Table E1 in this article's Online Repository at www.jacionline.org. A Manhattan plot of the GWAS findings is shown in Fig 1. The quantile-quantile plot (see Fig E1 in this article's Online Repository at www.jacionline.org) does not show strong departure from the distribution of expected *P* values by chance, with a genomic control parameter of 1.029, suggesting that familial relationships and population stratification were appropriately controlled for in the analysis.

In the FHS GWAS 13 SNPs met genome-wide significance, as determined by using the commonly accepted significance threshold of 5×10^{-8}.[15] All 13 SNPs were within 60 kb of 3 genes: *FCER1A*, *STAT6*, and *IL13*. Details of these 13 SNPs, as well as all 527 SNPs with a nominal *P* value of less than 10^{-4}, can be seen in Figs E2 to E4 and Table E2, respectively, in this article's Online Repository at www.jacionline.org.

Of the top 70 SNPs selected for the meta-analysis with replication cohorts (see Table E3), 10 SNPs demonstrated replication based on a Bonferroni-corrected α criterion of $P < .05/70 = 0.0007$ in a meta-analysis of the replication cohorts (Table II). Two additional SNPs near the gene regions *HLA-A* and *HLA-G* did not meet the *P* value of less than .0007 criterion in the replication cohorts but had association *P* values meeting the genome-wide significance criterion of less than 5×10^{-8} in a meta-analysis of the replication cohorts together with the FHS discovery cohort (Table II). Cohort-specific association results for these 12 SNPs are shown in Table E4. The top 2 SNPs, rs2251746 and rs2494264, which were located in noncoding regions of *FCER1A*, had combined (FHS plus replication cohorts) meta-analysis *P* values of 4.52×10^{-26} and 9.40×10^{-20}, respectively. SNPs rs1059513 in *STAT6* and rs20541 in *IL13* were also associated with total IgE concentrations at genome-wide significance, each with a combined meta-analysis *P* value of less than 10^{-11}.

Among the genome-wide significant associations based on combined meta-analysis *P* values were SNPs in or near the *HLA-A*, *HLA-G*, *HLA-DQA2*, and Duffy blood group, chemokine receptor *(DARC)* genes (Table II). Two SNPs within a single linkage disequilibrium (LD) block near the *HLA-A* gene were found to have meta-analysis *P* values of less than 5×10^{-8} (www.broad.mit.edu.mpg/haploview). rs2571391 is located within 60 kb of the *HLA-A* gene and was the most highly associated SNP in this region, with a combined *P* value of 1.23×10^{-15}. Association plots for the regions encompassing *HLA-A* and *HLA-G* (see Fig E5 in this article's Online Repository at www.jacionline.org) and *HLA-DQA2* (see Fig E6 in this article's Online Repository at www.jacionline.org) depict the associations in these regions in the FHS cohort.

The SNP rs13962 is a missense SNP in the *DARC* gene and was associated with total IgE concentrations with a combined *P* value of 2.21×10^{-11}. Given its close proximity to the *FCER1A* gene, a conditional model regression analysis was performed to assess the independence of this association. After adjusting for rs2251746, the top *FCER1A* SNP, the association of *DARC* was not found to be significant in the FHS cohort ($P = .6$). Similar findings were seen in all of the replication cohorts.

The GABRIEL consortium recently reported evidence of associations for both asthma and total IgE concentration with SNPs in the *HLA-DQB1–HLA-DRB1* region.[5] The total IgE concentration peak was distinct from the asthma peak and best represented by rs9271300, which was not included in our meta-analysis because it is not part of the HapMap 2 panel. However, we were able to impute rs9271300 with moderate accuracy (observed/expected variance ratio, 0.5) using the 1000 Genomes Project June 2010 haplotypes as a template.[16] The association of this imputed SNP with the $\log_{10}$-transformed total IgE concentration in the FHS dataset was not significant ($P = .06$); however, the 95% CI (−0.001 to +0.061) around the regression coefficient of 0.03 in the FHS cohort included the GABRIEL regression

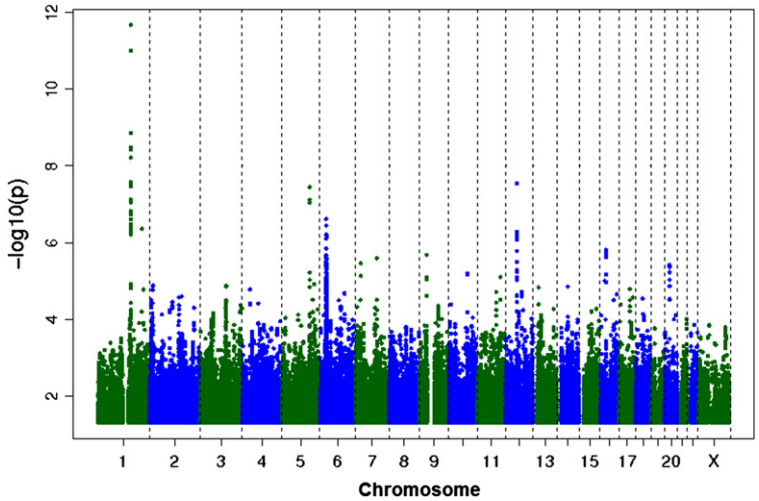

FIG 1. Genome-wide association results for imputed SNPs and plasma total IgE concentrations in the FHS cohort. Coordinates on the *x-axis* represent chromosomes. Negative logarithmic *P* values are shown on the *y-axis*.

TABLE II. Association results in the FHS cohort and in meta-analysis of replication cohorts for the 12 SNPs with the strongest evidence of association with IgE concentration*

Nearest gene	SNP	Chromosome	Position	Minor allele	MAF	FHS β	FHS *P* value	Replication† β	Replication† *P* value	Combined‡ β	Combined‡ *P* value
FCER1A	rs2251746	1	157538684	C	0.26	−0.084	**2.11E-12**	−0.089	**3.07E-15**	−0.087	**4.52E-26**
FCER1A	rs2494264	1	157533462	A	0.46	−0.064	**1.37E-09**	−0.067	**1.15E-11**	−0.066	**9.40E-20**
STAT6	rs1059513	12	55775976	C	0.09	−0.164	**2.87E-08**	−0.095	**2.08E-06**	−0.116	**1.99E-12**
IL13	rs20541	5	132023863	A	0.19	0.075	**3.55E-08**	0.086	**1.41E-11**	0.081	**3.41E-18**
HLA-G	rs2523809	6	29957598	T	0.13	0.085	2.40E-07	0.041	8.19E-03	0.062	**4.34E-08**
HLA-A	rs2517754	6	30004659	A	0.53	0.054	3.59E-07	0.060	2.73E-03	0.055	**3.61E-09**
FCER1A	rs4656784	1	157593504	G	0.19	−0.075	3.84E-07	−0.084	**7.43E-11**	−0.080	**1.68E-16**
STAT6	rs167769	12	55790042	T	0.35	0.056	5.18E-06	0.045	**1.47E-05**	0.049	**4.02E-10**
IL13	rs2243297	5	132027070	A	0.04	0.128	7.19E-05	0.127	**5.58E-05**	0.128	**1.54E-08**
HLA-A	rs2571391	6	30031817	C	0.32	−0.054	2.13E-06	−0.069	**7.43E-11**	−0.062	**1.23E-15**
DARC	rs13962	1	157442151	A	0.13	−0.087	1.52E-05	−0.087	**3.29E-07**	−0.087	**2.21E-11**
HLA-DQA2	rs2858331	6	32789255	G	0.44	0.048	2.03E-05	0.039	**1.51E-04**	0.043	**1.44E-08**

P values are expressed in scientific E notation in which 1.2E-3 denotes 1.2×10^{-3}.

*The SNPs in this table demonstrate an association with either a *P* value of less than .0007 in the meta-analysis of replication cohorts or a *P* value of less than 5×10^{-8} in the combined meta-analysis of the FHS discovery cohort and the replication cohorts. For the FHS analysis and the combined meta-analysis, *P* values that demonstrate genome-wide significance are shown in boldface. For the replication analysis, *P* values that demonstrate significance based on a value of less than .0007 are shown in boldface.

†Meta-analysis of replication cohorts only.

‡Meta-analysis of replication cohorts combined with the FHS cohort.

coefficient (0.06) for this association, suggesting that the findings are not heterogeneous with those of the GABRIEL study.

DISCUSSION

We found that SNPs in 3 gene regions, *FCER1A*, *STAT6*, and *IL13*, were associated with total IgE concentrations at a genome-wide significant level in the FHS cohort. The results confirm the findings from prior studies that have implicated these genes in the pathogenesis of IgE dysregulation. Additionally, we observed associations with SNPs near 3 other genes, *HLA-A*, *HLA-G*, and *HLA-DQA2*, for which relationships to IgE concentrations have not been clearly established.

Our analysis reveals associations that replicate in independent cohorts and/or reach genome-wide significance in meta-analyses combining the FHS cohort with replication cohorts in the region of the MHC superlocus on chromosome 6. Although MHC II antigens, particularly HLA-DRB1 and HLA-DQB1, have been consistently associated with atopic phenotypes in the genetic literature,[17,18] evidence for a genetic susceptibility through the classical MHC I antigens (HLA-A, HLA-B, and HLA-C) is less clear. The stronger association of MHC II antigens versus MHC I antigens in the literature is consistent with their functional roles in the immune system, with MHC I responsible for initiating cell-mediated immunity and targeting infected and cancer cells and MHC II responsible for mediating humoral immunity, including the production of IgE antibodies to allergenic antigens.

Three SNPs in or near the *HLA-A* gene, an MHC I antigen, were found to have *P* values of less than 2×10^{-7} in the FHS cohort, with the highest association seen for rs2571391 with a combined (FHS plus replication cohorts) meta-analysis *P* value of 1.23×10^{-15}. The first study to identify a linkage between *HLA-A*

haplotypes and ragweed allergy was published in 1972 by Levine et al,[19] although a subsequent larger study was unable to replicate the original findings.[20] In 1979, Marsh et al[21] published a regression analysis evaluating total IgE concentrations and found both positive (HLA-A2) and negative (HLA-A3) associations among the HLA-A antigens in patients with varying degrees of ragweed sensitivity. More recent studies have been unable to find significant associations between HLA-A and total IgE concentrations,[22] intrinsic or extrinsic asthma,[20] and mite-sensitive allergy in Greek and Venezuelan populations.[23,24] However, results published online from the B58C show associations (at conventional levels of significance) between log-transformed total IgE concentrations and the directly measured *HLA-A* subtypes *HLA*02*, **03*, and **29* (see the following: www.b58cgene.sgul.ac.uk/phenotype0.php?snp=hlaa_02&pheno=1; www.b58cgene.sgul.ac.uk/phenotype0.php?snp=hlaa_03&pheno=1; and www.b58cgene.sgul.ac.uk/phenotype0.php?snp=hlaa_29&pheno=1).

In the clinical literature many studies in children have demonstrated a relationship between viral infection, particularly respiratory syncytial virus, and the later development of asthma and increases in specific IgE concentrations.[25,26] One hypothesis is that MHC I polymorphisms might influence IgE concentrations through the processing of infectious pathogens, leading to immune dysregulation and, eventually, the clinical findings of atopy and asthma.

Our findings suggest that *HLA-A* might represent a susceptibility locus for IgE dysregulation. Although both MHC I and MHC II loci were found to be associated with total IgE concentrations, the association of *HLA-A* was consistently stronger in both the original FHS GWAS and in the meta-analysis than the association of the MHC II antigens *HLA-DQB1* and *HLA-DRB1*.

Additionally, an SNP near the *HLA-G* gene, a nonclassical MHC I antigen that has been associated with asthma and bronchial hyperresponsiveness in a positional candidate gene study,[27] was also found to reach genome-wide significance in the combined meta-analysis. *HLA-G* has not previously been associated with total IgE dysregulation but is thought to have immunomodulatory effects through actions on natural killer cells, T lymphocytes, and antigen-presenting cells.[28]

The *HLA-DQA2* region had the strongest association among MHC II loci, with rs2858331, an SNP within 27 kb from the *HLA-DQA2* gene, observed at a genome-wide significant level in the combined meta-analysis ($P = 1.44 \times 10^{-8}$). *HLA-DQA2* is thought to play a central role in peptide loading of MHC II molecules. Although it has never been associated with total IgE concentrations in the literature, a GWAS by Li et al[29] found a strong association of asthma with a nearby SNP, rs3916765, in the same region.

In the GABRIEL Consortium study[5] the rs9271300 SNP near *HLA-DRB1* was significantly associated with the total IgE concentration and was the strongest association observed for this phenotype. As discussed previously, this SNP was not found to be strongly associated with total IgE concentrations in the FHS cohort. It is not clear why the association with *HLA-DRB1* was considerably weaker in the FHS population compared with that seen in the GABRIEL population. This finding might be partly explained by the difference in study populations, as well as the difficulty in discriminating separate signals from the MHC superlocus. This discordance could also reflect the imperfect imputation of rs9271300 in our study.

The *DARC* gene on chromosome 1, which is in close proximity to *FCER1A*, was also identified as a susceptibility locus in the meta-analysis. The *DARC* gene was of particular interest given the biologic plausibility of DARC as a modulator of the body's inflammatory response and literature suggesting a role for *DARC* in the development of asthma and IgE dysregulation. A recent study by Vergara et al[30] investigated the relationship between *DARC* and asthma phenotypes in subjects of African descent. An SNP in the *DARC* promoter region, rs2814778, which is located in the same LD block as the top *DARC* SNP in the FHS cohort (www.broad.mit.edu.mpg/haploview), was found to be significantly associated with total IgE concentrations in Colombian and African Caribbean populations and with asthma in Colombian, Brazilian, and African Caribbean populations.

On the basis of the HapMap CEPH sample, there is low-to-moderate LD between the highest associated SNP in *DARC*, rs13962, and the nearby top SNP in *FCER1A*, rs2251746, with an r^2 value of 0.27 (see Fig E1; http://broad.mit.edu/mpg/snap). Conditional regression analysis, performed in both the FHS cohort and the 5 independent replication cohorts, revealed that the association of *DARC* with total IgE concentrations was not significant once rs2251746 was included in the model. Although this suggests that the *DARC* association in the study by Vergara et al[30] might be confounded by the effect of the neighboring *FCER1A* gene, differences in the populations studied in this meta-analysis (predominantly white and of European descent) and the Vergara et al study (African descent) likely play a role because the minor allele frequencies of the *DARC* SNP are significantly higher in populations of African descent compared with populations of European descent. Given the known function of the *DARC* receptor to act as a chemokine sink and modulate the inflammatory cascade,[31] the *DARC* associations with asthma and total IgE concentrations remain plausible, particularly in African populations. Further studies to better delineate the roles of *DARC* and *FCER1A* in IgE dysregulation are warranted.

Our study also confirmed, at a genome-wide significant level, the findings from prior genetic literature implicating *FCER1A*, *STAT6,* and *IL13* as susceptibility loci for IgE dysregulation. In the first published GWAS of total IgE concentrations, Weidinger et al[4] identified *FCER1A* as a susceptibility gene in a population-based German cohort. The top *FCER1A* SNP in the Weidinger et al study, rs2427837, was also highly associated with total IgE concentrations in the FHS cohort and had the second lowest *P* value among all top SNPs ($P = 9.82 \times 10^{-12}$). *STAT6 and IL13* are known to play significant roles in the pathogenesis of IgE dysregulation. *IL13*, in conjunction with *IL4*, is a critical mediator of the T_H2 allergic response, and *STAT6* is considered the master regulator of IgE class-switch recombination.[32,33] Our observation of a strong association of *STAT6* SNPs with IgE concentration confirms previous linkage and candidate gene studies that have shown *STAT6* genetic variants to be associated with food allergy,[34] atopic dermatitis,[35] asthma,[36] and total IgE concentrations.[37] In a recent review of asthma and atopy genetics, Ober and Hoffjan[3] identified *IL13* as one of 8 "elite" genes that had been associated with an asthma or atopy phenotype in greater than 10 studies.

