

**Combining Genome Wide Association Study and lung eQTL analysis provides  
evidence for genes associated with asthma.**

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## Supplementary information

### Methods

#### Study populations

##### *Dutch Asthma Genetics Consortium*

For GWAS I, we selected trios from our genetic studies with adequate DNA quantity and quality.

##### *Genotyping*

For GWAS I, raw fluorescence data were generated, and subsequently transformed to binary files with averaged red and green fluorescence values per SNP bead. The amplitudes for the red signal were matched to the green signal by estimating a multiplication factor per subarray and per SNP such that heterozygote genotypes were mapped to zero and the homozygote genotypes to  $-1$  and  $+1$ . The transformation  $Z = (\text{green} - \text{correction array} \times \text{correction SNP} \times \text{red}) / (\text{green} + \text{corrected red})$  was used as the mapping function. The mean heterozygote  $Z$ -transformed red/green value for each SNP and each subarray was shifted to zero by iterative adjustment of the correction factors. Ten iterations were used, which was sufficient for convergence. This procedure resulted in high quality, one-dimensional genotype clusters, allowing genotyping based on arrays rather than individual SNPs. The  $Z$  values were converted to genotypes. For amplitude analysis the green+corrected red score was used for each SNP, and the average for all SNPs was subtracted, resulting in a residue amplitude score. This procedure removed more than 90% of the variance of amplitude differences between SNPs. We compared the results of this procedure with the Illumina standardization and found only very marginal differences. Therefore, in GWAS II the genotypes were scored with Illumina standardized software Beadstudio.

*Quality control* measures included Hardy-Weinberg equilibrium of  $p > 10^{-7}$ , missing genotype rate per individual  $< 0.01$ , missing genotype rate per SNP  $< 0.01$  and a minor allele frequency

cut off of 0.01. Markers with Mendelian errors in phase I were excluded from analysis. We excluded related subjects (IBD >12.5 %) and non-Caucasian subjects, as assessed by principal components analysis performed with EIGENSTRAT (1). All statistical analysis were performed using PLINK v1.07 (2).

#### *Multicenter Asthma Genetics in Childhood Study (MAGICS)*

Asthma cases from the Multicentre Asthma Genetics in Childhood Study were diagnosed by a pediatric pulmonologist or allergologist on the basis of clinical examination, case history and objective tests of lung function (3). Asthmatics (mean age 10.95yr) were recruited from 7 centers located in Germany and Austria (Wesel, Bochum Cologne, Freiberg, Munich, Feldkirch and Vienna), and as a reference, 800 German children (mean age 9.62yr) from Dresden (n = 400) and Munich (n = 400) were randomly drawn from all German children with DNA available in the cross sectional ISAAC Phase II study (4). DNA of all these children was genotyped with the Illumina Sentrix HumanHap300 BeadChip. After quality control and elimination of markers with low minor-allele frequencies (<0.5%), extreme Hardy–Weinberg equilibrium statistics ( $\chi^2 > 25$ ) or low genotyping call rates (<95%), we retained 307,328 SNPs for analysis. SNPs selected for replication were tested using PLINK version v1.07 (2). All study methods were approved by the appropriate ethics committees and written parental consent was obtained for all participants.

#### *The Avon Longitudinal Study of Parents and Children (ALSPAC)*

ALSPAC is a longitudinal, population-based birth cohort study whose protocol has been described previously (5). Ethical approval was obtained from the ALSPAC Ethics and Law Committee and Local Research Ethics Committees, and written informed consent was obtained for all measurements.

ALSPAC recruited 14,541 pregnant women resident in Avon, UK with expected dates of delivery 1st April 1991 to 31st December 1992(5) 14,541 is the *initial* number of pregnancies for which the mother enrolled in the ALSPAC study and had either returned at least one questionnaire or attended a “Children in Focus” clinic by 19/07/99. Of these *initial* pregnancies, there were a total of 14,676 fetuses, resulting in 14,062 live births and 13,988 children who were alive at 1 year of age.

A total of 9912 children were genotyped using the Illumina HumanHap550 quad genome-wide SNP genotyping platform by 23andMe subcontracting the Wellcome Trust Sanger Institute, Cambridge, UK and the Laboratory Corporation of America, Burlington, NC, USA. Children were excluded from further analysis on the basis of having incorrect gender assignments; minimal or excessive heterozygosity ( $<0.320$  and  $>0.345$  for the Sanger data and  $<0.310$  and  $>0.330$  for the LabCorp data); disproportionate levels of individual missingness ( $>3\%$ ); evidence of cryptic relatedness (measured as proportion of identity by descent (IBD  $>0.1$ ) and insufficient sample replication (IBD  $<0.8$ ). The remaining children were assessed for evidence of population stratification by multidimensional scaling analysis and compared with Hapmap II (release 22) European descent (CEU), Han Chinese, Japanese and Yoruba reference populations; all children with non-European ancestry were removed to avoid population stratification, however this step removed very few children given the nature of the study and as a result had very little impact in the overall findings of the study. SNPs with a minor allele frequency of  $<1\%$ , a call rate of  $<95\%$  or evidence for violations of Hardy-Weinberg equilibrium ( $p < 5E-7$ ) were removed. Autosomal genotypic data were subsequently imputed using Markov Chain Haplotyping software (MACH v.1.0.16, Li et al. 2010) and phased haplotype data from CEU children (Hapmap release 22, Phase II NCBI B36, dbSNP 126) based on a cleaned dataset of 8,365 children and 464,311 autosomal SNPs. After imputation, all SNPs with indication of poor imputation quality ( $r^2 < 0.30$ ) were removed. Genotyping and cleaning has been previously documented (6).

Asthma at 7½ years was defined as a positive response to the question, “Has a doctor ever told you that your child has asthma?” in a questionnaire sent to their mothers at 91 months after birth.

Of 8,365 children with clean GWAS data, 5,562 had asthma status at age 7½ years available and 1,096 (19.7%) had asthma. Replication studies of selected SNPS were performed in PLINK regressing expected allelic dosage on case-control status.

*The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) multicenter study*

Subjects with severe or difficult to treat asthma were recruited as part of the TENOR study (7). These 438 cases represent adult subjects with asthma (mean age 47 years, 63% female), with mean FEV1 of 78.4 % of predicted, and a high percentage of atopy (394/409 patients had one or more positive skin tests) (8). DNA was isolated by using standard protocols, and SNP genotyping was performed with the Illumina HumanCNV370 BeadChip (Illumina, Inc, San Diego, California). QC and statistical analysis is described in the next section.

*CSGA /SARP/CAG*

The SARP non-Hispanic white population was composed of subjects from the NHLBI-funded SARP, and the CSGA population was from the NHLBI CSGA studies. Subjects with mild-to-severe asthma were recruited at SARP centers and carefully characterized, including baseline spirometric results and total serum IgE levels (9), (10). Subjects with asthma who were studied in CSGA by the Wake Forest investigators using a similar protocol were included in the analyses (11). In addition, healthy subjects without asthma recruited by SARP and CSGA investigators were included in the analysis. Controls were recruited from the same medical centers, and had no personal or first-degree relative family history of asthma. SARP and CSGA studies were approved by the appropriate Institutional Review Board at the participating sites including appropriate informed consent.

This sample consisted of 661 cases with asthma (mean age 33.1 years) and 363 age matched controls. The majority (65%) was female. Mean FEV<sub>1</sub> was 79.6 % of predicted, and 487 of 590 tested had a positive skin prick test for one or more aeroallergens (8).

Genotyping and QC: Genotyping was performed on the Illumina 1Mv1 platform, with individual genotypes called using clustering algorithms as implemented in the BeadStudio software by Illumina. For TENOR, CSGA and SARP: Samples were removed if they (1) had low genotyping call rates (<95%), (2) were discrepant or ambiguous for genetic sex (heterozygous haploid genotype percentage >0.01 or X-chromosome homozygosity F >0.9), (3) were not non-Hispanic whites as described), (4) failed the check for family relatedness (PI\_HAT >0.125), or (5) were detected as an outlier (>6 SDs for the first or second principal component). After subjects meeting these criteria were excluded, SNPs were removed if (1) the call rates were still low (95%), (2) inconsistent with Hardy-Weinberg equilibrium ( $p < 10^{-4}$ ) and (3) minor allele frequency was less than 0.05.

## Lung eQTL analysis

Non-tumor lung tissues were collected from patients who underwent lung resection surgery at three participating sites: Laval University (Quebec City, Canada), University of Groningen (Groningen, The Netherlands), and University of British Columbia (Vancouver, Canada) (12). At Laval, lung specimens were collected from patients undergoing lung cancer surgery and stored at the “Institut universitaire de cardiologie et de pneumologie de Québec” (IUCPQ) site of the Respiratory Health Network Tissue Bank of the “Fonds de recherche du Québec – Santé” ([www.tissuebank.ca](http://www.tissuebank.ca)). Written informed consent was obtained from all subjects and the study was approved by the IUCPQ ethics committee. At Groningen, lung specimens were provided by the local tissue bank of the Department of Pathology and the study protocol was consistent with the Research Code of the University Medical Center Groningen and Dutch national ethical and professional guidelines (“Code of conduct; Dutch federation of biomedical scientific societies”; <http://www.federa.org>). At Vancouver, the lung specimens were provided by the James Hogg Research Center Biobank at St Paul's Hospital and subjects provided written informed consent. The study was approved by the ethics committees at the UBC-Providence Health Care Research Institute Ethics Board.

Genome-wide gene expression and genotyping profiles were obtained using a custom Affymetrix array, Gene Expression Omnibus (GEO) platform GPL10379, and the Illumina Human1M-Duo BeadChip array, respectively. Gene expression data are available through the GEO repository with the accession number GSE23546. Standard quality controls were performed as described previously (12). Only 1095 subjects from Laval, Groningen, and UBC subjects that passed genotyping and expression quality controls were included in this study.

Probes located two Mb to the left and right of the base pair position of the top SNP were selected for the *cis*-eQTL analysis for that SNP (genome build reference 36.3). EQTL analyses were performed per site and then meta-analyzed. To correct for technical variance, principal components were calculated on the residuals of a linear regression on the gene-expression data with correction for gender, disease, age and smoking. Principal components which explained more than 5% of the variance were added as covariates in the eQTL

analysis on the gene-expression data. eQTL analysis was performed using a linear regression with correction for gender, disease, age, smoking and technical variance (principal components).

Selected probes were checked for any known polymorphisms in the probe (primer polymorphisms) (13). If primer polymorphisms were found with a minor allele frequency  $\geq 0.05$ , the gene transcript are shown in table E7b, but not used in the conclusions. A p-value of  $p < 6 \times 10^{-5}$  was considered significant, using a Bonferroni correction for all tests performed ( $p = 0.05/825$ ).



## **Association of additional phenotypes within asthma patients in the DAG cohort**

### *Airway wall biopsies*

In 98 of the asthmatics (11%) in this GWAS, airway wall biopsies were taken (14). In these biopsies the following markers were determined: CD4<sup>+</sup> cells, neutrophils and eosinophils. Values were log transformed to reach normal distribution.

### *Spirometry measurements and severity of BHR*

In 909 asthmatics (98%), Force Expiratory Volume in one second (FEV<sub>1</sub>) was measured with a calibrated water-sealed spirometer according to the standardized guidelines(15).

650 Subjects (71%), performed a BHR test using tidal breathing of a directly acting stimulus (histamine or methacholine) (15). Patients were bronchial hyperresponsive when a 20% fall of FEV<sub>1</sub> compared to baseline was reached, when nebulizing with a concentration  $\leq 9.8$  mg/ml methacholine bromide (equaling  $\leq 8$  mg/ml methacholine chloride) or  $\leq 8$  mg/ml histamine. Only asthmatics with data on smoking and steroid use were included for these analyses.

Severity of BHR was measured with a slope. The slope was calculated by dividing the difference between FEV<sub>1</sub> at baseline and at the dose step at which a 20% fall or more in FEV<sub>1</sub> was reached, by the dose was taken at this last step. We divided the BHR slopes of the 30-second tidal breathing method by 4 in order to compare the slope of the 30-second tidal breathing method with the 2-minute method. Values were log transformed to reach normal distribution.

### *Blood*

IgE and eosinophils were determined in blood. Total IgE was determined in 781 asthmatics (85%) (Mini Vidas, Biomerieux, France) and eosinophils in 777 asthmatics (84%).