The *RAD50* gene is located within 20 kb of *IL13* on chromosome 5. In the study by Weidinger et al,[4] as well as the subsequent GWAS investigating asthma by Li et al,[29] the *RAD50* gene was found to be more highly associated with total IgE concentrations and asthma, respectively, than the neighboring *IL13* gene. This is

in contrast to the FHS cohort, in which SNPs located in *IL13* were found to have the strongest associations in the region, with no SNPs within the *RAD50* gene found to have a *P* value of less than 10^{-4} (see Fig E3). The highest associated SNPs in each (rs1295686 for *IL13* rs2240032 for *RAD50*) were in moderate LD, with an r^2 value of 0.58 in the HapMap CEPH sample. Given the findings from 3 separate GWASs, it is difficult to separate the 2 signals on a genetic level. With murine models showing a T_H2 locus control region in the 3′ end of *RAD50*,[38] both *IL13* and *RAD50* are plausible candidate genes in the pathogenesis of IgE dysregulation and asthma.

In summary, this GWAS of plasma total IgE concentrations in the FHS cohort has identified potential susceptibility loci in the *HLA-A*, *HLA-G*, and *HLA-DQA2* gene regions for which an association with total IgE concentration has not been clearly established in the previous literature. We have also confirmed the associations of previously described genetic variants in *FCER1A*, *STAT6*, and *IL13* as risk factors for IgE dysregulation. On the basis of these findings, further genetic investigation of the relationship between *HLA* loci and total IgE concentrations and other atopic phenotypes is warranted. These findings might help target molecular pathways for future interventions to prevent or treat IgE-mediated allergy.

Clinical implications: This GWAS identified genetic loci near *HLA* genes that are associated with plasma total IgE concentrations. It also confirmed the association of susceptibility loci in *the FCER1A*, *STAT6*, and *IL13* genes.

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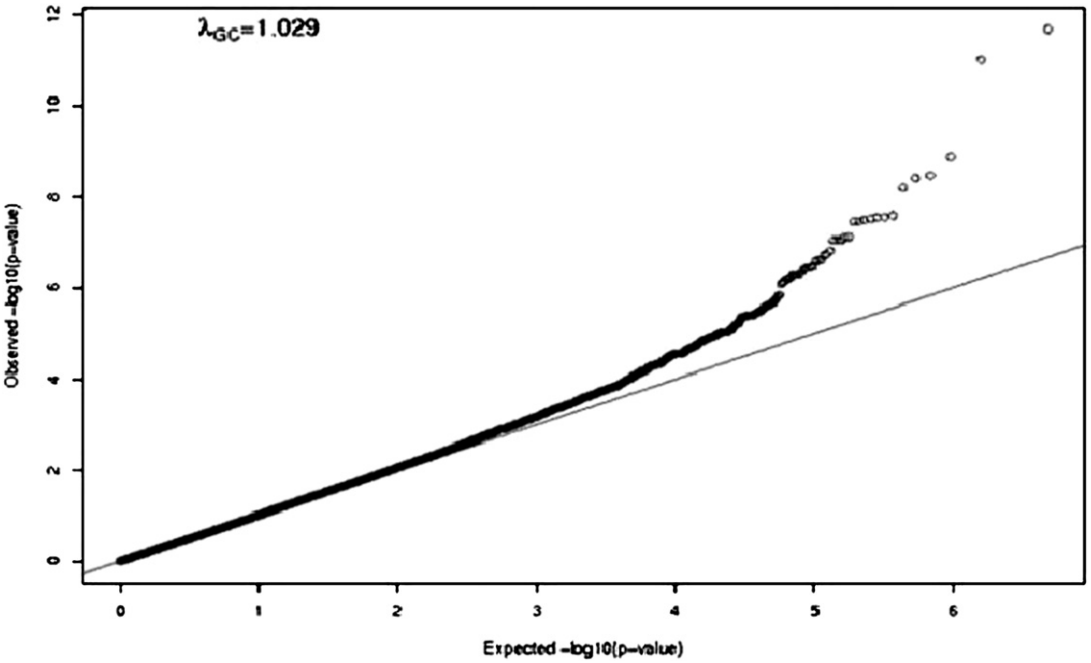

FIG E1. Quantile-quantile plot of log total IgE concentration GWAS results in the FHS cohort.

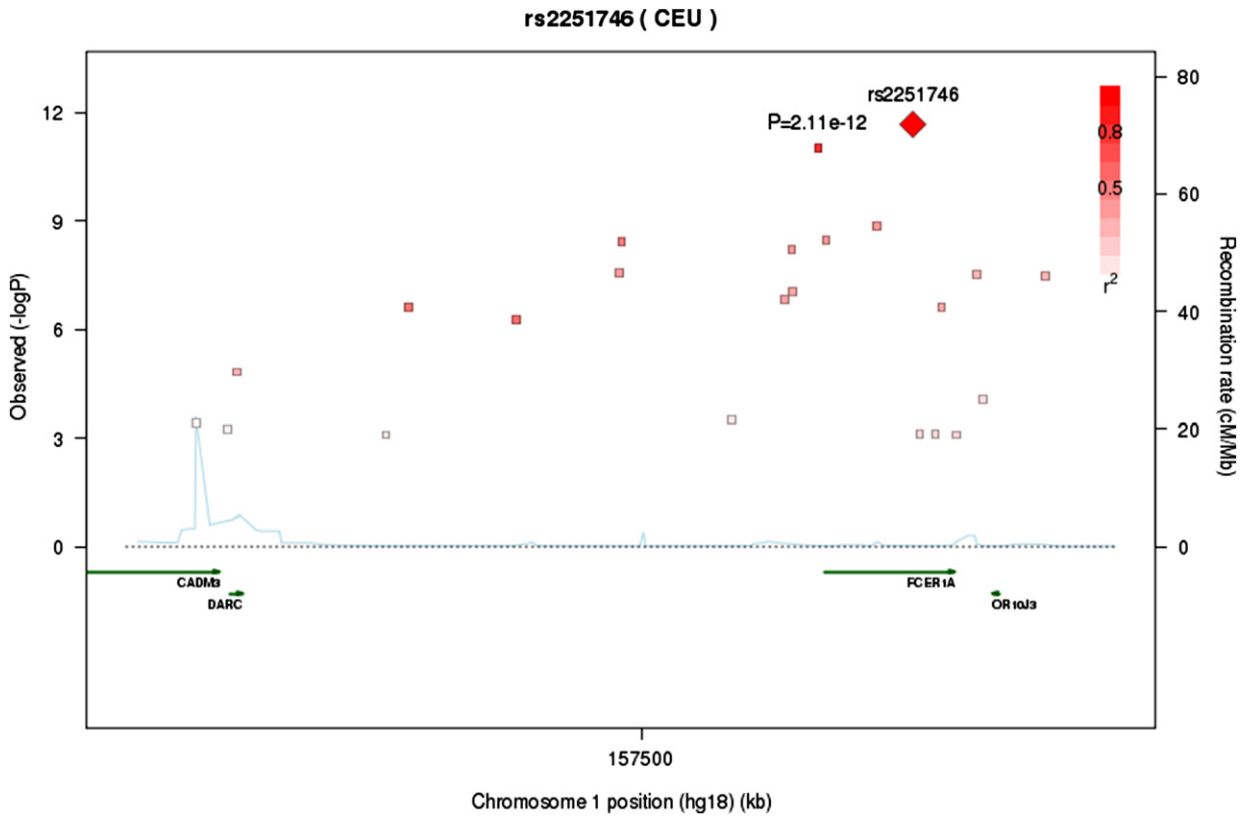

FIG E2. Association plot for SNPs in the *FCER1A* region in the FHS cohort. Negative log-transformed *P* values are on the *left y-axis*, and the recombination rate is on the *right y-axis*. The r^2 color scheme for SNPs based on the color gradient key is in the upper right corner of the figure. Only SNPs with *P* values of less than 10^{-3} are shown. *cM/Mb*, Centimorgans per megabase.

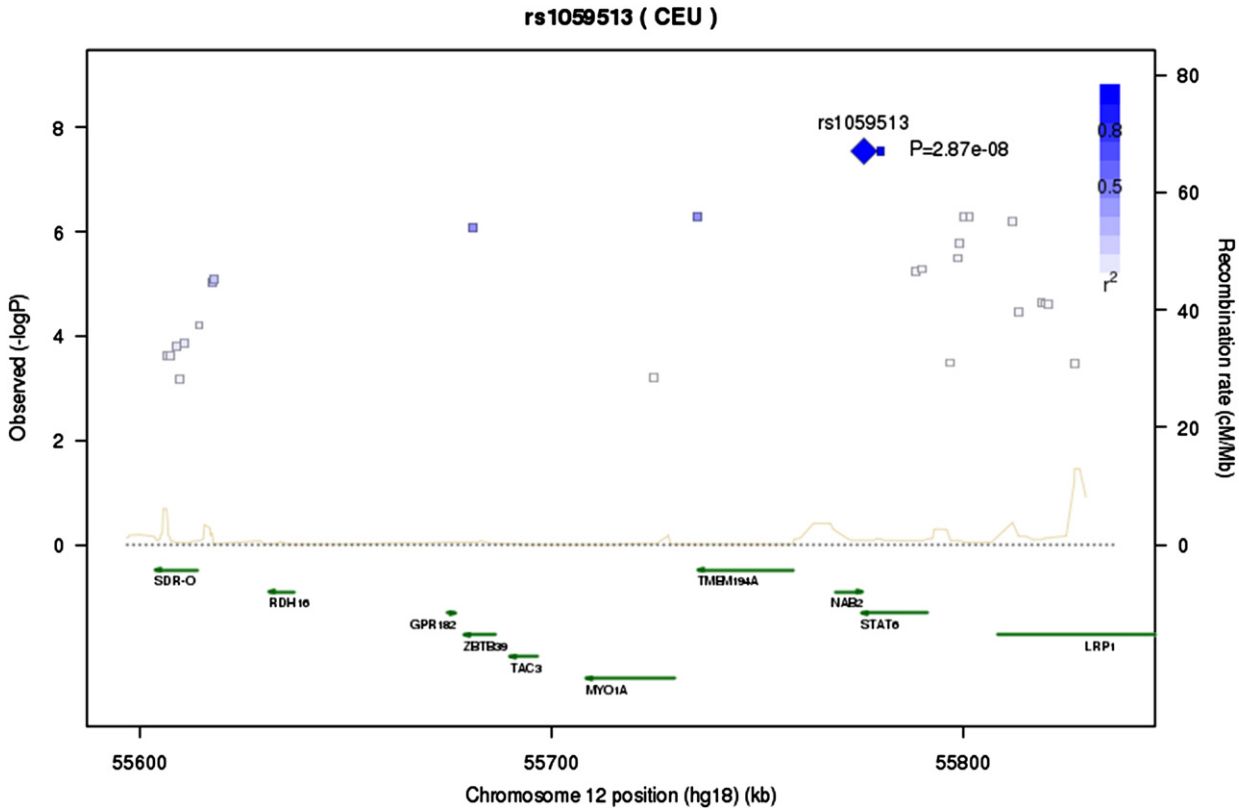

FIG E3. Association plot for SNPs in the *STAT6* region in the FHS cohort. Negative log-transformed *P* values are on the *left y-axis*, and the recombination rate is on the *right y-axis*. The r^2 color scheme for SNPs based on the color gradient key is in the upper right corner of the figure. Only SNPs with *P* values of less than 10^{-3} are shown. *cM/Mb*, Centimorgans per megabase.

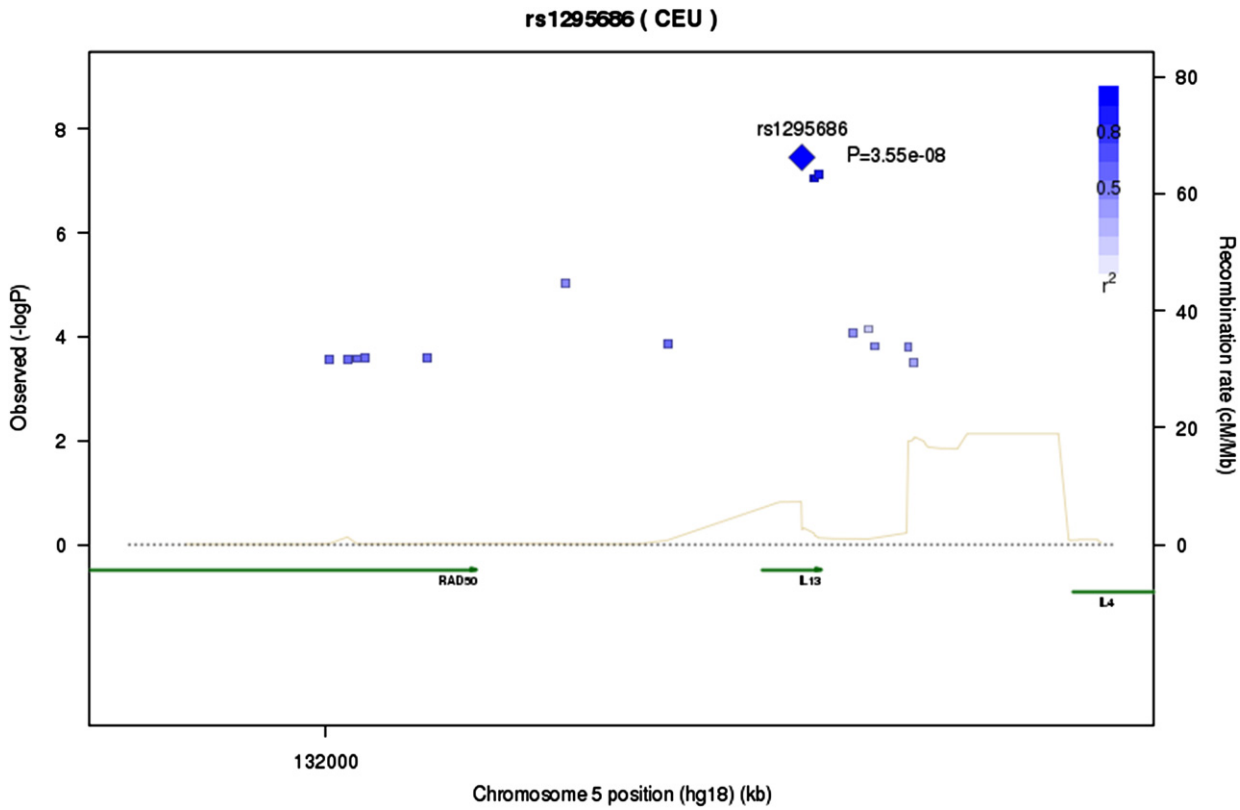

FIG E4. Association plot for SNPs in the *IL13* region in the FHS cohort. Negative log-transformed *P* values are on the *left y-axis*, and the recombination rate is on the *right y-axis*. The r^2 color scheme for SNPs based on the color gradient key is in the upper right corner of the figure. Only SNPs with *P* values of less than 10^{-3} are shown. *cM/Mb*, Centimorgans per megabase.