### *Age of onset*

In 729 asthmatics (79%), age of onset of the disease was assessed with a self-reported questionnaire or by examining the medical history of asthmatics.

#### *Corticosteroid use*

Data on corticosteroid use in the last 12 months before the airway responsiveness challenge test was available for 905 asthmatics (98%).

#### *Atopy*

Atopy was measured in 673 asthmatics (74%) and defined as one or more positive tests either via intracutaneous or a skin prick test.

Supplementary table E1: Genome wide association studies in asthma: phenotype definition and Odds Ratios

First author (ref)	Asthma definition	Chr.	Gene	rs number	Risk allele	OR, 95%CI	Comments
Torgerson (16)	Doctor's diagnosis (+ in subset + symptoms and reversibility or BHR)	1	<i>PYHIN1</i>	rs1102000	T	1.32(1.17-1.46)	Afr Am /Carib pop.
		2	<i>IL1RL1</i>	rs10173081	C	1.20(1.11-1.29)	All US ethnicities
		5	<i>TSLP</i>	rs1837235	C	1.19(1.12-1.27)	All US ethnicities
		9	<i>IL33</i>	rs2381416	C	1.18(1.08-1.28)	All US ethnicities
		17	<i>GSDMB</i>	rs11078927	C	1.27(1.20-1.34)	All US ethnicities
Ferreira (17)	Doctor's diagnosis	1	<i>IL6R</i>	rs41296267	T	1.09 (1.06-1.12)	Australian discovery
		11	11q13.5	rs7130588	G	1.09 (1.06-1.13)	<i>LRRC32</i> is closest gene
Himes (18)	Childhood onset asthma, all patients had BHR	5	<i>PDE4D</i>	rs1588265	A	G: Protective Allele 0.85 (0.77-0.93) A: Risk allele 1.18 (1.08-1.30)	OR in discovery and replication populations; OR in discovery: 0.60 (0.48-0.71)
Moffatt (3, 19)	Doctor's diagnosis, Childhood onset asthma	17	<i>ORMDL3</i>	rs7216398	T	NA	OR = 1.45 in replication sample
		17	<i>GSDMA</i>	rs3894194	A	1.17 (1.11-1.23)	GABRIEL meta-analysis
		17	<i>GSDMB</i>	rs2305480	G	1.18 (1.11-1.23)	GABRIEL
		6	<i>HLA-DQ</i>	rs9273349	C	1.18 (1.13-1.24)	GABRIEL
		22	<i>IL2RB</i>	rs2284033	G	1.12 (1.08-1.16)	GABRIEL
		2	<i>IL18R1/IL1RL1</i>	rs3771166	G	1.15 (1.10-1.20)	GABRIEL
		9	<i>IL33</i>	rs1342326	C	1.20 (1.13-1.28)	GABRIEL
		15	<i>SMAD3</i>	rs744910	G	1.12 (1.09-1.16)	GABRIEL
Sleiman (20)	Children with persistent asthma on inhaled corticosteroids	1	<i>DENND1B</i>	rs2786098	C	1.42 (1.28-1.59)	European Ancestry population (CHOP)
Noguchi (21)	Doctor's diagnosis in children	6	HLA-DP	rs987870	G	1.40 (1.26–1.55)	Japanese population

Hirota (22)	Doctor's diagnosis in adults	4		rs7686660	T	1.16 (1.11-1.21)	Japanese population
		6	<i>HLA-DQ</i>	rs404860	A	1.21 (1.16-1.25)	Japanese population
		10	Gene desert, <i>GATA3</i> 1mB	rs10508372	C	1.16 (1.12-1.21)	Japanese population
		12	a.o. <i>IKZF4</i>	rs1701704	G	1.19 (1.14-1.25)	Japanese population
Schauberger (23)	Doctor's diagnosis in children	1	<i>ATPAF1</i>	rs2289447	C	NA	Caucasian European ancestry population
Anantharaman (24)	Doctor's diagnosis and questionnaire and atopy status by skin prick test	17	<i>PERLD1</i>	rs2941504	G	0.78 (0.653-0.941)	Chinese population
Lasky-Su (25)	Doctor's diagnosis	6	<i>HLA-DQA1</i>	rs9272346	G	NA	Adult Caucasian population
Bonnelyke (26)	with repeated acute hospitalization	7	<i>CDHR3</i>	rs6967330	A	1.26 (1.18-1.33)	Caucasian population of children

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Only studies with genome wide significant results after replication (  $p < 5 \times 10^{-8}$  ) were selected. Odds Ratios of initial study are reported. CHR: Chromosome; OR: Odds Ratio; CI: Confidence interval; BHR: Bronchial Hyperresponsiveness; NA: Not annotated

Supplementary table E2: Characteristics GWAS I and GWAS II of Dutch Asthma GWAS Cohort

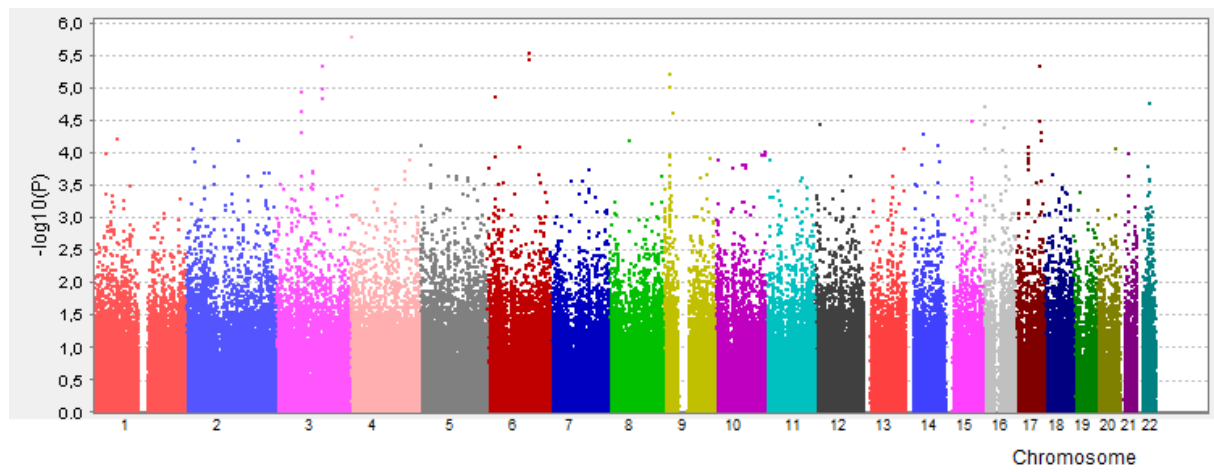
	ALL GWAS		GWAS I		GWAS II	
	Cases (n=920)	Controls (n=631)	Cases (n=468)	Controls (n=120)	Cases (n=452)	Controls (n=511)
<b>Characteristics</b>						
Height (m)	1.68 ± 0.17	1.78 ± 0.07	1.69 ± 0.15	1.70 ± 0.08	1.68 ± 0.79	1.79 ± 0.06
Weight (kg)	71 ± 22	76 ± 12	71 ± 21	76 ± 12	71 ± 24	
Gender (male)	430 (47)	557 (84)	215 (46)	46 (38)	215 (48)	511 (100)
Age (years)	34 ± 16	57 ± 6	33 ± 15.3	50 ± 8.2	36 ± 16	58 ± 5
<i>Smoking, n (%)</i>						
Current smoker	147 (16)	556 (88)	69 (15)	45 (37)	78 (18)	511 (100)
Never smoker	544 (59)	32 (5)	280 (60)	32 (27)	264 (58)	-
Ex-smoker	226 (25)	43 (7)	118 (25)	43 (36)	108 (24)	-
Pack years	7 [2;16]	34 [25;44]	5 [2;13]	14 [6;25]	8 [2;19]	34 [28;44]
<i>Steroids use in last 12 months, n (%)</i>						
Oral steroids	51 (6)	1 (1)	16 (4)	-	35 (8)	-
Inhaled steroids	506 (55)	-	298 (64)	-	208 (58)	-
Oral and inhaled steroids	23 (2)	-	13 (3)	-	10 (2)	-
No steroids	325 (35)	631 (100)	130 (29)	119 (100)	195 (43)	511 (100)
<b>Lung function</b>						
FEV <sub>1</sub> % predicted	86 ± 21	103 ± 12	85 ± 21	101 ± 13	88 ± 21	104 ± 11
<i>Hyperresponsiveness</i>						
PC20 methacholine (mg/ml)	0.67 [0.18;2.37]	-	1.89 [0.59;4.82]	-	0.41 [0.12;1.12]	-
					5.89	
PC20 histamine (mg/ml)	3.48 [1.14;11.23]	-	2.98 [0.90;9.45]	-	[1.70;12.76]	-
<b>Blood</b>						
Eosinophils, 10 <sup>-7</sup> /l	17 [10;29]	7 [3;12]	15 [8;26]	7 [3;12]	18 [10;32]	-
Total IgE, kU/l	130 [44;375]	20 [9;52]	143 [45;469]	20 [9;52]	115 [42;309]	-
<b>Atopy (yes) (n=673)</b>	575 (74%)	-	380 (83%)	-	195 (90%)	-
<b>Studies included in the DAG cohort (number of asthmatics %)</b>	920 (100)	980 (100)	468 (100)	469 (100)	452 (100)	511 (100)

SITA (27)	35 (4)	-	-	-	35 (8)	-
AST (28)	22 (2)	-	-	-	22 (5)	-
Nocturnal asthma (29)	39 (4)	-	-	-	36 (8)	-
SGO (30)	10 (1)	-	10 (2)	-	-	-
Stepdown (31)	64 (7)	-	-	-	64 (14)	-
KGO (32)	50 (6)	-	50 (11)	-	-	-
PIAMA (33)	63 (7)	-	22 (5)	-	41 (9)	-
Prevasc (34)	21 (2)	-	-	-	21 (4)	-
ELON (35)	6 (1)	-	-	-	6 (1)	-
Beatrixoord families (36)	229 (25)	150 (16)	130 (28)	150 (33)	99 (22)	-
Trios (36)	299 (32)	316 (32)	256 (54)	316 (67)	43 (10)	-
Van Lookeren (37)	60 (6)	-	-	-	60 (13)	-
Smoking in asthma (14)	25 (3)	-	-	-	25 (6)	-
Copacetic (11)	-	511 (52)	-	-	-	511 (100)