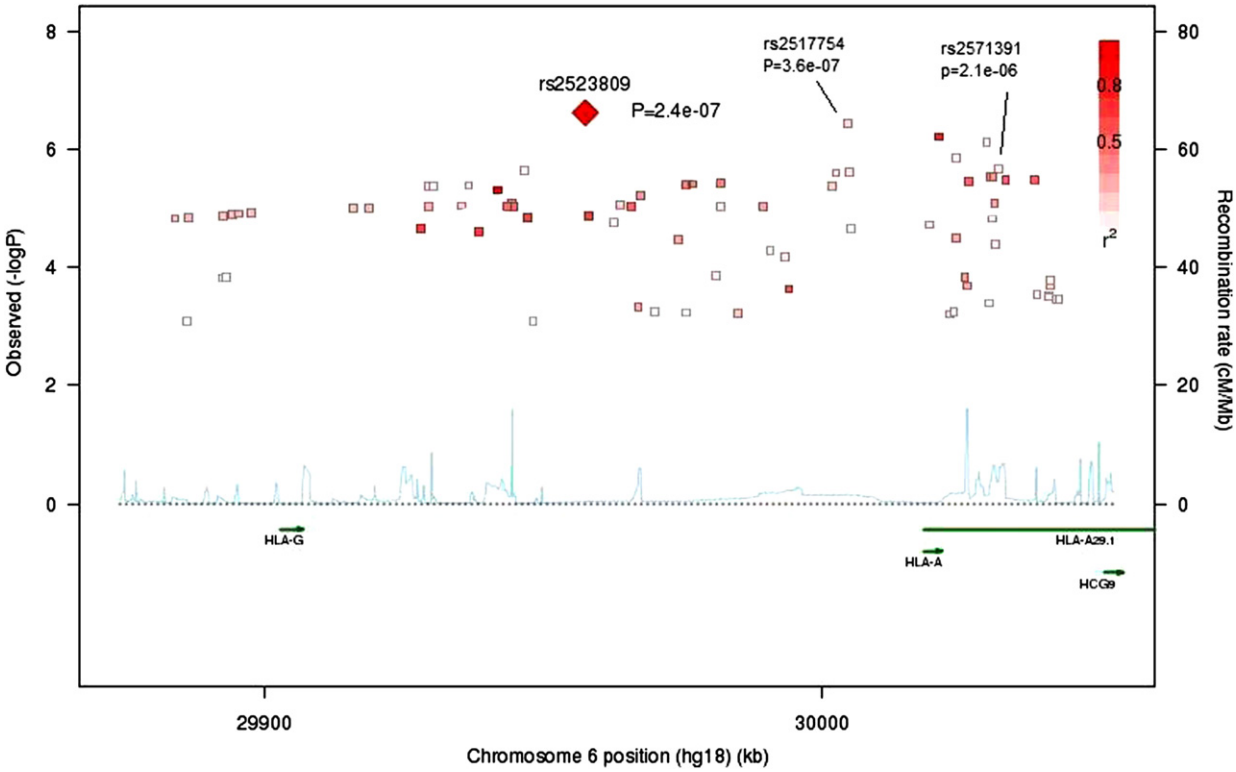

FIG E5. Association plot for SNPs in the *HLA-A* and *HLA-G* region in the FHS cohort. Negative log-transformed *P* values are on the *left y-axis,* and the recombination rate is on the *right y-axis*. The r^2 color scheme for SNPs based on the color gradient key is in the upper right corner of the figure. Only SNPs with *P* values of less than 10^{-3} are shown. *cM/Mb*, Centimorgans per megabase.

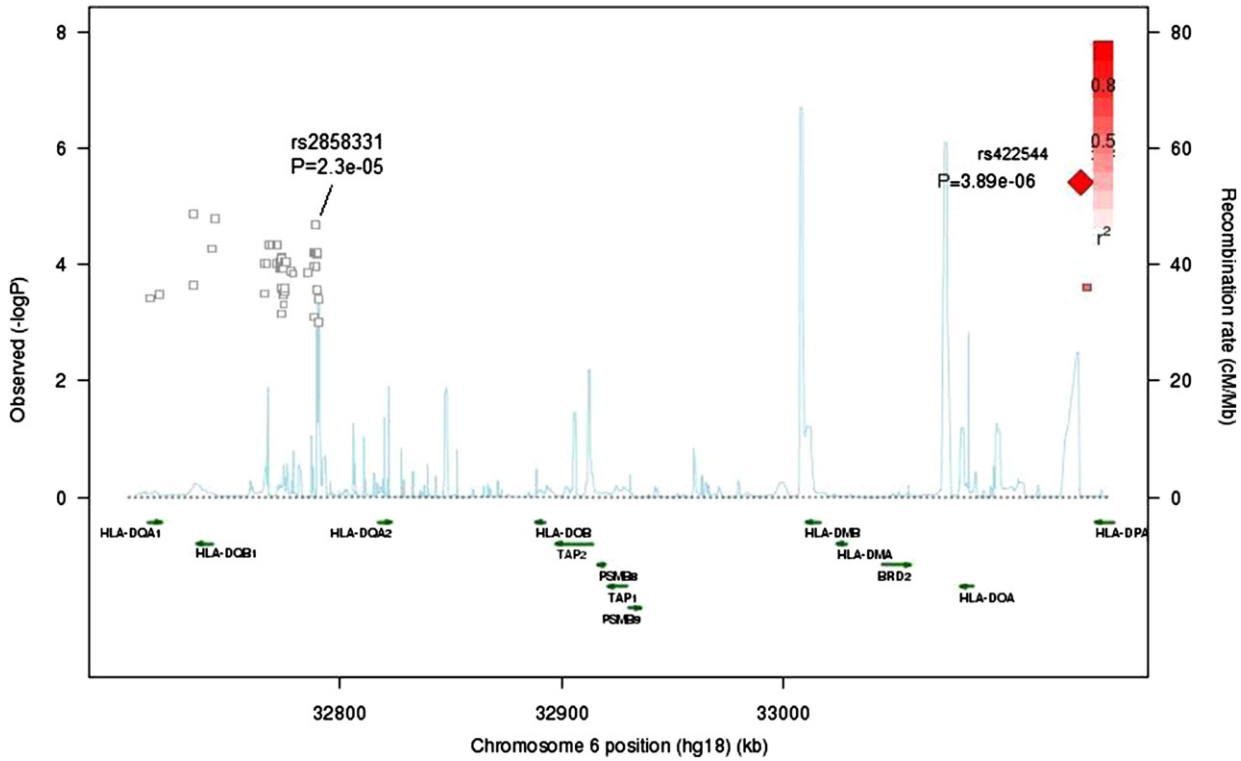

FIG E6. Association plot for SNPs in the *HLA-DQA2* region in the FHS cohort. Negative log-transformed *P* values are on the *left y-axis*, and the recombination rate is on the *right y-axis*. The r^2 color scheme for SNPs based on the color gradient key is in the upper right corner of the figure. Only SNPs with *P* values of less than 10^{-3} are shown. *cM/Mb*, Centimorgans per megabase.

TABLE E1. Descriptive characteristics of FHS cohorts and replication cohorts

	FHS original cohort (n = 860)	FHS offspring cohort (n = 2377)	FHS generation 3 cohort (n = 3681)	B58C (n = 3940)	KORA S3 (n = 1530)	KORA S4 (n = 1764)	CAMP (n = 575)
Age (y)	73 (11)	60 (9)	40 (9)	45 (0.4)	52 (10)	54 (9)	9 (2)
Female sex	56%	55%	53%	51%	50%	51%	41%
Current smoker	34%	11%	16%	23%	18%	20%	1%
Pack years	30 (22)	27 (23)	13 (13)	16 (12)	NA	NA	NA
Asthma	NA	8%	16%	17%	4%	6%	100%
Hay fever	NA	29%*	47%	23%	18%	17%	51%
Log IgE	1.59 (0.64)	1.55 (0.59)	1.51 (0.56)	1.50 (0.61)	1.63 (0.60)	1.54 (0.64)	2.63 (0.68)

For continuous variables, mean (SD) are shown.

NA, Not applicable.

*Prevalence of hay fever in the FHS offspring cohort were ascertained 3 years after plasma collection for total IgE measurement.