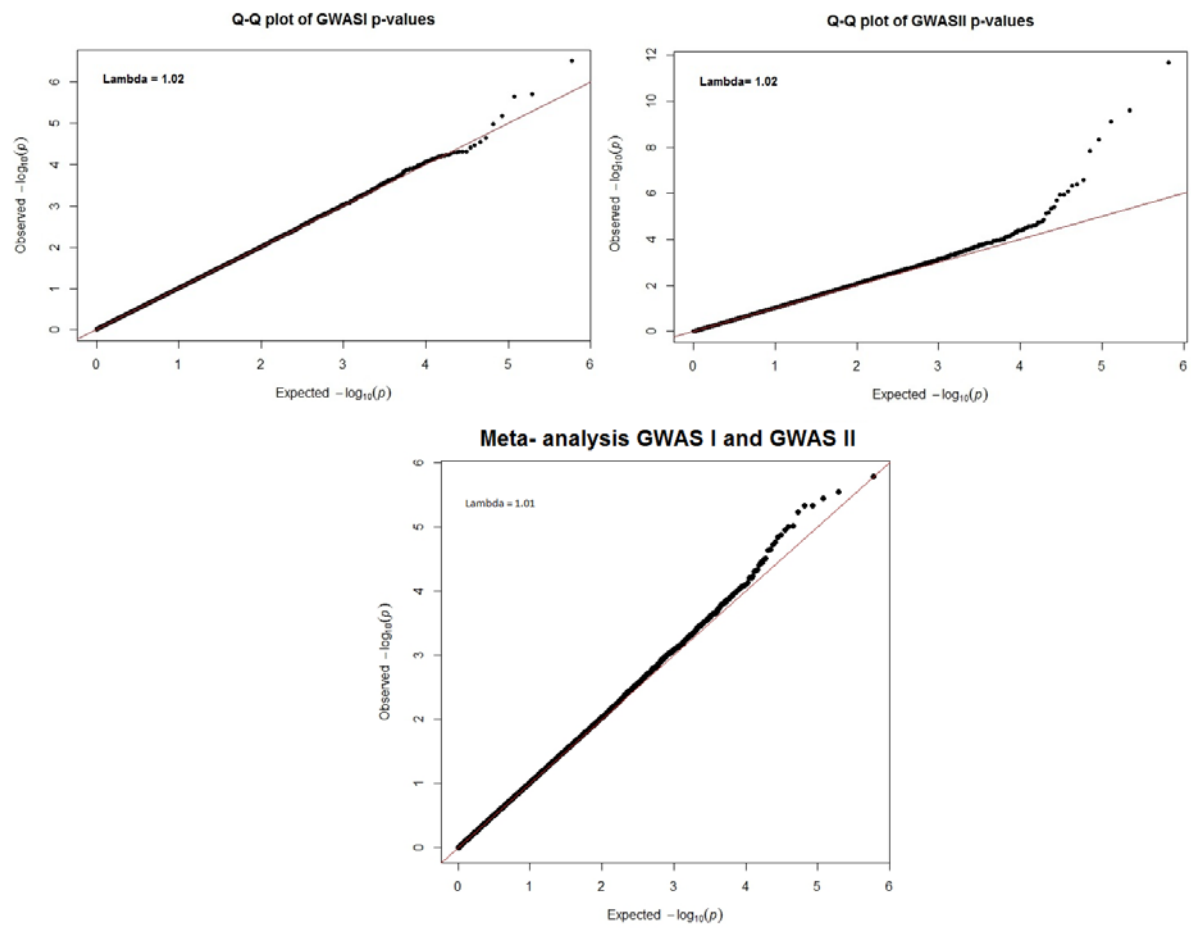
\*Not all controls in GWAS I have a phenotype; this is due to the 349 pseudo controls. In these controls the untransmitted alleles from father and mother of asthmatics out of GWAS I were used as the genotype.

Mean ±Standard deviation; Median [range]; Number (%)

Supplementary figure E3: Manhattan plot of Dutch Asthma GWAS on asthma with presence of bronchial hyperresponsiveness

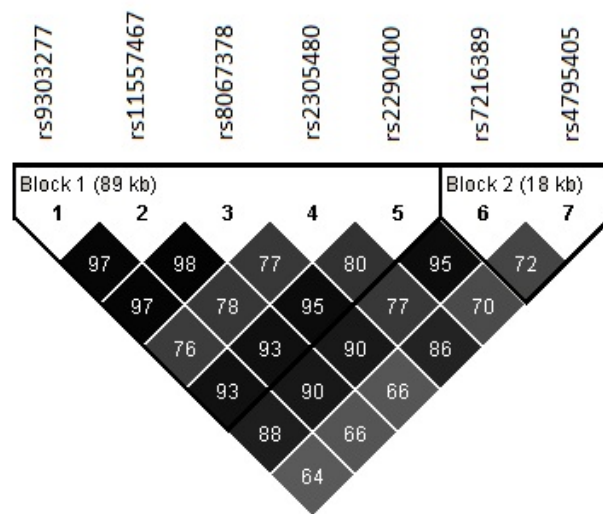


Supplementary figure E4: QQ-plots of GWAS I, GWAS II and the meta-analysis of the Dutch Asthma GWAS.