TABLE E2. Association results in the FHS cohort for the 527 SNPs with nominal *P* values < 10^{-4} for the association with IgE concentration*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
1	rs2251746	157538684	0.26	−0.08	**2.11E-12**	C	T	0.99	*FCER1A*	*OR10J3; FCER1A*
1	rs2427837	157525169	0.27	−0.08	**9.82E-12**	A	G	1.01		*OR10J3; FCER1A*
1	rs2494264	157533462	0.46	−0.06	**1.37E-09**	A	T	0.99	*FCER1A*	*OR10J3; FCER1A*
1	rs2247584	157526304	0.46	−0.06	**3.34E-09**	G	T	0.99	*FCER1A*	*OR10J3; FCER1A*
1	rs2511211	157497095	0.22	−0.08	**3.80E-09**	G	T	0.82		*OR10J3; CADM3; DARC; FCER1A*
1	rs2427836	157521388	0.46	−0.06	**6.07E-09**	C	T	1		*OR10J3; FCER1A*
1	rs2494257	157496722	0.46	−0.06	**2.63E-08**	A	T	0.99		*OR10J3; CADM3; DARC; FCER1A*
12	rs1059513	55775976	0.09	−0.16	**2.87E-08**	C	T	0.39	*STAT6*	*KIAA0286; NAB2; STAT6; MYO1A; LRP1*
12	rs3024971	55779994	0.09	−0.17	**2.88E-08**	G	T	0.38	*STAT6*	*KIAA0286; NAB2; STAT6; MYO1A; LRP1*
1	rs2494251	157547775	0.44	−0.06	**3.12E-08**	A	G	0.97		*OR10J3; FCER1A*
1	rs12724895	157557669	0.44	−0.06	**3.38E-08**	A	T	0.97		*OR10J3; FCER1A*
5	rs1295686	132023742	0.19	0.07	**3.55E-08**	T	C	0.99	*IL13*	*RAD50;IL13; KIF3A; IL4*
5	rs20541	132023863	0.19	0.07	**3.55E-08**	A	G	0.99	*IL13*	*RAD50; IL13; KIF3A; IL4*
1	rs12141365	157606923	0.09	−0.12	7.52E-08	C	T	0.64		*OR10J3*
5	rs847	132024568	0.19	0.08	7.60E-08	T	C	0.9	*IL13*	*RAD50; IL13; KIF3A; IL4*
5	rs1295685	132024344	0.19	0.07	8.93E-08	A	G	0.92	*IL13*	*RAD50; IL13; KIF3A; IL4*
1	rs2511214	157521490	0.48	0.06	8.99E-08	G	T	0.97		*OR10J3; FCER1A*
5	rs848	132024399	0.19	0.07	9.01E-08	A	C	0.92	*IL13*	*RAD50; IL13; KIF3A; IL4*
1	rs2494262	157520296	0.48	0.06	1.51E-07	C	A	0.98		*OR10J3; FCER1A*
1	rs4656236	157677599	0.25	−0.06	1.77E-07	A	G	1.01		*OR10J1*
1	rs7540542	157696951	0.25	−0.06	1.87E-07	T	G	1.01		*OR10J1*
6	rs2523809	29957598	0.13	0.08	2.40E-07	T	G	0.93		*HLA-G*
1	rs863013	157466644	0.32	−0.06	2.43E-07	T	G	0.95		*CADM3; DARC; FCER1A*
1	rs2252226	157542777	0.45	0.06	2.49E-07	C	T	0.98	*FCER1A*	*OR10J3; FCER1A*
1	rs12133577	157698902	0.46	0.05	3.33E-07	C	T	0.98		*OR10J1*
1	rs11265204	157706537	0.46	0.05	3.39E-07	A	G	0.98		*OR10J1*
1	rs12034243	157708065	0.46	0.05	3.55E-07	G	A	0.97		*OR10J1*
6	rs2517754	30004659	0.53	0.05	3.59E-07	A	G	0.96		*HLA-A; HCG9*
1	rs4656784	157593504	0.19	−0.07	3.84E-07	G	A	0.8		*OR10J3; FCER1A*
1	rs17019567	210922546	0.1	−0.09	4.33E-07	G	A	0.98		*NSL1; SNFT; FAM71A*
1	rs12118201	157663565	0.19	−0.07	4.69E-07	T	C	0.82		*OR10J1*
12	rs11172086	55735473	0.05	−0.15	5.22E-07	T	C	0.66		*KIAA0286; NAB2; STAT6; ZBTB39; MYO1A; TAC3; GPR182*
1	rs863018	157481950	0.32	−0.06	5.25E-07	T	C	0.93		*CADM3; DARC; FCER1A*
12	rs12298170	55801630	0.37	0.06	5.30E-07	G	A	0.88		*KIAA0286; NAB2; STAT6; LRP1*
12	rs12309413	55800146	0.37	0.06	5.31E-07	G	C	0.88		*KIAA0286; NAB2; STAT6; LRP1*
1	rs10908714	157606977	0.46	0.05	6.07E-07	T	A	0.97		*OR10J3*
6	rs3823343	30021090	0.2	0.07	6.12E-07	G	A	1	*HLA-A*	*HLA-A; HCG9*
12	rs4759275	55812023	0.37	0.06	6.53E-07	A	G	0.85	*LRP1*	*KIAA0286; NAB2; STAT6; LRP1*
6	rs3130214	33182690	0.12	−0.08	6.57E-07	C	G	0.92		*COL11A2; HLA-DPB1; HLA-DPA1*
6	rs3135021	33153536	0.26	0.06	7.23E-07	A	G	0.95	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2517703	30029679	0.31	−0.06	7.77E-07	T	C	0.91		*HLA-A; HCG9*
12	rs3741578	55680902	0.05	−0.14	8.30E-07	C	G	0.73	*ZBTB39*	*KIAA0286; ZBTB39; MYO1A; RDH16; TAC3; GPR182*
6	rs2517719	30024232	0.23	−0.07	1.43E-06	C	G	0.79		*HLA-A; HCG9*
16	rs1801275	27281901	0.2	−0.06	1.54E-06	G	A	1	*IL4R*	*IL21R; IL4R*
12	rs11172106	55799142	0.39	0.05	1.65E-06	G	C	0.92		*KIAA0286; NAB2; STAT6; LRP1*
16	rs2234900	27281473	0.1	−0.08	1.81E-06	C	T	0.97	*IL4R*	*IL21R; IL4R*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
16	rs1805012	27281465	0.1	−0.08	1.87E-06	C	T	0.97	*IL4R*	*IL21R; IL4R*
9	rs13295276	33843118	0.15	0.07	2.07E-06	A	G	1.01	*UBE2R2*	*PRSS3; UBE2R2*
6	rs2571391	30031817	0.32	−0.05	2.13E-06	C	A	0.94		*HLA-A; HCG9*
6	rs2844821	29946621	0.29	−0.06	2.24E-06	C	T	0.95		*HLA-G*
16	rs2234898	27281416	0.1	−0.08	2.37E-06	T	G	0.98	*IL4R*	*IL21R; IL4R*
16	rs1805011	27281373	0.1	−0.08	2.39E-06	C	A	0.98	*IL4R*	*IL21R; IL4R*
6	rs404655	30004947	0.06	0.11	2.46E-06	A	G	0.98		*HLA-A; HCG9*
6	rs386014	30002608	0.06	0.11	2.50E-06	C	G	0.98		*HLA-A; HCG9*
7	rs17469756	100924034	0.52	−0.05	2.57E-06	G	A	0.97	*EMID2*	*EMID2*
6	rs2395175	32513004	0.14	−0.07	2.71E-06	A	G	0.93		*HLA-DRA; BTNL2*
6	rs9260607	30030835	0.09	0.09	2.93E-06	C	T	0.98		*HLA-A; HCG9*
6	rs9260587	30030471	0.09	0.09	2.95E-06	G	A	0.99		*HLA-A; HCG9*
12	rs12368672	55798737	0.36	0.05	3.21E-06	G	C	0.98		*KIAA0286; NAB2; STAT6; LRP1*
6	rs2523942	30033065	0.08	0.09	3.32E-06	G	T	1.01		*HLA-A; HCG9*
6	rs2517688	30038302	0.08	0.09	3.33E-06	T	C	1.01		*HLA-A; HCG9*
7	rs10282247	25045068	0.25	0.1	3.43E-06	C	T	0.31		*OSBPL3*
6	rs660895	32685358	0.18	−0.07	3.46E-06	G	A	0.97		*HLA-DQA1; HLA-DQB1; HLA-DRB1*
6	rs3094674	30026517	0.09	0.09	3.58E-06	G	C	1.02		*HLA-A; HCG9*
6	rs3115637	30026432	0.09	0.09	3.59E-06	G	A	1.02		*HLA-A; HCG9*
6	rs433518	29981788	0.09	0.09	3.80E-06	C	G	1.01		*HLA-A*
20	rs6049203	23813477	0.13	−0.07	3.85E-06	T	C	0.98		*CST2; CST5*
20	rs6049205	23815670	0.13	−0.07	3.87E-06	G	A	0.99		*CST5*
6	rs2517904	29976963	0.09	0.09	3.87E-06	G	A	1.01		*HLA-A*
6	rs2517905	29976812	0.09	0.09	3.88E-06	C	T	1.01		*HLA-A*
6	rs422544	33134088	0.25	0.06	3.89E-06	C	A	0.85		*HLA-DPB1; HLA-DPA1; HLA-DOA*
20	rs6049224	23837307	0.14	−0.07	3.91E-06	C	G	0.98		*CST5*
6	rs1611575	29975788	0.09	0.09	3.92E-06	C	T	1.01		*HLA-A*
20	rs6036568	23831788	0.14	−0.07	4.00E-06	G	A	0.98		*CST5*
20	rs6138159	23821518	0.14	−0.07	4.11E-06	G	A	0.98		*CST5*
6	rs2523822	29936639	0.28	−0.05	4.12E-06	G	A	0.97		*HLA-G*
20	rs6138158	23820072	0.14	−0.07	4.22E-06	G	A	0.99		*CST5*
6	rs2517774	30001961	0.03	0.18	4.26E-06	T	C	0.72		*HLA-A; HCG9*
6	rs2975033	29930240	0.28	−0.05	4.27E-06	A	G	0.97		*HLA-G*
6	rs2734982	29929546	0.28	−0.05	4.30E-06	T	G	0.97		*HLA-G*
20	rs4074167	23816926	0.14	−0.07	4.37E-06	C	G	0.99		*CST5*
6	rs3117224	33167603	0.17	−0.07	4.90E-06	C	G	0.93		*HLA-DPA1; HLA-DPB1*
6	rs2734973	29941927	0.14	0.07	4.93E-06	T	C	1.01		*HLA-G*
12	rs167769	55790042	0.35	0.06	5.18E-06	T	C	0.83	*STAT6*	*KIAA0286; NAB2;STAT6; MYO1A; LRP1*
12	rs324011	55788449	0.37	0.06	5.82E-06	T	C	0.79	*STAT6*	*KIAA0286; NAB2; STAT6; MYO1A; LRP1*
20	rs6049227	23839497	0.19	−0.06	5.90E-06	C	G	0.95		*CST5*
5	rs11745587	131824821	0.34	0.05	5.95E-06	A	G	1	*LOC441108*	*LOC441108; IRF1*
6	rs2517817	29967496	0.09	0.08	6.13E-06	T	C	1.01		*HLA-A*
10	rs10458771	88152218	0.14	−0.07	6.37E-06	A	G	1.01		*GRID1; WAPAL*
6	rs2905715	31459509	0.14	0.07	6.39E-06	C	T	0.86		*HLA-B*
16	rs1805015	27281681	0.16	−0.07	6.70E-06	C	T	0.99	*IL4R*	*IL21R; IL4R*
10	rs10788500	88146819	0.14	−0.07	6.77E-06	A	G	1.01		*GRID1; WAPAL*
7	rs17208431	24696636	0.05	0.18	7.36E-06	C	T	0.37		*MPP6; DFNA5*
6	rs9268543	32492779	0.14	−0.07	7.36E-06	T	A	0.88		*HLA-DRA; BTNL2; C6orf10*
11	rs17565975	111092160	0.53	0.05	7.89E-06	A	G	0.97	*SNF1LK2*	*SNF1LK2; PPP2R1B*
9	rs13302810	33878000	0.17	0.06	7.98E-06	A	C	1.02	*UBE2R2*	*UBAP2; UBE2R2*
12	rs725956	55618203	0.11	−0.08	8.11E-06	G	A	1.02		*RDH16; GPR182; SDR-O*
6	rs1611634	29944345	0.09	0.08	8.17E-06	T	C	1.02		*HLA-G*
6	rs9260622	30031107	0.1	0.08	8.30E-06	C	G	0.91		*HLA-A; HCG9*
9	rs13287325	33919030	0.17	0.06	9.02E-06	A	G	1.02	*UBAP2*	*UBAP2; UBE2R2*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
6	rs1611610	29963797	0.04	0.12	9.02E-06	T	G	1		*HLA-A; HLA-G*
6	rs1611697	29935364	0.04	0.12	9.10E-06	C	A	1		*HLA-G*
20	rs6083320	23839641	0.24	−0.05	9.28E-06	A	G	0.98		*CST5*
5	rs2158177	132011957	0.18	0.07	9.31E-06	G	A	0.69		*RAD50; IL13; KIF3A; IL4*
6	rs2571410	29989443	0.13	0.07	9.33E-06	G	C	1.01		*HLA-A*
6	rs1611628	29965751	0.09	0.08	9.34E-06	C	T	1.02		*HLA-A; HLA-G*
6	rs9259594	29981942	0.28	0.05	9.38E-06	G	A	0.91		*HLA-A*
12	rs10506348	55617637	0.11	−0.07	9.40E-06	G	A	1.02		*RDH16; GPR182; SDR-O*
6	rs4711206	30095163	0.27	−0.05	9.40E-06	A	G	0.98		*PPP1R11; RNF39; ZNRD1; HCG9*
6	rs9348835	30093609	0.27	−0.05	9.40E-06	G	A	0.98		*PPP1R11; RNF39; ZNRD1; HCG9*
6	rs1611636	29944682	0.04	0.12	9.49E-06	C	A	1		*HLA-G*
6	rs2247726	29929413	0.04	0.12	9.51E-06	A	G	1		*HLA-G*
6	rs9357092	30092231	0.27	−0.05	9.55E-06	A	G	0.98		*PPP1R11; RNF39; ZNRD1; HCG9*
6	rs1611638	29944832	0.09	0.08	9.58E-06	C	G	1.02		*HLA-G*
6	rs1611631	29943633	0.09	0.08	9.59E-06	T	C	1.02		*HLA-G*
6	rs2517808	30058990	0.04	0.13	9.61E-06	T	C	1.01		*HLA-A; HCG9*
6	rs1611135	29918719	0.04	0.12	9.92E-06	C	T	1		*HLA-G*
16	rs9929374	21151451	0.4	0.08	9.92E-06	G	A	0.32		*TMEM159; CRYM; ZP2; ANKS4B*
6	rs1233320	29916011	0.04	0.12	1.00E-05	G	C	1		*HLA-G*
6	rs2844510	31518387	0.11	0.07	1.01E-05	T	G	1.01		*MICB; HCP5*
6	rs9295826	30078906	0.27	−0.05	1.04E-05	T	C	0.98		*HLA-A; ZNRD1; HCG9*
6	rs4959039	30065048	0.26	−0.05	1.04E-05	G	A	0.98		*HLA-A; HCG9*
16	rs3024676	27281059	0.16	−0.06	1.07E-05	A	C	1	*IL4R*	*IL21R; IL4R*
6	rs4947244	30062343	0.26	−0.05	1.07E-05	G	C	0.98		*HLA-A; HCG9*
6	rs9393986	30081505	0.27	−0.05	1.07E-05	C	T	0.98		*HLA-A; ZNRD1; HCG9*
6	rs4713281	30086331	0.27	−0.05	1.14E-05	A	G	0.98		*PPP1R11; RNF39; ZNRD1; HCG9*
6	rs9277557	33164672	0.25	−0.05	1.15E-05	C	T	0.95		*HLA-DPB1; HLA-DPA1*
6	rs2275855	30084768	0.27	−0.05	1.18E-05	C	T	0.98		*PPP1R11; HCG9; ZNRD1*
5	rs12655409	153940678	0.27	−0.05	1.20E-05	G	A	1.01		
6	rs9405044	30114744	0.27	−0.05	1.21E-05	A	G	0.97		*PPP1R11; RNF39; ZNRD1*
1	rs12132451	157580466	0.45	−0.05	1.21E-05	A	G	0.96		*OR10J3; FCER1A*
6	rs1611146	29897502	0.04	0.12	1.22E-05	C	T	0.99		*HLA-G*
1	rs12128960	157580071	0.45	−0.05	1.22E-05	T	A	0.96		*OR10J3; FCER1A*
1	rs10908709	157586804	0.45	−0.05	1.22E-05	A	C	0.96		*OR10J3; FCER1A*
1	rs10908710	157587603	0.45	−0.05	1.22E-05	A	G	0.96		*OR10J3; FCER1A*
1	rs11265178	157595670	0.45	−0.05	1.23E-05	A	C	0.97		*OR10J3; FCER1A*
6	rs2246283	29895216	0.04	0.12	1.24E-05	T	C	0.99		*HLA-G*
6	rs2743932	29894222	0.04	0.12	1.25E-05	T	C	0.99		*HLA-G*
6	rs2743933	29894199	0.04	0.12	1.26E-05	C	T	0.99		*HLA-G*
6	rs3128928	33182590	0.18	−0.06	1.29E-05	A	C	0.93		*COL11A2; HLA-DPB1; HLA-DPA1*
6	rs9380150	30118471	0.27	−0.05	1.30E-05	C	T	0.92		*PPP1R11; RNF39; ZNRD1*
2	rs7579979	15729712	0.39	−0.05	1.31E-05	G	A	0.98		*DDX1*
6	rs6906021	32734289	0.49	0.05	1.33E-05	C	T	0.98		*HLA-DQB1; HLA-DQA1*
3	rs1801725	123486447	0.17	0.06	1.33E-05	T	G	0.96	*CASR*	*CSTA; CASR*
2	rs10929380	15730028	0.39	−0.05	1.34E-05	A	G	0.98		*DDX1*
6	rs2743934	29892496	0.04	0.12	1.34E-05	T	C	0.98		*HLA-G*
20	rs13037793	23820373	0.35	−0.05	1.36E-05	A	T	0.85		*CST5*
6	rs2523807	29958253	0.11	0.08	1.38E-05	G	A	0.98		*HLA-G*
14	rs7158953	51870485	0.11	−0.08	1.40E-05	A	C	0.9		*PTGDR; PTGER2*
3	rs17251221	123475937	0.17	0.06	1.40E-05	G	A	0.96	*CASR*	*CSTA; CASR*
6	rs886398	29947247	0.11	0.08	1.41E-05	T	C	0.98		*HLA-G*
5	rs6894249	131825446	0.36	0.05	1.43E-05	G	A	1	*LOC441108*	*LOC441108; IRF1*
6	rs9393987	30117148	0.27	−0.05	1.45E-05	T	C	0.97		*PPP1R11; RNF39; ZNRD1*
6	rs1611174	29886261	0.04	0.12	1.45E-05	C	T	0.97		*HLA-G*
13	rs9512492	26488400	0.46	0.05	1.48E-05	T	C	0.94		*USP12*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
6	rs16896742	30030719	0.35	−0.05	1.48E-05	G	A	0.93		*HLA-A; HCG9*
6	rs3998759	29883883	0.04	0.12	1.48E-05	T	G	0.97		*HLA-G*
6	rs2523755	29874061	0.04	0.12	1.51E-05	G	A	0.97		*HLA-G*
1	rs13962	157442151	0.13	−0.09	1.52E-05	A	G	0.6	*DARC*	*CADM3; DARC*
6	rs4711207	30113733	0.27	−0.05	1.55E-05	A	C	0.96		*PPP1R11; RNF39; ZNRD1; HCG9*
6	rs2735036	29864850	0.04	0.12	1.55E-05	T	C	0.96		*HLA-G*
6	rs3828800	32744041	0.16	−0.06	1.59E-05	A	G	0.99		*HLA-DQB1; HLA-DQA1*
17	rs11657292	52877854	0.33	−0.06	1.62E-05	T	C	0.65	*MSI2*	*MSI2*
4	rs3893296	37576766	0.25	0.05	1.66E-05	C	A	0.96	*TBC1D1*	*PGM2; TBC1D1*
4	rs3893297	37576777	0.25	0.05	1.66E-05	A	G	0.97	*TBC1D1*	*PGM2; TBC1D1*
1	rs1391565	218194851	0.27	0.05	1.67E-05	G	C	0.85		*EPRS; SLC30A10*
2	rs7593726	15731291	0.4	−0.05	1.72E-05	T	C	1		*DDX1*
6	rs1054175	29962774	0.23	−0.06	1.74E-05	C	G	0.72		*HLA-A; HLA-G*
6	rs6905389	30427909	0.06	0.1	1.76E-05	A	C	0.97		*RPP21; TRIM39*
6	rs2844519	31479409	0.17	−0.06	1.80E-05	T	C	0.98		*HLA-B; HCP5*
6	rs9277518	33162280	0.31	−0.05	1.85E-05	C	T	0.95	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277458	33161145	0.31	−0.05	1.86E-05	C	A	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277431	33160006	0.31	−0.05	1.89E-05	T	C	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2517725	30019305	0.03	0.14	1.89E-05	G	A	0.85	*HLA-A*	*HLA-A; HCG9*
11	rs4420222	90644663	0.02	−0.15	1.94E-05	C	T	0.92		
12	rs10506786	77376000	0.15	0.06	1.95E-05	A	G	1.01		
6	rs9277424	33159843	0.31	−0.05	1.98E-05	C	A	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277421	33159798	0.31	−0.05	1.98E-05	A	G	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
12	rs4761417	77373718	0.15	0.06	1.98E-05	A	G	1		
6	rs9277410	33159618	0.31	−0.05	2.00E-05	A	G	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277409	33159602	0.31	−0.05	2.01E-05	G	C	0.94	*HLA-DPB1*	*HLA-DPA1; HLA-DPB1*
6	rs9277396	33159117	0.31	−0.05	2.01E-05	A	G	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277395	33159029	0.31	−0.05	2.02E-05	G	A	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2858331	32789255	0.44	0.05	2.03E-05	G	A	0.92		*HLA-DQB1; HLA-DQA2*
6	rs9277394	33158948	0.31	−0.05	2.03E-05	T	A	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs6904594	117628064	0.04	0.13	2.04E-05	C	G	0.86		
6	rs3097652	33165813	0.3	−0.05	2.10E-05	T	C	0.98		*HLA-DPA1; HLA-DPB1*
6	rs3117225	33165689	0.3	−0.05	2.11E-05	A	G	0.98		*HLA-DPB1; HLA-DPA1*
6	rs3128921	33178727	0.26	−0.05	2.12E-05	A	C	0.99		*COL11A2; HLA-DPB1; HLA-DPA1*
12	rs12579704	77378878	0.16	0.06	2.14E-05	A	T	1.02		
6	rs2508050	29928026	0.1	0.08	2.17E-05	C	T	0.99		*HLA-G*
6	rs3135024	33155444	0.23	−0.05	2.17E-05	C	T	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9400988	117621203	0.04	0.13	2.18E-05	A	C	0.86		
6	rs2517749	30005238	0.23	−0.06	2.20E-05	A	T	0.73		*HLA-A; HCG9*
12	rs11109877	77379733	0.16	0.06	2.21E-05	G	A	1.02		
16	rs4533297	77994546	0.41	−0.05	2.22E-05	T	A	0.68		
6	rs3091282	33165176	0.3	−0.05	2.22E-05	C	G	0.98		*HLA-DPB1; HLA-DPA1*
6	rs3130188	33165154	0.3	−0.05	2.24E-05	C	T	0.98		*HLA-DPB1; HLA-DPA1*
12	rs11109950	77391717	0.16	0.06	2.26E-05	G	T	0.95		
6	rs2295118	33168870	0.3	−0.05	2.32E-05	T	C	0.98		*HLA-DPB1; HLA-DPA1*
12	rs1385526	55819016	0.31	0.05	2.35E-05	C	G	0.99	*LRP1*	*NAB2; STAT6; LRP1*
12	rs4759277	55819957	0.31	0.05	2.38E-05	A	C	0.99	*LRP1*	*NAB2; STAT6; LRP1*
6	rs9277412	33159667	0.31	−0.05	2.39E-05	T	C	0.93	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
12	rs1466535	55820737	0.31	0.05	2.41E-05	A	G	0.99	*LRP1*	*NAB2; STAT6; LRP1*
9	rs13296914	34044826	0.17	0.06	2.42E-05	T	C	0.97		*UBAP2; WDR40A*
12	rs12315707	77404575	0.16	0.06	2.51E-05	T	C	0.9		
2	rs1401743	154255169	0.42	0.05	2.52E-05	G	A	0.97		
6	rs2517829	29938508	0.1	0.08	2.54E-05	G	C	1		*HLA-G*
6	rs885912	30282612	0.22	0.05	2.60E-05	A	C	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
6	rs2064476	33181300	0.31	−0.05	2.65E-05	G	A	0.98		*COL11A2; HLA-DPB1; HLA-DPA1*
2	rs6732761	141051207	0.45	0.04	2.65E-05	C	A	0.98	*LRP1B*	*LRP1B*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
6	rs3117228	33164413	0.3	−0.05	2.67E-05	T	G	0.98		*HLA-DPB1; HLA-DPA1*
17	rs10163516	66519729	0.02	0.23	2.70E-05	A	G	0.43		
6	rs9277554	33163516	0.3	−0.05	2.77E-05	T	C	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277555	33163583	0.3	−0.05	2.77E-05	A	G	0.98		*HLA-DPB1; HLA-DPA1*
6	rs3128963	33163758	0.3	−0.05	2.77E-05	T	C	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277553	33163494	0.3	−0.05	2.77E-05	C	T	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277547	33163345	0.3	−0.05	2.77E-05	A	C	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277548	33163368	0.3	−0.05	2.77E-05	T	C	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277546	33163324	0.3	−0.05	2.77E-05	G	T	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277542	33163225	0.3	−0.05	2.77E-05	C	T	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277541	33163136	0.3	−0.05	2.77E-05	G	A	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277540	33163101	0.3	−0.05	2.77E-05	G	A	0.98		*HLA-DPB1;HLA-DPA1*
6	rs9277359	33158002	0.31	−0.05	2.77E-05	A	C	0.94	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277538	33163025	0.3	−0.05	2.77E-05	G	A	0.98		*HLA-DPB1; HLA-DPA1*
6	rs9277534	33162785	0.3	−0.05	2.77E-05	G	A	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277533	33162699	0.3	−0.05	2.77E-05	T	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs1042544	33162435	0.3	−0.05	2.77E-05	G	A	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs929	33162597	0.3	−0.05	2.77E-05	A	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs1042448	33162320	0.3	−0.05	2.78E-05	A	T	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277515	33162246	0.3	−0.05	2.78E-05	A	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277497	33162069	0.3	−0.05	2.78E-05	T	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277492	33161960	0.3	−0.05	2.78E-05	C	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277479	33161767	0.3	−0.05	2.78E-05	G	A	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277477	33161750	0.3	−0.05	2.78E-05	A	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277470	33161455	0.3	−0.05	2.78E-05	C	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277468	33161433	0.3	−0.05	2.78E-05	T	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277469	33161446	0.3	−0.05	2.78E-05	T	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277463	33161285	0.3	−0.05	2.79E-05	T	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2021722	30282110	0.22	0.05	2.80E-05	T	C	1.01	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
6	rs9277460	33161230	0.3	−0.05	2.80E-05	A	G	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277450	33160673	0.3	−0.05	2.81E-05	G	T	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277437	33160228	0.3	−0.05	2.82E-05	G	A	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2904781	31565396	0.2	0.06	2.83E-05	G	C	0.94		*NFKBIL1; MICB; BAT1; HCP5; ATP6V1G2; MCCD1*
6	rs9277434	33160164	0.3	−0.05	2.83E-05	G	A	0.98	*HLA-DPB1*	*HLA-DPA1; HLA-DPB1*
6	rs9277432	33160050	0.3	−0.05	2.83E-05	T	A	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
18	rs11874847	34336514	0.01	0.28	2.85E-05	G	A	0.51		
6	rs9277426	33159888	0.3	−0.05	2.86E-05	A	C	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2523713	30281309	0.22	0.05	2.87E-05	A	G	1.01	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
6	rs2517673	30045221	0.13	0.07	2.92E-05	A	G	0.98		*HLA-A; HCG9*
6	rs2254618	31535118	0.26	0.05	2.92E-05	T	A	0.89		*MICB; HCP5*
6	rs2596503	31428789	0.17	−0.06	2.93E-05	A	G	0.93		*HLA-B*
6	rs9277568	33165033	0.25	−0.05	2.93E-05	C	T	0.99		*HLA-DPB1; HLA-DPA1*
20	rs1857051	23841840	0.23	−0.06	2.95E-05	T	A	0.85		*CST5*
20	rs2995108	23842550	0.25	−0.06	3.09E-05	G	A	0.82		*CST5*
5	rs7724608	146417829	0.35	0.05	3.09E-05	G	A	0.94	*PPP2R2B*	*PPP2R2B*
11	rs10502148	111153208	0.36	0.05	3.09E-05	T	C	0.99		*ALG9; SNF1LK2; PPP2R1B*
7	rs6967280	100962760	0.06	0.1	3.10E-05	T	C	0.89	*EMID2*	*EMID2*
11	rs10891290	111110425	0.36	0.05	3.13E-05	C	T	0.99	*PPP2R1B*	*ALG9; SNF1LK2; PPP2R1B*
6	rs971570	30280492	0.22	0.05	3.14E-05	C	A	1.01	*TRIM26*	*TRIM10; TRIM26; TRIM15; TRIM40; FLJ45422*
16	rs12598268	63646305	0.08	0.09	3.14E-05	T	C	0.83	*CDH11*	*CDH11*
7	rs1054766	22111640	0.36	0.05	3.14E-05	G	A	1.01		*RAPGEF5*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
2	rs3097276	8349583	0.14	0.07	3.16E-05	C	T	0.78		
17	rs2877824	52878222	0.24	−0.05	3.16E-05	T	C	0.92	*MSI2*	*MSI2*
2	rs3102947	8351636	0.14	0.07	3.17E-05	G	C	0.78		
6	rs964626	90056015	0.17	−0.08	3.17E-05	C	T	0.56	*GABRR2*	*UBE2J1; GABRR2*
3	rs17265703	123531334	0.18	0.06	3.18E-05	G	A	0.99	*CSTA*	*CSTA; CASR; C3orf28; CCDC58*
6	rs9260285	30024077	0.08	0.08	3.22E-05	C	T	0.93		*HLA-A; HCG9*
2	rs2931130	8352399	0.14	0.07	3.27E-05	A	G	0.79		
6	rs1611567	29974179	0.08	0.08	3.33E-05	T	G	0.95		*HLA-A*
6	rs9277558	33164689	0.25	−0.05	3.36E-05	T	C	0.99		*HLA-DPB1; HLA-DPA1*
6	rs3091281	33164544	0.25	−0.05	3.41E-05	C	T	0.99		*HLA-DPB1; HLA-DPA1*
6	rs3128968	33164231	0.25	−0.05	3.47E-05	A	T	0.99		*HLA-DPB1; HLA-DPA1*
6	rs3130186	33164185	0.25	−0.05	3.50E-05	T	C	0.99		*HLA-DPB1; HLA-DPA1*
2	rs11690981	108982543	0.02	0.19	3.52E-05	A	G	0.72		*EDAR*
6	rs3128967	33164075	0.25	−0.05	3.52E-05	G	T	0.99		*HLA-DPB1; HLA-DPA1*
12	rs11172113	55813550	0.36	0.05	3.53E-05	C	T	0.84	*LRP1*	*KIAA0286; NAB2; STAT6; LRP1*
6	rs9277464	33161330	0.25	−0.05	3.54E-05	T	C	0.99	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
3	rs5008830	123513152	0.18	0.06	3.54E-05	A	G	0.99		*CSTA; CASR; CCDC58*
6	rs9277480	33161790	0.25	−0.05	3.54E-05	G	A	0.99	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277489	33161920	0.25	−0.05	3.54E-05	C	T	0.99	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs9277535	33162839	0.25	−0.05	3.55E-05	G	A	0.99	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs3117229	33164047	0.25	−0.05	3.55E-05	A	G	0.99		*HLA-DPB1; HLA-DPA1*
2	rs3102956	8384895	0.15	0.06	3.68E-05	A	G	0.98		
11	rs6483107	90642599	0.02	−0.16	3.70E-05	G	A	0.87		
2	rs2914424	8384366	0.15	0.06	3.72E-05	T	A	0.98		
1	rs11265196	157684836	0.36	0.05	3.72E-05	G	A	1.01		*OR10J1*
2	rs11884512	14444382	0.03	−0.13	3.73E-05	C	G	0.91		
4	rs11942966	77709168	0.17	−0.06	3.87E-05	A	C	0.78	*SHROOM3*	*SHROOM3*
4	rs3860062	37577174	0.23	0.05	3.92E-05	C	T	1	*TBC1D1*	*PGM2; TBC1D1*
3	rs2001548	123515479	0.18	0.06	3.94E-05	A	G	0.99		*CSTA; CASR; CCDC58*
6	rs2844776	30279806	0.21	0.05	4.04E-05	C	T	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
13	rs7329290	26487418	0.51	−0.04	4.06E-05	G	C	0.92		*USP12*
6	rs2904758	30031330	0.29	0.05	4.07E-05	G	A	0.89		*HLA-A; HCG9*
10	rs12414220	9926686	0.07	0.1	4.08E-05	C	T	0.81		
17	rs9896736	10146721	0.18	−0.07	4.11E-05	C	T	0.6	*MYH13*	*MYH13*
4	rs10010366	37577217	0.23	0.05	4.16E-05	A	G	1	*TBC1D1*	*PGM2; TBC1D1*
6	rs9277378	33158257	0.3	−0.05	4.17E-05	G	A	0.97	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
3	rs1949751	192799909	0.38	−0.05	4.26E-05	A	G	0.9		
3	rs4686582	192796773	0.38	−0.05	4.26E-05	C	T	0.9		
3	rs6444578	192800486	0.38	−0.05	4.26E-05	G	A	0.9		
2	rs6723267	141047276	0.46	0.04	4.27E-05	G	C	0.99	*LRP1B*	*LRP1B*
3	rs10446354	192797745	0.38	−0.05	4.27E-05	A	G	0.9		
2	rs11676729	108957841	0.01	0.19	4.43E-05	A	G	0.96	*EDAR*	*EDAR*
6	rs2523716	30278504	0.21	0.05	4.43E-05	T	C	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
9	rs11142142	89975367	0.07	0.08	4.44E-05	G	A	1.01		
9	rs10780903	89974990	0.07	0.08	4.48E-05	C	T	1.01		
9	rs2578250	89983909	0.07	0.08	4.53E-05	A	G	1.01		
17	rs920747	52878433	0.23	−0.05	4.54E-05	A	G	0.99	*MSI2*	*MSI2*
3	rs6791616	123589925	0.19	0.06	4.56E-05	T	C	0.99	*C3orf28*	*CSTA; WDR5B; KPNA1; C3orf28; CCDC58*
6	rs2647017	32771750	0.11	0.07	4.57E-05	G	T	1.01		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
2	rs260695	108954807	0.01	0.19	4.58E-05	G	C	0.97	*EDAR*	*EDAR*
6	rs6933093	99836622	0.49	0.04	4.58E-05	G	A	0.96	*C6orf168*	*C6orf168*
6	rs2647015	32772071	0.11	0.07	4.58E-05	G	T	1.01		*HLA-DQB1; HLA-DQA1; HLA-DQA2*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
2	rs2562016	8377259	0.15	0.06	4.58E-05	G	C	0.97		
9	rs2183881	89973612	0.07	0.08	4.60E-05	C	A	1.01		
9	rs2814840	89982069	0.07	0.08	4.60E-05	A	G	1.01		
2	rs3097289	8376644	0.15	0.06	4.65E-05	T	C	0.97		
6	rs1117490	30278489	0.21	0.05	4.65E-05	C	T	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
9	rs2183879	89973445	0.07	0.08	4.65E-05	C	T	1.01		
6	rs2647009	32769593	0.11	0.07	4.65E-05	A	T	1.01		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
6	rs928976	33157189	0.3	−0.05	4.68E-05	T	C	0.97	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
6	rs2856673	32767800	0.11	0.07	4.69E-05	T	G	1.01		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
9	rs17053839	89980533	0.07	0.08	4.71E-05	A	G	1.01		
9	rs11142149	89980151	0.07	0.08	4.73E-05	T	C	1.02		
9	rs4877415	89971602	0.07	0.08	4.75E-05	T	C	1.01		
6	rs13206094	99879095	0.26	−0.05	4.75E-05	C	T	0.92	*C6orf168*	*COQ3; C6orf168*
6	rs2735071	30052958	0.16	0.06	4.76E-05	C	G	0.91	*HCG9*	*HLA-A; HCG9*
9	rs11142148	89979974	0.07	0.08	4.79E-05	A	T	1.02		
7	rs1897414	7095599	0.31	−0.05	4.80E-05	A	G	0.95		
6	rs2517611	30277306	0.21	0.05	4.80E-05	G	A	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15; FLJ45422*
9	rs11142147	89979859	0.07	0.08	4.82E-05	T	C	1.02		
9	rs4877414	89971481	0.07	0.08	4.83E-05	T	C	1.01		
9	rs11142146	89979595	0.07	0.08	4.83E-05	G	T	1.02		
9	rs17053832	89978984	0.07	0.08	4.87E-05	A	T	1.02		
9	rs7039913	89971388	0.07	0.08	4.88E-05	T	C	1.01		
2	rs404236	8373454	0.15	0.06	4.88E-05	A	G	0.96		
9	rs11142143	89975474	0.07	0.08	4.90E-05	G	A	1.02		
9	rs11142145	89976374	0.07	0.08	4.90E-05	T	G	1.02		
6	rs2523721	30274245	0.21	0.05	4.92E-05	T	C	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15*
6	rs2523722	30273252	0.21	0.05	4.96E-05	T	C	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15*
9	rs7020342	89971319	0.07	0.08	4.96E-05	A	G	1.01		
3	rs12107092	123606538	0.19	0.06	4.97E-05	T	C	0.99	*C3orf28*	*WDR5B; KPNA1; C3orf28; CCDC58*
6	rs2517614	30271934	0.21	0.05	4.98E-05	A	G	1.02	*TRIM26*	*TRIM26; TRIM40; TRIM10; TRIM15*
2	rs11694335	108954788	0.01	0.18	5.00E-05	T	C	0.98	*EDAR*	*EDAR*
7	rs2282978	92102346	0.35	0.04	5.01E-05	C	T	1.02	*CDK6*	*CDK6; FAM133B*
2	rs12328640	213567430	0.13	−0.06	5.01E-05	G	T	0.98		*IKZF2*
6	rs721150	99841733	0.49	0.04	5.02E-05	A	G	0.96	*C6orf168*	*C6orf168*
3	rs2280670	120700002	0.2	−0.05	5.05E-05	T	C	0.99		*C3orf1; TMEM39A; CD80; KTELC1*
9	rs7847987	89970585	0.07	0.08	5.07E-05	G	C	1.01		
3	rs2686084	198706920	0.27	0.05	5.07E-05	T	C	1.01		*BDH1*
2	rs11691107	108952869	0.01	0.18	5.08E-05	T	C	0.98	*EDAR*	*EDAR*
3	rs4688011	120709937	0.2	−0.05	5.11E-05	A	G	0.99	*C3orf1*	*C3orf1; TMEM39A; CD80; KTELC1*
3	rs4688013	120712176	0.2	−0.05	5.13E-05	A	G	0.99	*C3orf1*	*C3orf1; TMEM39A; CD80; KTELC1*
3	rs1599796	120726624	0.2	−0.05	5.14E-05	A	G	0.99	*CD80*	*ADPRH; C3orf1; CD80; KTELC1*
3	rs1599795	120726545	0.2	−0.05	5.15E-05	A	T	0.99	*CD80*	*ADPRH; C3orf1; CD80; KTELC1*
6	rs2734922	29990777	0.38	0.04	5.16E-05	G	A	0.97		*HLA-A*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
6	rs9295829	30136779	0.29	−0.05	5.16E-05	G	A	0.9		*TRIM31; PPP1R11; RNF39; ZNRD1*
2	rs10174201	108951680	0.01	0.18	5.19E-05	T	A	0.98	*EDAR*	*EDAR*
3	rs11719448	120717284	0.2	−0.05	5.20E-05	T	C	0.99	*C3orf1*	*C3orf1; TMEM39A; CD80; KTELC1*
3	rs2567357	198703634	0.27	0.05	5.20E-05	G	C	1.01		*BDH1*
6	rs4840026	99843821	0.49	0.04	5.30E-05	G	C	0.96	*C6orf168*	*C6orf168*
15	rs8028925	81425129	0.02	0.16	5.31E-05	G	A	0.97		*BTBD1; C15orf40; FAM103A1; HOMER2*
6	rs3117242	33177871	0.27	−0.05	5.36E-05	G	A	0.99		*HLA-DPB1; HLA-DPA1*
6	rs2395314	33170651	0.27	−0.05	5.36E-05	T	G	0.95		*HLA-DPB1; HLA-DPA1*
15	rs8027909	81452020	0.02	0.16	5.36E-05	C	G	0.97		*BTBD1; C15orf40; FAM103A1; HOMER2*
6	rs3128923	33179300	0.27	−0.05	5.37E-05	G	C	0.99		*COL11A2; HLA-DPB1; HLA-DPA1*
13	rs9584885	98096292	0.23	0.05	5.37E-05	A	G	1.01		*SLC15A1*
6	rs3891175	32742445	0.23	0.05	5.37E-05	T	C	1		*HLA-DQB1; HLA-DQA1*
3	rs10934504	121239637	0.02	0.16	5.46E-05	C	T	0.83	*GSK3B*	*GSK3B*
2	rs17806210	141049302	0.45	0.04	5.48E-05	G	A	0.97	*LRP1B*	*LRP1B*
5	rs888934	169856310	0.08	−0.12	5.53E-05	A	G	0.44	*KCNIP1*	*KCNIP1*
6	rs2144014	33173791	0.27	−0.05	5.53E-05	A	G	0.99		*HLA-DPB1; HLA-DPA1*
6	rs2132678	99821818	0.49	0.04	5.62E-05	C	A	0.96		*C6orf168*
1	rs12048482	157676481	0.36	0.04	5.64E-05	A	G	1.02	*OR10J1*	*OR10J1*
11	rs2196517	90634708	0.03	−0.13	5.66E-05	G	A	0.99		
11	rs965994	90637022	0.03	−0.13	5.69E-05	A	G	0.99		
6	rs1045731	99827724	0.49	0.04	5.70E-05	C	T	0.97		*C6orf168*
6	rs1045728	99827770	0.49	0.04	5.70E-05	G	A	0.97		*C6orf168*
7	rs39348	103254061	0.29	−0.05	5.71E-05	T	A	0.96	*RELN*	*RELN*
9	rs1888875	89966314	0.07	0.08	5.72E-05	T	G	1.01		
6	rs3117213	33172583	0.27	−0.05	5.72E-05	T	G	0.98		*HLA-DPB1; HLA-DPA1*
12	rs17354637	84871883	0.21	−0.06	5.74E-05	G	A	0.78		*MGAT4C*
2	rs749458	96159584	0.26	−0.05	5.75E-05	T	C	0.86	*ASTL*	*ASTL; DUSP2; ADRA2B; STARD7*
6	rs6914651	33171677	0.27	−0.05	5.86E-05	G	A	0.98		*HLA-DPB1; HLA-DPA1*
6	rs2394994	31499597	0.17	−0.06	5.86E-05	A	T	0.98		*HCP5*
1	rs11265191	157666983	0.36	0.04	6.05E-05	T	C	1.01		*OR10J1*
17	rs12949258	52877684	0.38	−0.06	6.15E-05	G	T	0.6	*MSI2*	*MSI2*
6	rs1431403	33155009	0.3	−0.05	6.18E-05	C	T	0.98	*HLA-DPB1*	*HLA-DPB1; HLA-DPA1*
12	rs747275	55614549	0.09	−0.07	6.19E-05	A	G	1.01		*RDH16; SDR-O*
15	rs9920962	58823842	0.13	−0.06	6.22E-05	G	A	1.01	*RORA*	*RORA*
6	rs3117217	33171249	0.26	−0.05	6.24E-05	A	G	0.98		*HLA-DPB1; HLA-DPA1*
3	rs9290877	189925174	0.32	0.04	6.24E-05	C	T	0.99	*LPP*	*LPP*
6	rs9391744	32788205	0.32	0.05	6.31E-05	T	C	0.94		*HLA-DQB1; HLA-DQA2*
9	rs10868719	89964390	0.07	0.08	6.31E-05	C	G	1.01		
1	rs9658807	210943525	0.15	0.06	6.33E-05	G	A	0.9		*NSL1; SNFT*
15	rs11632684	58827883	0.13	−0.06	6.33E-05	G	T	0.93	*RORA*	*RORA*
3	rs9815874	189923855	0.32	0.04	6.33E-05	T	C	0.99	*LPP*	*LPP*
6	rs17581425	32788563	0.32	0.05	6.35E-05	C	T	0.93		*HLA-DQB1; HLA-DQA2*
15	rs10519068	58855996	0.12	−0.07	6.37E-05	A	G	0.91	*RORA*	*RORA*
6	rs2858333	32789063	0.32	0.05	6.38E-05	G	A	0.93		*HLA-DQB1; HLA-DQA2*
6	rs2647087	32789027	0.32	0.05	6.39E-05	C	A	0.93		*HLA-DQB1; HLA-DQA2*
6	rs3957148	32790115	0.08	−0.1	6.40E-05	G	A	0.6		*HLA-DQB1; HLA-DQA2*
6	rs7745656	32788948	0.32	0.05	6.41E-05	T	G	0.93		*HLA-DQB1; HLA-DQA2*
15	rs7172011	58826679	0.13	−0.06	6.42E-05	T	C	0.93	*RORA*	*RORA*
5	rs11167957	146416716	0.34	0.05	6.42E-05	C	T	0.82	*PPP2R2B*	*PPP2R2B*
6	rs2647088	32789496	0.32	0.05	6.42E-05	G	A	0.92		*HLA-DQB1; HLA-DQA2*
6	rs3916766	32789623	0.32	0.05	6.42E-05	A	T	0.92		*HLA-DQB1; HLA-DQA2*
6	rs2647089	32789546	0.32	0.05	6.42E-05	C	T	0.92		*HLA-DQB1; HLA-DQA2*
1	rs11265190	157658025	0.36	0.04	6.45E-05	G	A	1.01		*OR10J1*
5	rs11746185	146416497	0.34	0.05	6.46E-05	A	C	0.82	*PPP2R2B*	*PPP2R2B*
3	rs2270859	123738398	0.17	0.06	6.47E-05	A	G	1	*PARP9*	*DTX3L; PARP9; KPNA1*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
12	rs11836463	64736239	0.29	−0.05	6.48E-05	A	C	0.91		
1	rs12034969	157651568	0.36	0.04	6.53E-05	T	C	1.01		*OR10J1*
3	rs9848114	189922870	0.32	0.04	6.57E-05	G	A	0.99	*LPP*	*LPP*
9	rs10868718	89964316	0.07	0.08	6.58E-05	G	A	1.01		
6	rs422055	29993525	0.08	0.08	6.60E-05	T	C	0.99		*HLA-A; HCG9*
2	rs4907304	96262023	0.26	−0.05	6.62E-05	T	C	0.89		*CIAO1; ASCC3L1; TMEM127; LOC285033; STARD7*
3	rs9810196	189922630	0.32	0.04	6.63E-05	G	C	0.99	*LPP*	*LPP*
10	rs17106692	88143743	0.09	−0.07	6.64E-05	G	A	0.96		*GRID1; WAPAL*
6	rs7451962	32690413	0.46	0.04	6.65E-05	A	G	0.95		*HLA-DQB1; HLA-DQA1; HLA-DRB1*
6	rs3130191	33169849	0.26	−0.05	6.75E-05	C	T	0.98		*HLA-DPB1; HLA-DPA1*
6	rs6935723	32789647	0.32	0.05	6.81E-05	C	T	0.91		*HLA-DQB1; HLA-DQA2*
9	rs7029261	89964260	0.07	0.08	6.87E-05	T	A	1.01		
2	rs13385301	14391354	0.03	−0.14	6.97E-05	A	C	0.89		
3	rs16833168	123737337	0.17	0.06	6.98E-05	T	C	1	*PARP9*	*DTX3L; PARP9; KPNA1*
2	rs10495639	14393140	0.03	−0.14	7.02E-05	T	C	0.9		
3	rs689236	61814920	0.34	0.04	7.03E-05	T	C	1	*PTPRG*	*PTPRG*
3	rs625177	61815335	0.34	0.04	7.08E-05	A	G	1	*PTPRG*	*PTPRG*
18	rs10163673	36171962	0.2	−0.05	7.19E-05	A	T	0.98		
5	rs2243297	132027070	0.04	0.13	7.19E-05	A	T	0.74		*RAD50; IL13; KIF3A;IL4*
6	rs2857778	29736345	0.04	0.11	7.20E-05	T	C	0.86	*MOG*	*MOG; GABBR1*
12	rs7975189	64732375	0.28	−0.05	7.24E-05	G	C	0.98		
6	rs3128919	33169604	0.26	−0.05	7.24E-05	A	T	0.98		*HLA-DPB1; HLA-DPA1*
6	rs2523943	30050906	0.13	0.06	7.24E-05	G	T	0.98	*HCG9*	*HLA-A; HCG9*
9	rs1929942	89959646	0.09	0.08	7.33E-05	T	C	0.8		
6	rs3130190	33169668	0.33	−0.05	7.37E-05	C	T	0.8		*HLA-DPA1; HLA-DPB1*
12	rs11176016	64728528	0.27	−0.05	7.40E-05	T	C	0.96		
9	rs10125321	89958706	0.07	0.08	7.40E-05	A	G	1.01		
6	rs2395184	32540624	0.22	0.05	7.42E-05	A	G	0.84		*HLA-DRB5; HLA-DRA; BTNL2*
6	rs2856665	32773575	0.11	0.07	7.42E-05	G	A	1		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
9	rs7025341	89957646	0.07	0.08	7.42E-05	T	A	1.01		
7	rs2282983	92117299	0.37	0.04	7.46E-05	C	T	1	*CDK6*	*CDK6; FAM133B*
6	rs537350	117495752	0.03	0.12	7.46E-05	G	A	0.93		
7	rs10269774	92091908	0.35	0.04	7.46E-05	A	G	1.02	*CDK6*	*CDK6; FAM133B*
9	rs2150922	89960665	0.07	0.08	7.47E-05	G	A	1.01		
9	rs2150923	89960769	0.07	0.08	7.49E-05	G	A	1.01		
2	rs17328175	59958779	0.28	0.05	7.51E-05	G	A	1.02		
9	rs7027288	89955112	0.07	0.08	7.54E-05	A	G	0.96		
6	rs3117231	33182886	0.26	−0.05	7.54E-05	G	A	0.98		*COL11A2; HLA-DPB1; HLA-DPA1*
2	rs2380887	141037653	0.45	0.04	7.57E-05	A	C	0.98	*LRP1B*	*LRP1B*
5	rs7707527	76466392	0.45	0.04	7.59E-05	C	G	0.97		*ZBED3*
6	rs2516687	30472566	0.04	0.11	7.61E-05	T	A	0.91		*RPP21; TRIM39*
9	rs7038901	89962712	0.07	0.08	7.66E-05	G	A	1.01		
3	rs17267388	123750236	0.18	0.05	7.69E-05	A	G	0.99	*PARP9*	*DTX3L; PARP9; KPNA1*
9	rs4877412	89963726	0.07	0.08	7.69E-05	C	T	1.01		
9	rs2150921	89953359	0.07	0.08	7.70E-05	C	T	0.93		
20	rs6025158	54785719	0.05	0.09	7.76E-05	G	C	0.99		
6	rs2646994	32773791	0.11	0.06	7.82E-05	T	C	1		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
6	rs1408300	17262835	0.44	0.05	7.88E-05	T	C	0.73		
6	rs4959041	30185946	0.27	−0.05	7.89E-05	C	T	0.96	*TRIM31*	*TRIM31; TRIM40; PPP1R11; RNF39; ZNRD1; TRIM10; TRIM15*
13	rs9548217	37616535	0.36	0.04	7.91E-05	T	G	0.98		