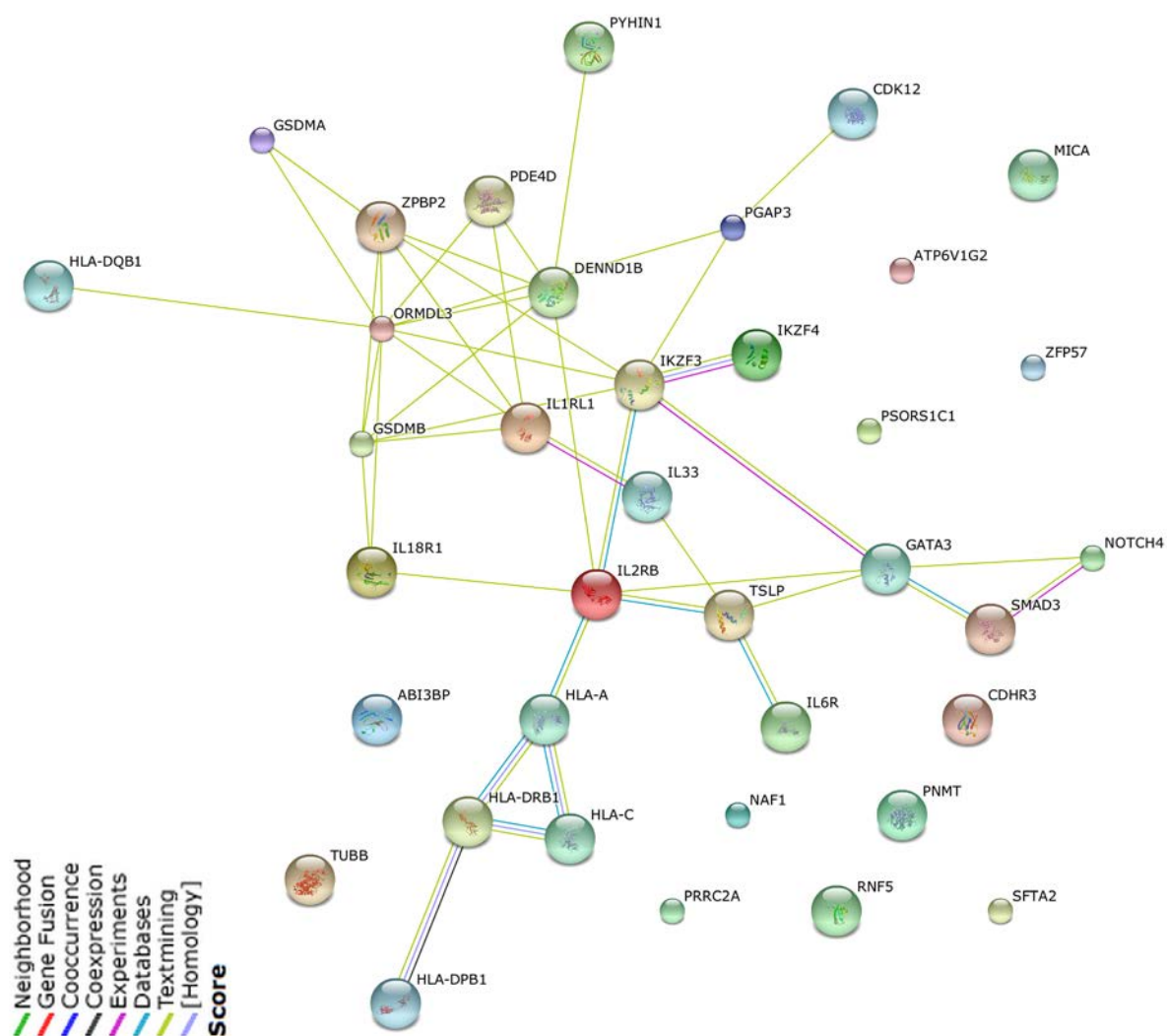




Supplementary figure E5: Linkage disequilibrium plot of asthma-associated SNPs at the 17q12 locus (LD shown as  $r^2 \times 100$ )



Supplemental figure E6: Pathway analysis of genes identified in GWAS and eQTL analysis



Supplementary table E7: An overview of function in the literature of the 7 top SNPs in our GWAS on asthma with presence of BHR

SNP	Suggested gene	Association in literature
rs1449302 & rs13091963	<i>ABI3BP</i>	Involved in stress induced premature senescence (SIPS), which could lead to cellular senescence and tumor suppression in lung cancer via oxidative stress. The precise mechanisms are unclear (38, 39)
rs4132177	<i>NAF1</i>	Knock-out mouse shows early senescence accompanied by a shortened lifespan via degenerations of the mitochondria thereby inducing autophagy which leads to cell death. A second mechanism is by endoplasmatic reticulum IP3 Ca2+ leak channels in skeletal muscle (40, 41)
rs2596560	<i>MICA</i>	<i>MICA</i> is associated with the RSV infection in young childhood which could lead to asthma (42)
rs2290400 & rs2305480	<b><u>GSDMB</u></b>	Association with early childhood asthma onset, precise mechanisms unclear (43)

# SNPs of genes in bold, italic and underlined are genic, other SNPs are intergenic

SNP; Single Nucleotide Polymorphism

Supplementary table E8: Overview of gene transcripts identified in the eQTL analysis

Locus of the identified gene, SNP which leads to an eQTL in the gene, risk allele of the SNP leading to the eQTL, up or down regulation of the gene transcript by risk allele of the SNP and function of the gene (known in genecards.org)

Gene	locus	SNP	Risk allele	regulation	function*
<i>ABI3BP</i>	3q12.2	rs13091963 rs1449302	A C	up	Involved in stress induced premature senescence (SIPS), which could lead to cellular senescence and tumor suppression in lung cancer via oxidative stress. Precise mechanisms are unclear
<i>HCG18</i>	6q21.3	rs2596560	C	down	Function unknown
<i>FLOT1</i>	6q21.3	rs2596560	C	up	May act as a scaffolding protein within caveolar membranes, functionally participating in formation of caveolae or caveolae-like vesicles
<i>HLA-A</i>	6q21.3	rs2596560	C	up&down	Involved in the presentation of foreign antigens to the immune system
<i>PSORS1C1</i>	6q21.3	rs2596560	C	down	This gene is one of several genes thought to confer susceptibility to psoriasis and systemic sclerosis.
<i>HLA-C</i>	6q21.3	rs2596560	C	down	Involved in the presentation of foreign antigens to the immune system
<i>ATP6V1G2</i>	6q21.3	rs2596560	C	down	Catalytic subunit of the peripheral V1 complex of vacuolar ATPase (V-ATPase). V-ATPase is responsible for acidifying a variety of intracellular compartments in eukaryotic cells
<i>NOTCH4</i>	6q21.3	rs2596560	C	down	Suggested to play a role in angiogenesis and airway remodeling
<i>TUBB</i>	6q21.3	rs2596560	C	up	Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha chain
<i>BAT2</i>	6q21.3	rs2596560	C	down	May play a role in the regulation of pre-mRNA splicing
<i>HLA-DQB1</i>	6q21.3	rs2596560	C	down	Binds peptides derived from antigens that access the endocytic route of antigen presenting cells (APC) and presents them on the cell surface for recognition by the CD4 T-cells.
<i>ZFP57</i>	6q21.3	rs2596560	C	up	Transcription regulator required to maintain maternal and paternal gene imprinting, a process by which gene expression is restricted in a parent of origin-specific manner by epigenetic modification of genomic DNA and chromatin, including DNA methylation
<i>SFTA2</i>	6q21.33	rs2596560	C	up	<i>SFTA2</i> (surfactant associated 2) is a protein-coding gene

<i>RNF5</i>	6q21.3	rs2596560	C	up	The protein encoded by this gene contains a RING finger, which is a motif known to be involved in protein-protein interactions. This protein is a membrane-bound ubiquitin ligase. It can regulate cell motility by targeting paxillin ubiquitination and altering the distribution and localization of paxillin in cytoplasm and cell focal adhesions
<i>HLA-DPB1</i>	6q21.3	rs2596560	C	up	HLA-DPB belongs to the HLA class II beta chain paralogues. This class II molecule is a heterodimer consisting of an alpha (DPA) and a beta chain (DPB), both anchored in the membrane. It plays a central role in the immune system by presenting peptides derived from extracellular protein
<i>HLA-DRB1</i>	6q21.3	rs2596560	C	up	HLA-DRB1 belongs to the HLA class II beta chain paralogues. The class II molecule is a heterodimer consisting of an alpha (DRA) and a beta chain (DRB), both anchored in the membrane. It plays a central role in the immune system by presenting peptides derived from extracellular proteins by presenting peptides derived from extracellular proteins
<i>GSDMB</i>	17q12.21	rs2305480 rs2290400	A C	down	May play a role as secretory or metabolic product involved in secretory pathway. May also play a role in achieving and maintaining the final differentiation state of epithelial cells
<i>GSDMA</i>	17q12.21	rs2305480 rs2290400	A C	up	Induces apoptosis
<i>CRKRS</i>	17q12.21	rs2305480 rs2290400	A C	up	Cyclin-dependent kinase which displays CTD kinase activity and is required for RNA splicing
<i>PERLD1</i>	17q12.21	rs2305480 rs2290400	A C	down	Involved in the lipid remodeling steps of GPI-anchor maturation.
<i>ORMDL3</i>	17q12.21	rs2305480 rs2290400	A C	down	Negative regulator of sphingolipid synthesis. May indirectly regulate endoplasmic reticulum-mediated Ca(+2) signaling
<i>PNMT</i>	17q12.21	rs2290400	C	down	Converts noradrenaline to adrenaline
<i>IKZF3</i>	17q12.21	rs2290400	C	up	Transcription factor that plays an important role in the regulation of lymphocyte differentiation. Plays an essential role in regulation of B-cell differentiation, proliferation and maturation to an effector state. Involved in regulating BCL2 expression and controlling apoptosis in T-cells in an IL2-dependent manner