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
16	rs11646632	4198092	0.06	0.09	7.95E-05	T	C	0.97	*SRL*	*TFAP4; SRL*
3	rs868925	61823057	0.34	0.04	8.02E-05	A	G	1	*PTPRG*	*PTPRG*
11	rs4501949	90611257	0.02	−0.18	8.03E-05	C	G	0.63		
3	rs677654	61824173	0.34	0.04	8.07E-05	T	G	1	*PTPRG*	*PTPRG*
1	rs6692378	157605865	0.36	0.04	8.10E-05	C	T	1		*OR10J3*
12	rs12230818	64723760	0.29	−0.05	8.13E-05	G	A	0.93		
6	rs3117222	33168927	0.26	−0.05	8.17E-05	T	C	0.98		*HLA-DPB1; HLA-DPA1*
18	rs11082403	40571788	0.22	0.05	8.25E-05	G	T	0.98	*SETBP1*	*SETBP1*
1	rs2427829	157548635	0.26	0.05	8.36E-05	A	G	0.96		*OR10J3; FCER1A*
3	rs4678192	123610282	0.36	0.05	8.39E-05	G	A	0.83	*C3orf28*	*WDR5B; KPNA1; C3orf28; CCDC58*
1	rs3027001	157436087	0.23	−0.05	8.44E-05	T	C	0.92	*CADM3*	*CADM3; DARC*
6	rs3128972	33166752	0.26	−0.05	8.46E-05	C	T	0.99		*HLA-DPB1; HLA-DPA1*
5	rs2069757	132026312	0.08	0.08	8.46E-05	A	G	0.98		*RAD50;IL13; KIF3A; IL4*
6	rs2179919	33167240	0.26	−0.05	8.51E-05	C	T	0.99		*HLA-DPB1; HLA-DPA1*
6	rs1367730	33166092	0.26	−0.05	8.52E-05	T	C	0.99		*HLA-DPB1; HLA-DPA1*
12	rs11176015	64727951	0.29	−0.05	8.54E-05	T	C	0.92		
6	rs2395313	33167314	0.26	−0.05	8.55E-05	C	A	0.99		*HLA-DPB1; HLA-DPA1*
14	rs11848946	51880550	0.12	−0.06	8.55E-05	G	A	1		*PTGER2*
1	rs4282816	157559474	0.26	0.05	8.57E-05	G	A	0.96		*OR10J3; FCER1A*
13	rs2225872	37439196	0.34	0.04	8.58E-05	G	A	0.97		
1	rs4498803	157571781	0.26	0.05	8.58E-05	C	T	0.96		*OR10J3; FCER1A*
3	rs6445243	61859908	0.33	0.04	8.58E-05	G	C	1	*PTPRG*	*PTPRG*
2	rs11888369	14395050	0.03	−0.13	8.63E-05	C	T	0.92		
18	rs17710169	40568007	0.22	0.05	8.77E-05	G	C	0.98	*SETBP1*	*SETBP1*
2	rs13416263	14398489	0.03	−0.13	8.80E-05	A	G	0.92		
6	rs3128917	33167974	0.26	−0.05	8.84E-05	G	T	0.99		*HLA-DPB1; HLA-DPA1*
6	rs3117223	33168042	0.26	−0.05	8.91E-05	A	G	0.99		*HLA-DPB1; HLA-DPA1*
2	rs13419213	14402607	0.03	−0.13	8.98E-05	G	A	0.92		
2	rs13410836	14405250	0.03	−0.13	9.01E-05	C	T	0.92		
10	rs6585111	113514361	0.07	0.08	9.04E-05	T	C	0.99		
18	rs17782904	40567708	0.22	0.05	9.04E-05	A	G	0.98	*SETBP1*	*SETBP1*
6	rs9275334	32775085	0.09	−0.07	9.06E-05	C	T	0.98		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
2	rs13428704	14410351	0.03	−0.13	9.06E-05	T	A	0.92		
2	rs10203925	14408786	0.03	−0.13	9.06E-05	C	T	0.92		
6	rs9275307	32772968	0.09	−0.07	9.08E-05	T	A	0.99		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
3	rs605580	61801108	0.32	0.05	9.08E-05	T	C	0.91	*PTPRG*	*PTPRG*
6	rs9275351	32775771	0.09	−0.07	9.10E-05	A	C	0.98		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
6	rs9275356	32775828	0.09	−0.07	9.13E-05	G	C	0.98		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
3	rs607882	61802734	0.33	0.04	9.16E-05	A	T	0.95	*PTPRG*	*PTPRG*
5	rs27453	16517596	0.07	−0.08	9.16E-05	G	A	1	*ZNF622*	*FAM134B; ZNF622*
3	rs622358	61802595	0.33	0.04	9.25E-05	T	A	0.95	*PTPRG*	*PTPRG*
3	rs9789994	123700541	0.17	0.05	9.36E-05	A	T	1	*KPNA1*	*PARP9; KPNA1*
1	rs1584252	157790252	0.43	−0.04	9.38E-05	T	A	1.01		*APCS; OR10J5*
6	rs6912685	99877040	0.45	−0.04	9.39E-05	C	A	0.96	*C6orf168*	*COQ3; C6orf168*
6	rs6925577	99875757	0.45	−0.04	9.41E-05	A	G	0.96	*C6orf168*	*COQ3; C6orf168*
6	rs3091283	33165191	0.26	−0.05	9.46E-05	T	C	0.99		*HLA-DPB1; HLA-DPA1*
13	rs2265458	37440152	0.34	0.04	9.46E-05	G	C	0.98		
6	rs9275293	32771286	0.09	−0.07	9.49E-05	C	T	0.99		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
13	rs1337647	37440845	0.34	0.04	9.51E-05	T	C	0.98		
1	rs7543174	152794296	0.15	−0.06	9.51E-05	C	T	0.97	*UBE2Q1*	*UBE2Q1; CHRNB2; ADAR; SHE; TDRD10*
13	rs2485488	37441039	0.34	0.04	9.51E-05	G	A	0.98		
6	rs9275221	32767077	0.09	−0.07	9.53E-05	C	T	1		*HLA-DQB1; HLA-DQA1; HLA-DQA2*

(Continued)

TABLE E2. *(Continued)*

Chromosome	SNP	Location	Minor allele frequency	β	*P* value	Minor	Major	Ratio	In reference gene	Reference genes <60 kb from SNP
6	rs9275207	32765688	0.09	−0.07	9.57E-05	G	A	1		*HLA-DQB1; HLA-DQA1; HLA-DQA2*
13	rs2485492	37448242	0.34	0.04	9.58E-05	A	G	0.98		
13	rs2255148	37449635	0.34	0.04	9.60E-05	A	G	0.98		
12	rs16920791	125610943	0.07	0.09	9.64E-05	G	C	0.78		
6	rs1526268	117625211	0.05	0.12	9.72E-05	C	G	0.72		
3	rs592179	61800481	0.32	0.05	9.74E-05	T	G	0.9	*PTPRG*	*PTPRG*
13	rs2243570	37455085	0.34	0.04	9.76E-05	G	A	0.99		
9	rs10125291	89958647	0.07	0.08	9.78E-05	A	G	1.01		
3	rs686553	61799747	0.32	0.05	9.83E-05	G	T	0.9	*PTPRG*	*PTPRG*
3	rs686518	61799732	0.32	0.05	9.87E-05	G	C	0.9	*PTPRG*	*PTPRG*
9	rs10761034	106334543	0.2	−0.05	9.92E-05	G	T	0.96		*OR13C8; OR13C3; OR13F1; OR13C4*
21	rs13050646	42585118	0.06	0.09	9.92E-05	T	G	0.93	*ABCG1*	*ABCG1; TFF2; TFF3*
7	rs1558015	100933715	0.39	0.04	9.96E-05	T	C	0.97	*EMID2*	*EMID2*

**P* values are expressed in scientific E notation in which 1.2E-3 denotes 1.2×10^{-3}.

TABLE E3. Cohort-specific association results in the FHS cohort and replication cohorts for the 70 SNPs included in replication analyses*

		FHS			T1DGC			WTCC			KORA F3			KORA F4			CAMP			Combined					
SNP	Effect allele	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	β	*P* value	Chr	Position	In reference gene	Closest reference gene
rs2251746	C	0.2643	−0.0844	2.11E-12	0.7107	−0.0796	2.95E-05	0.7114	−0.0942	1.33E-04	0.7443	−0.1140	1.07E-05	0.7531	−0.0850	8.14E-04	0.7333	0.0530	2.41E-01	0.09	4.52E-26	1	157538684	*FCER1A*	*FCER1A*
rs2494264	A	0.4574	−0.0644	1.37E-09	0.4807	−0.0673	7.74E-05	0.5173	−0.0706	1.57E-03	0.5388	−0.0807	2.46E-04	0.5349	−0.0330	1.29E-01	0.4572	−0.1146	2.74E-03	−0.07	9.40E-20	1	157533462	*FCER1A*	*FCER1A*
rs20541	A	0.1842	0.0747	3.55E-08	0.8245	0.0883	7.59E-05	0.8196	0.1033	4.34E-03	0.7914	0.0922	3.63E-04	0.8049	0.0743	6.09E-03	0.7801	−0.0677	1.38E-01	0.08	3.41E-18	5	132023863	*IL13*	*IL13*
rs4656784	G	0.1960	−0.0748	3.84E-07	0.7944	−0.0795	2.49E-04	0.2093	−0.1046	8.33E-04	0.1403	−0.0683	2.52E-02	0.1943	−0.1069	1.14E-04	0.7435	0.0329	4.73E-01	0.08	1.68E-16	1	157593504		*OR10J3*
rs2571391	C	0.3226	−0.0545	2.13E-06	0.3243	−0.0718	7.13E-05	0.3426	−0.0839	5.59E-04	0.3207	−0.0633	6.12E-03	0.3125	−0.0751	1.47E-03	0.6225	−0.0010	9.82E-01	0.06	1.23E-15	6	30031817		*HLA-A*
rs1059513	C	0.0867	−0.1645	2.87E-08	0.8853	−0.0913	6.79E-04	0.9135	−0.0992	1.15E-01	0.9888	−0.1538	1.46E-02	0.9664	−0.0517	2.96E-01	0.9147	−0.1231	7.23E-02	0.12	1.99E-12	12	55775976	*STAT6*	*NAB2*
rs13962	A	0.1281	−0.0871	1.52E-05	0.8577	−0.0628	1.97E-02	0.8716	−0.1765	8.10E-05	0.9572	−0.0738	7.77E-02	0.9110	−0.1287	7.15E-04	0.8280	−0.0203	7.22E-01	−0.09	2.21E-11	1	157442151	*DARC*	*DARC*
rs167769	T	0.3485	0.0555	5.18E-06	0.6082	0.0399	2.41E-02	0.4194	0.0552	2.36E-02	0.3567	0.0775	7.23E-04	0.3401	0.0239	3.01E-01	0.4200	0.0075	8.50E-01	0.05	4.02E-10	12	55790042	*STAT6*	*STAT6*
rs2517754	A	0.5307	0.0542	3.59E-07	NA			NA			NA			0.4773	0.0779	3.64E-04	0.6439	−0.0313	5.23E-01	0.06	3.61E-09	6	30004659		*HLA-A*
rs2858331	G	0.4336	0.0481	2.03E-05	0.6198	0.0495	4.77E-03	0.3689	0.0209	3.77E-01	0.4029	−0.0175	4.43E-01	0.4130	0.0660	3.30E-03	0.6196	0.1137	3.32E-03	−0.04	1.44E-08	6	32789255		*HLA-DQA2*
rs2243297	A	0.0370	0.1281	7.19E-05	0.9672	0.1540	3.77E-03	0.9708	0.0143	8.62E-01	0.9866	0.1082	1.04E-01	0.9913	0.2590	1.12E-03	0.9467	0.0493	5.84E-01	0.13	1.54E-08	5	132027070		*IL13*
rs2523809	T	0.1266	0.0846	2.40E-07	0.8796	0.0677	1.05E-02	0.1082	0.0129	7.35E-01	0.0968	0.0432	2.07E-01	0.0992	0.0317	3.53E-01	0.8726	−0.0002	9.97E-01	0.06	4.34E-08	6	29957598		*HLA-G*
rs3823343	G	0.1936	0.0666	6.12E-07	NA			NA			NA			0.1764	0.0633	2.27E-02	0.8665	0.0042	9.48E-01	−0.06	6.65E-08	6	30021090	*HLA-A*	*HLA-A*
rs1801275	G	0.2019	−0.0636	1.54E-06	0.7851	−0.0271	1.92E-01	0.2341	−0.0373	2.03E-01	0.1783	−0.0135	6.41E-01	0.2076	−0.0549	3.77E-02	0.9005	−0.0657	3.71E-01	0.05	1.45E-07	16	27281901	*IL4R*	*IL4R*
rs2234900	C	0.1024	−0.0840	1.81E-06	NA			NA			NA			0.8879	−0.0645	5.54E-02	0.9015	−0.0588	3.83E-01	0.08	2.20E-07	16	27281473	*IL4R*	*IL4R*
rs3102947	G	0.1432	0.0714	3.17E-05	0.1414	0.0521	3.19E-02	0.1280	0.0678	1.00E-01	0.0931	0.0470	1.73E-01	0.1419	0.0571	6.40E-02	0.8362	−0.0350	5.32E-01	−0.06	2.36E-07	2	8351636		*ID2*
rs9290877	C	0.3191	0.0450	6.24E-05	0.6856	0.0053	7.73E-01	0.7045	0.0618	1.25E-02	0.6859	0.0525	2.36E-02	0.6851	0.0039	8.62E-01	0.3183	0.0710	9.19E-02	−0.04	1.95E-06	3	189925174	*LPP*	*LPP*
rs386014	C	0.0571	0.1071	2.50E-06	NA			NA			NA			0.9576	0.0460	3.59E-01	0.9618	0.0395	7.27E-01	0.09	3.26E-06	6	30002608		*HLA-A*
rs9275207	G	0.0917	−0.0722	9.57E-05	0.1051	−0.0442	1.17E-01	0.1153	−0.0172	6.30E-01	0.0895	−0.0007	9.85E-01	0.0950	−0.0574	1.17E-01	0.8776	−0.1338	2.26E-02	0.05	9.89E-06	6	32765688		*HLA-DQB1*
rs9920962	G	0.1305	−0.0625	6.22E-05	0.8821	−0.0448	9.11E-02	0.1189	−0.0322	3.75E-01	0.1263	−0.0279	3.72E-01	0.1216	−0.0016	9.61E-01	0.8683	−0.0825	1.56E-01	0.05	1.56E-05	15	58823842	*RORA*	*RORA*
rs1599796	A	0.1984	−0.0537	5.14E-05	0.8138	0.0249	2.57E-01	0.8123	−0.0292	3.03E-01	0.8223	−0.0583	3.45E-02	0.8216	−0.0744	8.36E-03	0.7926	−0.0225	6.46E-01	−0.04	1.82E-05	3	120726624	*CD80*	*CD80*
rs2905715	C	0.1395	0.0737	6.39E-06	0.8788	0.0762	4.63E-03	0.8667	−0.0025	9.44E-01	0.9008	−0.0405	2.53E-01	0.8817	0.0354	2.91E-01	0.7275	0.0099	8.18E-01	−0.05	2.08E-05	6	31459509		*HLA-B*
rs12598268	T	0.0807	0.0889	3.14E-05	0.9239	0.0542	1.49E-01	0.0718	0.0190	6.92E-01	0.0646	0.1110	9.21E-03	0.0839	−0.0299	4.36E-01	0.9161	0.0073	9.30E-01	0.06	3.64E-05	16	63646305	*CDH11*	*CDH11*
rs17565975	A	0.5310	0.0475	7.89E-06	0.4310	−0.0003	9.86E-01	0.4444	0.0050	8.41E-01	0.4648	−0.0067	7.77E-01	0.4658	0.0441	4.45E-02	0.5704	0.0626	1.14E-01	0.03	5.45E-05	11	111092160	*SNF1LK2*	*SNF1LK2*
rs17265703	G	0.1806	0.0571	3.18E-05	0.8539	0.0159	5.21E-01	0.1526	0.0642	3.97E-02	0.1742	0.0265	3.54E-01	0.1542	−0.0041	8.90E-01	0.8486	−0.0294	5.93E-01	−0.04	6.48E-05	3	123531334	*CSTA*	*CSTA*
rs13050646	T	0.0656	0.0863	9.92E-05	0.9522	0.0420	2.97E-01	0.0565	0.0770	1.19E-01	0.0549	0.0136	7.80E-01	0.0475	0.0367	4.39E-01	0.9572	−0.0745	5.11E-01	0.06	8.22E-05	21	42585118	*ABCG1*	*ABCG1*
rs11874847	G	0.0121	0.2849	2.85E-05	0.9842	0.0091	9.27E-01	0.0145	−0.0760	5.28E-01	0.0065	0.1278	1.91E-01	0.0047	0.3001	9.17E-03	NA			−0.16	9.12E-05	18	34336514		*BRUNOL4*
rs4678192	G	0.3646	0.0467	8.39E-05	0.5983	0.0233	1.87E-01	0.3647	−0.0024	9.26E-01	0.3698	0.0446	6.39E-02	0.3941	−0.0079	7.30E-01	0.6224	0.0500	2.28E-01	−0.03	9.88E-05	3	123610282	*C3orf28*	*C3orf28*
rs11745587	A	0.3382	0.0503	5.95E-06	0.3546	0.0027	8.80E-01	0.6440	0.0182	4.44E-01	0.6409	0.0258	2.46E-01	0.6598	0.0139	5.49E-01	0.6400	−0.0405	3.11E-01	0.03	1.53E-04	5	131824821	*LOC441108*	*LOC441108*
rs3893297	A	0.2494	0.0528	1.66E-05	0.2516	0.0305	1.24E-01	0.7444	−0.0110	7.92E-01	0.8606	−0.0085	8.33E-01	0.7435	−0.0115	6.41E-01	0.6623	0.0526	2.83E-01	0.03	1.64E-04	4	37576777	*TBC1D1*	*TBC1D1*
rs39348	T	0.2925	−0.0481	5.71E-05	0.7059	0.0223	2.53E-01	0.2938	−0.0307	2.39E-01	0.2509	0.0107	6.64E-01	0.2584	−0.0182	4.60E-01	0.3435	0.0000	1.00E+00	0.03	2.12E-04	7	103254061	*RELN*	*RELN*
rs3135021	A	0.2613	0.0610	7.23E-07	0.2429	−0.0006	9.77E-01	0.7648	0.0239	4.14E-01	0.6871	0.0156	5.06E-01	0.8212	−0.0089	7.50E-01	0.7351	−0.0227	6.02E-01	0.03	2.18E-04	6	33153536	*HLA-DPB1*	*HLA-DPB1*
rs13295276	A	0.1454	0.0701	2.07E-06	0.8450	−0.0022	9.28E-01	0.8632	0.0281	4.37E-01	0.9528	−0.0565	1.15E-01	0.8619	0.0610	5.32E-02	0.8553	−0.0632	2.44E-01	0.04	4.95E-04	9	33843118	*UBE2R2*	*UBE2R2*
rs10506786	A	0.1524	0.0618	1.95E-05	0.8586	0.0566	1.95E-02	0.8517	0.0025	9.39E-01	0.8440	−0.0195	5.07E-01	0.8538	−0.0222	4.63E-01	0.8511	−0.0143	7.94E-01	0.03	6.20E-04	12	77376000		*NAV3*
rs13037793	A	0.3526	−0.0520	1.36E-05	0.6344	0.0103	5.90E-01	0.6541	0.0195	4.44E-01	0.6643	0.0123	6.21E-01	0.6847	−0.0458	5.86E-02	0.7080	0.0606	1.87E-01	−0.03	1.30E-03	20	23820373		*CST5*