\* function as known on [genecards.org](http://genecards.org)

SNP; Single Nucleotide Polymorphism

Supplementary table E9: Results of eQTL analysis.

A. Gene transcripts without a primer polymorphism in one of the probes.

SNP	Risk allele	eQTL gene	(ref 36.3) start eQTL	(ref 36.3) stop eQTL	beta	p-value
rs13091963	G	<i>ABI3BP</i>	102127882	102190794	-0.11	1.95*10 <sup>-15</sup>
		<i>ABI3BP</i>	101950689	101951270	-0.06	2.52*10 <sup>-07</sup>
rs1449302	T	<i>ABI3BP</i>	102127882	102190794	-0.06	2.38*10 <sup>-08</sup>
rs2596560	T	<i>ZFP57</i>	29748256	29766468	0.53	2.66*10 <sup>-19</sup>
		<i>HLA-A</i>	30019070	30085606	0.10	1.32*10 <sup>-11</sup>
		<i>HLA-C</i>	31344828	31347827	-0.04	5.41*10 <sup>-10</sup>
		<i>TUBB</i>	30796135	30801172	0.05	5.88*10 <sup>-10</sup>
		<i>HLA-DQB1</i>	32735222	32742439	-0.06	5.43*10 <sup>-08</sup>
		<i>ATP6V1G2</i>	31620220	31622606	-0.12	7.52*10 <sup>-08</sup>
		<i>HLA-DQB1</i>	32735634	32742444	-0.06	1.11*10 <sup>-07</sup>
		<i>HLA-DQB1</i>	32735641	32742443	-0.06	1.44*10 <sup>-07</sup>
		<i>NOTCH4</i>	32270598	32299822	-0.07	2.73*10 <sup>-07</sup>
		<i>HLA-DRB1</i>	32594309	32665569	0.13	5.99*10 <sup>-07</sup>
		<i>HLA-A</i>	30018309	30021632	-0.10	1.19*10 <sup>-06</sup>
		<i>BAT2</i>	31696428	31713533	-0.04	1.26*10 <sup>-06</sup>
		<i>SFTA2</i>	31007105	31007931	0.06	1.85*10 <sup>-06</sup>
		<i>PSORS1C1</i>	31190601	31215816	-0.17	2.42*10 <sup>-06</sup>
		<i>RNF5</i>	32254139	32256548	0.04	2.75*10 <sup>-06</sup>
		<i>HLA-DPB1</i>	33151737	33162954	0.09	8.07*10 <sup>-06</sup>
rs2290400	T	<i>GSDMB</i>	35314375	35328429	0.14	2.24*10 <sup>-46</sup>
		<i>GSDMA</i>	35372751	35387545	-0.33	3.95*10 <sup>-25</sup>
		<i>CRKRS</i>	34942504	34943280	-0.08	3.80*10 <sup>-24</sup>
		<i>ORMDL3</i>	35330821	35337380	0.07	4.61*10 <sup>-19</sup>
		<i>CRKRS</i>	34941825	34942053	-0.10	1.82*10 <sup>-15</sup>
		<i>CRKRS</i>	34871264	34944326	-0.10	2.64*10 <sup>-14</sup>
		<i>PERLD1</i>	35080901	35097836	0.04	1.30*10 <sup>-08</sup>
		<i>IKZF3</i>	35174726	35273967	-0.07	4.70*10 <sup>-06</sup>
		<i>PNMT</i>	35078032	35080254	0.11	7.65*10 <sup>-06</sup>
rs2305480	G	<i>GSDMB</i>	35314375	35328429	0.14	3.41*10 <sup>-42</sup>
		<i>GSDMA</i>	35372751	35387545	-0.40	3.55*10 <sup>-37</sup>
		<i>CRKRS</i>	34942504	34943280	-0.07	9.38*10 <sup>-17</sup>
		<i>ORMDL3</i>	35330821	35337380	0.06	5.61*10 <sup>-16</sup>
		<i>CRKRS</i>	34941825	34942053	-0.09	1.22*10 <sup>-12</sup>
		<i>CRKRS</i>	34871264	34944326	-0.09	9.40*10 <sup>-12</sup>
		<i>PERLD1</i>	35080901	35097836	0.03	9.38*10 <sup>-07</sup>

SNP; Single Nucleotide Polymorphism

B. Gene transcripts with a primer polymorphism in one of the probes of the gene transcripts, are not used in the conclusions

SNP	Risk allele	eQTL gene	(ref 36.3) start eQTL	(ref 36.3) stop eQTL	beta	p-value
rs2596560	T	<i>HLA-C</i>	31344506	31347861	-0.16	$1.12 \cdot 10^{-27}$
		<i>MICB</i>	31573944	31586877	0.10	$6.83 \cdot 10^{-14}$
		<i>APOM</i>	31731649	31733965	-0.08	$3.19 \cdot 10^{-11}$
		<i>HLA-G</i>	29903802	29905448	-0.10	$1.24 \cdot 10^{-10}$
		<i>HCP5</i>	31538937	31541460	-0.09	$4.85 \cdot 10^{-09}$
		<i>C6orf12</i>	30081147	30081403	0.13	$6.23 \cdot 10^{-09}$
		<i>NCR3</i>	31664650	31668741	0.12	$6.70 \cdot 10^{-09}$
		<i>VAR52</i>	30989960	31002212	-0.07	$4.52 \cdot 10^{-08}$
		<i>HLA-DQB2</i>	32831853	32839245	0.32	$1.02 \cdot 10^{-07}$
		<i>LST1</i>	31661949	31664664	0.06	$6.32 \cdot 10^{-07}$
		<i>HLA-G</i>	29902734	29906878	-0.10	$4.05 \cdot 10^{-06}$
		<i>HCG4P6</i>	30000478	30002971	0.12	$1.03 \cdot 10^{-05}$

SNP; Single Nucleotide Polymorphism

Supplementary table E10: All results of the in depth phenotyping

Association of top hit SNPs with age of onset of asthma, steroid use, atopy (positive skin prick test), FEV<sub>1</sub>% predicted, BHR severity, eosinophils, total IgE, CD4<sup>+</sup>, neutrophils and eosinophils (EPX) (analyzed in an additive regression model).