(Continued)

ARTICLE IN PRESS

TABLE E3. *(Continued)*

		FHS			T1DGC			WTCC			KORA F3			KORA F4			CAMP			Combined					
SNP	Effect allele	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	MAF	β	*P* value	β	*P* value	Chr	Position	In reference gene	Closest reference gene
rs6904594	C	0.0363	0.1285	2.04E-05	0.9613	0.0100	8.23E-01	0.9687	−0.0616	3.79E-01	0.9628	0.0035	9.46E-01	0.9486	0.0448	3.46E-01	0.9484	0.0994	2.70E-01	0.06	1.34E-03	6	117628064		*VGLL2*
rs6049203	T	0.1344	−0.0711	3.85E-06	0.8595	0.0143	5.69E-01	0.1298	−0.0324	3.44E-01	0.1331	0.0339	2.96E-01	0.1168	−0.0185	5.71E-01	0.8756	−0.0103	8.70E-01	−0.03	1.80E-03	20	23813477		*CST5*
rs1408300	T	0.4447	0.0485	7.88E-05	0.4507	−0.0176	3.06E-01	0.4763	0.0216	4.21E-01	0.4338	0.0365	1.53E-01	0.4096	0.0382	1.21E-01	0.5672	−0.0470	2.46E-01	0.03	1.91E-03	6	17262835		*RBM24*
rs9512492	T	0.4563	0.0470	1.48E-05	0.5673	0.0319	6.10E-02	0.4462	−0.0169	4.69E-01	0.4270	−0.0102	6.46E-01	0.4344	−0.0034	8.74E-01	0.4147	−0.0491	2.29E-01	0.02	1.96E-03	13	26488400		*USP12*
rs27453	G	0.0735	−0.0792	9.16E-05	0.9261	−0.0550	1.02E-01	0.0720	0.0102	8.21E-01	0.0659	0.0368	3.98E-01	0.0793	−0.0286	4.79E-01	0.9166	0.0726	3.08E-01	0.04	2.13E-03	5	16517596	*ZNF622*	*ZNF622*
rs6933093	G	0.4910	0.0433	4.58E-05	0.4917	0.0030	8.59E-01	0.4892	0.0009	9.69E-01	0.4804	0.0223	2.98E-01	0.4595	−0.0032	8.80E-01	0.5293	−0.0185	6.32E-01	−0.02	2.19E-03	6	99836622	*C6orf168*	*C6orf168*
rs10891290	C	0.3586	0.0459	3.13E-05	0.6083	−0.0149	3.89E-01	0.6250	0.0075	7.43E-01	0.6356	−0.0094	6.75E-01	0.6468	0.0354	1.15E-01	0.5578	0.0232	5.67E-01	−0.02	2.43E-03	11	111110425	*PPP2R1B*	*PPP2R1B*
rs2282978	C	0.3532	0.0443	5.01E-05	0.6805	0.0239	1.93E-01	0.6709	−0.0239	3.21E-01	0.6550	−0.0363	1.11E-01	0.6358	0.0214	3.34E-01	0.6506	0.0368	3.67E-01	−0.02	2.82E-03	7	92102346	*CDK6*	*CDK6*
rs4420222	C	0.0237	−0.1517	1.94E-05	0.9777	−0.1156	5.71E-02	0.9793	0.1024	2.00E-01	0.9788	0.0093	8.90E-01	0.9794	−0.0297	6.85E-01	0.9507	0.1445	1.35E-01	0.07	3.01E-03	11	90644663		*CHORDC1*
rs7707527	C	0.4443	0.0425	7.59E-05	0.5876	−0.0129	4.65E-01	0.5827	−0.0077	8.23E-01	0.6554	0.0363	2.22E-01	0.6099	−0.0255	3.61E-01	0.4373	0.0579	1.42E-01	0.02	3.54E-03	5	76466392		*ZBED3*
rs7579979	G	0.3921	−0.0475	1.31E-05	0.3933	0.0008	9.62E-01	0.3813	−0.0114	6.25E-01	0.3852	−0.0016	9.40E-01	0.4075	0.0038	8.61E-01	0.5852	0.0386	3.43E-01	0.02	3.92E-03	2	15729712		*DDX1*
rs2877824	T	0.2391	−0.0538	3.16E-05	0.7390	−0.0246	2.07E-01	0.2659	−0.0008	9.79E-01	0.1463	0.0404	1.71E-01	0.1621	0.0506	8.47E-02	0.7578	−0.0651	1.46E-01	−0.03	4.69E-03	17	52878222	*MSI2*	*MSI2*
rs11646632	T	0.0562	0.0908	7.95E-05	0.9384	−0.0446	4.39E-01	0.0574	−0.0405	6.52E-01	0.0556	−0.0038	9.36E-01	0.0443	0.0181	7.37E-01	0.0459	−0.0338	8.26E-01	0.05	5.43E-03	16	4198092	*SRL*	*SRL*
rs7724608	G	0.3567	0.0474	3.09E-05	0.6135	0.0043	8.07E-01	0.3659	0.0068	7.76E-01	0.3563	−0.0074	7.45E-01	0.3777	−0.0077	7.26E-01	0.3899	0.0040	9.21E-01	−0.02	5.56E-03	5	146417829	*PPP2R2B*	*PPP2R2B*
rs11942966	A	0.1735	−0.0641	3.87E-05	0.7948	−0.0065	7.62E-01	0.8153	0.0157	6.19E-01	0.8926	−0.0035	9.06E-01	0.7863	−0.0051	8.41E-01	0.7959	−0.0164	7.36E-01	−0.03	5.68E-03	4	77709168	*SHROOM3*	*SHROOM3*
rs9584885	A	0.2332	0.0502	5.37E-05	0.2602	−0.0008	9.67E-01	0.7537	−0.0077	7.65E-01	0.7822	0.0171	5.17E-01	0.7704	−0.0098	7.00E-01	0.7255	−0.0015	9.72E-01	0.02	7.01E-03	13	98096292		*SLC15A1*
rs749458	T	0.2604	−0.0520	5.75E-05	0.7961	0.0004	9.85E-01	0.1975	0.0064	8.35E-01	0.2054	−0.0007	9.80E-01	0.2106	−0.0163	5.37E-01	0.8097	0.0852	8.90E-02	−0.02	8.36E-03	2	96159584	*ASTL*	*ASTL*
rs11657292	T	0.3359	−0.0595	1.62E-05	0.6171	0.0035	8.46E-01	0.3475	−0.0046	8.83E-01	0.2560	0.0306	2.91E-01	0.2655	0.0290	3.12E-01	0.6512	−0.0830	4.87E-02	−0.02	1.12E-02	17	52877854	*MSI2*	*MSI2*
rs16920791	G	0.0742	0.0874	9.64E-05	0.9414	0.0241	5.29E-01	0.0671	0.0038	9.38E-01	0.0536	−0.0323	4.99E-01	0.0666	−0.0126	7.72E-01	0.9340	−0.0565	5.20E-01	−0.04	1.15E-02	12	125610943		*TMEM132B*
rs888934	A	0.0797	−0.1173	5.53E-05	0.9248	0.0066	8.37E-01	0.9250	0.0153	8.08E-01	0.9965	−0.0151	8.14E-01	0.9902	−0.0769	1.99E-01	0.9167	0.0694	3.43E-01	−0.05	1.15E-02	5	169856310	*KCNIP1*	*KCNIP1*
rs11082403	G	0.2213	0.0504	8.25E-05	0.7771	0.0086	6.73E-01	0.8248	0.0321	3.48E-01	0.8822	−0.0547	7.65E-02	0.7859	−0.0349	1.82E-01	0.7893	0.0698	1.35E-01	−0.02	1.19E-02	18	40571788	*SETBP1*	*SETBP1*
rs11142142	G	0.0718	0.0836	4.44E-05	0.9240	0.0297	3.60E-01	0.0752	0.0084	8.41E-01	0.0716	−0.0824	4.84E-02	0.0836	−0.0065	8.66E-01	0.9157	−0.0303	6.69E-01	−0.03	1.68E-02	9	89975367		*CCRK*
rs964626	C	0.1741	−0.0757	3.17E-05	0.8265	−0.0234	3.12E-01	0.8249	0.0428	2.55E-01	0.9455	−0.0056	8.90E-01	0.8588	0.0423	1.72E-01	0.8955	−0.0113	8.68E-01	0.03	1.84E-02	6	90056015	*GABRR2*	*GABRR2*
rs9548217	T	0.3592	0.0437	7.91E-05	0.6292	0.0077	6.62E-01	0.3502	−0.0035	8.86E-01	0.3477	−0.0409	6.52E-02	0.3499	−0.0055	8.10E-01	0.6269	0.0348	4.04E-01	0.02	2.31E-02	13	37616535		*UFM1*
rs6967280	T	0.0611	0.0966	3.10E-05	0.9581	−0.0330	4.43E-01	0.0386	0.0076	9.05E-01	0.0372	−0.0463	3.86E-01	0.0551	−0.0816	8.16E-02	0.9228	0.1293	8.42E-02	0.04	2.68E-02	7	100962760	*EMID2*	*EMID2*
rs689236	T	0.3391	0.0443	7.03E-05	0.6669	−0.0078	6.66E-01	0.3483	−0.0047	8.44E-01	0.3084	−0.0217	3.53E-01	0.3176	0.0058	8.00E-01	0.3560	−0.0337	4.09E-01	0.02	3.56E-02	3	61814920	*PTPRG*	*PTPRG*
rs11676729	A	0.0135	0.1859	4.43E-05	0.9685	−0.0360	4.67E-01	0.9853	0.0874	3.65E-01	0.9840	0.0452	6.01E-01	0.9816	−0.1094	1.73E-01	NA			0.06	4.03E-02	2	108957841	*EDAR*	*EDAR*
rs1949751	A	0.3840	−0.0463	4.26E-05	0.5968	0.0243	1.66E-01	0.6152	0.0209	3.91E-01	0.5957	0.0137	5.50E-01	0.6308	−0.0045	8.38E-01	0.3711	−0.0321	4.40E-01	−0.01	5.80E-02	3	192799909		*POP2*
rs11836463	A	0.2917	−0.0481	6.48E-05	0.7308	0.0162	3.97E-01	0.7137	0.0183	4.69E-01	0.7236	0.0076	7.53E-01	0.7280	0.0127	5.99E-01	0.7384	−0.0053	9.06E-01	−0.02	6.45E-02	12	64736239		*C12orf31*
rs9929374	G	0.3969	0.0836	9.92E-06	0.6293	−0.0258	1.42E-01	0.3815	−0.0243	5.46E-01	0.1667	−0.0229	5.95E-01	0.2593	−0.0019	9.59E-01	0.6109	0.0769	5.57E-02	−0.02	6.72E-02	16	21151451		*ANKS4B*
rs11884512	C	0.0316	−0.1311	3.73E-05	0.9673	0.1389	5.61E-03	0.9709	−0.0998	1.65E-01	0.9660	0.0129	8.18E-01	0.9695	0.0378	5.34E-01	0.9762	−0.0907	4.70E-01	−0.04	7.08E-02	2	14444382		*FAM84A*
rs9896736	C	0.1799	−0.0725	4.11E-05	0.8092	0.0188	4.26E-01	0.7912	0.0449	2.44E-01	0.8269	−0.0417	2.49E-01	0.8166	0.0500	7.13E-02	0.7820	−0.0787	1.48E-01	0.02	7.16E-02	17	10146721	*MYH13*	*MYH13*
rs10934504	C	0.0202	0.1618	5.46E-05	0.9762	−0.0761	2.47E-01	0.9825	0.0024	9.79E-01	0.9852	−0.1090	1.64E-01	0.9892	−0.0555	5.66E-01	NA			−0.05	9.00E-02	3	121239637	*GSK3B*	*GSK3B*
rs6732761	C	0.4527	0.0449	2.65E-05	0.4029	−0.0412	1.56E-02	0.3943	−0.0361	1.52E-01	0.4086	−0.0033	8.83E-01	0.4306	0.0089	6.78E-01	0.4131	0.0237	5.43E-01	−0.01	1.02E-01	2	141051207	*LRP1B*	*LRP1B*
rs17469756	G	0.5262	−0.0501	2.57E-06	0.4796	0.0330	5.30E-02	0.4923	0.0258	2.63E-01	0.4834	−0.0147	5.16E-01	0.5123	0.0529	1.81E-02	0.5036	−0.0237	5.50E-01	0.01	1.11E-01	7	100924034	*EMID2*	*EMID2*

MAF, Minor allele frequency; *NA*, SNP not available for analysis; *T1DGC*, Type 1 Diabetes Genetics Consortium (British 1958 Birth Cohort); *WTCCC*, Wellcome Trust Case Control Consortium (British 1958 Birth Cohort).
**P* values are expressed in scientific E notation in which 1.2E-3 denotes 1.2×10^{-3}.

TABLE E4. Association results for FHS and each replication cohort for the 12 SNPs with the strongest association with IgE concentration in the meta-analysis combining all of these cohorts*†

		FHS (n = 6918)		KORA S3 (n = 1530)		KORA S4 (n = 1764)		T1DGC (n = 2504)		WTCCC (n = 1436)		CAMP (n = 568)	
Nearest gene	**SNP**	**β**	***P* value**	**β**	***P* value**	**β**	***P* value**	**β**	***P* value**	**β**	***P* value**	**β**	***P* value**
FCER1A	rs2251746	−0.084	2.11E-12	−0.114	1.07E-05	−0.085	8.13E-04	−0.080	2.95E-05	−0.094	1.33E-04	−0.053	2.41E-01
FCER1A	rs2494264	−0.064	1.37E-09	−0.081	2.45E-04	−0.033	1.28E-01	−0.067	7.74E-05	−0.071	1.57E-03	−0.115	2.74E-03
IL13	rs20541	0.074	3.55E-08	0.092	3.63E-04	0.074	6.08E-03	0.088	7.59E-05	0.103	4.34E-03	0.068	1.38E-01
FCER1A	rs4656784	−0.075	3.84E-07	−0.068	2.52E-02	−0.107	1.14E-04	−0.079	2.49E-04	−0.105	8.33E-04	−0.033	4.73E-01
HLA-A	rs2571391	−0.054	2.13E-06	−0.063	6.11E-03	−0.075	1.47E-03	−0.072	7.13E-05	−0.084	5.59E-04	−0.001	9.82E-01
STAT6	rs1059513	−0.164	2.87E-08	−0.154	1.46E-02	−0.052	2.96E-01	−0.091	6.79E-04	−0.099	1.15E-01	−0.123	7.23E-02
DARC	rs13962	−0.087	1.52E-05	−0.074	7.77E-02	−0.129	7.15E-04	−0.063	1.97E-02	−0.177	8.10E-05	0.020	7.22E-01
STAT6	rs167769	0.055	5.18E-06	0.077	7.22E-04	0.024	3.01E-01	0.040	2.41E-02	0.055	2.36E-02	0.008	8.50E-01
HLA-A	rs2517754	0.054	3.59E-07	NA	NA	0.078	3.63E-04	NA	NA	NA	NA	−0.031	5.23E-01
HLA-DQA2	rs2858331	0.048	2.03E-05	−0.017	4.43E-01	0.066	3.29E-03	0.049	4.77E-03	0.021	3.77E-01	0.114	3.32E-03
IL13	rs2243297	0.128	7.19E-05	0.108	1.04E-01	0.259	1.11E-03	0.154	3.77E-03	0.014	8.62E-01	0.049	5.84E-01
HLA-G	rs2523809	0.085	2.40E-07	0.043	2.06E-01	0.032	3.53E-01	−0.068	1.05E-02	0.013	7.35E-01	0.000	9.97E-01

NA, SNP not available for analysis; *T1DGC*, Type 1 Diabetes Genetics Consortium (B58C); *WTCCC*, Wellcome Trust Case Control Consortium (B58C).
*The modeled allele in the meta-analysis is equal to the minor allele in the original FHS GWAS (Table II).
†*P* values are expressed in scientific E notation in which 1.2E-3 denotes 1.2×10^{-3}.