	CHR	3	3	4	6	17	17
	SNP	rs1449302	rs13091963	rs4132177	rs2596560	rs2305480	rs2290400
	risk allele	T	G	A	C	G	T
Phenotypes	MAF	0.56	0.72	0.05	0.29	0.56	0.51
Age onset	OR	0.84	0.85	1.09	1.13	1.15	1.12
≤4 years n=312	Se	0.11	0.12	0.22	0.12	0.12	0.11
≥4 years n=417	P	0.11	0.18	0.7	0.31	0.24	0.32
Age onset	OR	0.86	1.06	0.86	1.1	1.12	1.08
≤16 years n=553	Se	0.12	0.13	0.23	0.13	0.12	0.12
≥16 years n=176	P	0.2	0.62	0.52	0.47	0.35	0.48
Steroids	OR	0.83	0.83	1.01	0.94	0.92	0.93
yes n=580	Se	0.1	0.11	0.2	0.11	0.1	0.1
no n=325	P	0.24	0.1	0.96	0.58	0.44	0.47
Atopy	OR	0.78	0.83	0.58	1.5	1.14	1.11
n=575	Se	0.16	0.18	0.26	0.18	0.16	0.15
no=98	P	0.11	0.3	<b>0.03</b>	<b>0.03</b>	0.4	0.49
Eos	Beta	-0.001	0.02	0.02	-0.02	-0.04	-0.02
n=777	Se	0.05	0.05	0.1	0.05	0.05	0.05
	P	0.98	0.71	0.87	0.67	0.49	0.67
FEV1 % predicted	Beta	-1.1	-0.96	-0.4	0.87	0.04	0.57
n=909	Se	0.96	1.09	1.93	1.05	0.99	0.97
	P	0.25	0.38	0.84	0.41	0.97	0.56
Total IgE	Beta	-0.19	-0.22	-0.05	-0.002	0.12	0.12
n=781	Se	0.08	0.09	0.16	0.09	0.08	0.08
	P	<b>0.02</b>	<b>9.50E-03</b>	0.76	0.98	0.14	0.13
BHR severity	Beta	0.01	-0.03	-0.22	-0.01	0.15	0.09
n=650	Se	0.09	0.1	0.17	0.09	0.09	0.08
	P	0.95	0.74	0.18	0.92	0.08	0.26
Neutrophils	Beta	-0.08	-0.09	0.4	-0.04	-0.02	-0.1
n=98	Se	0.14	0.15	0.3	0.14	0.14	0.14
	P	0.55	0.56	0.18	0.76	0.86	0.45
CD4	Beta	0.2	0.18	-0.36	0.12	0.4	0.34
n=98	Se	0.16	0.18	0.36	0.16	0.16	0.16
	P	0.23	0.34	0.32	0.47	<b>0.02</b>	<b>0.04</b>
EPX	Beta	-0.17	-0.14	0.14	0.14	0.31	0.21
n=98	Se	0.15	0.17	0.33	0.15	0.15	0.15
	P	0.26	0.39	0.67	0.36	<b>0.04</b>	0.15

\* Not all subphenotype are measure in all asthmatics

SNP: Single Nucleotide Polymorphism; CHR: Chromosome; MAF: Minor allele frequency; OR: Odds Ratio; Se: Standard error; P: p-value



Supplementary table E11: Overview of STRING network analyses; all FDR significant GO biological processes (A) and KEGG (B) pathway analysis.

A:

Go biological pathway	Number of genes	P-value*	Genes
Regulation of interferon-gamma production	8	1.47E-8	<i>HLA-DPB1, HLA-DRB1, HLA-A, IL18R1, PDE4D, GATA3, IL1RL1, IL33</i>
Positive regulation of interleukin-5 production	4	9.11E-7	<i>IL33, IL1RL1, GATA3, PDE4D</i>
Regulation of interleukin-5 production	4	4.01E-5	<i>IL33, IL1RL1, GATA3, PDE4D</i>
Positive regulation of cytokine production	8	2.04E-4	<i>HLA-DPB1, HLA-A, IL1RL1, GATA3, IL18R1, PDE4D, IL6R, SMAD3</i>
Cellular response to cytokine stimulus	9	2.96E-4	<i>HLA-DPB1, HLA-DRB1, HLA-C, HLA-A, IL2RB, IL18R1, GATA3, IL1RL1, HLA-DQB1</i>
Cytokine-mediated signaling pathway	8	2.96E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, GATA3, PDE4D</i>
Negative regulation of interferon-gamma production	4	2.96E-4	<i>HLA-C, HLA-DRB1, IL33, IL1RL1, HLA-DQB1</i>
Interferon-gamma-mediated signaling pathway	5	3.87E-4	<i>HLA-DPB1, HLA-DRB1, HLA-C, HLA-A, HLA-DQB1</i>
Regulation of leukocyte activation	8	3.95E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, IL-33, IL1RL1, IKZF3, MICA</i>
Positive regulation of leukocyte activation	7	4.11E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, IL-33, IL1RL1, GATA3</i>
Positive regulation of cell activation	7	4.73E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, IL-33, IL1RL1, GATA3</i>
Regulation of cell activation	8	5.05E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, IL-33, IL1RL1, IKZF3, MICA</i>
Response to cytokine	9	5.83E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A, IL18R1, IL2RB, GATA3, IL1RL1</i>
T cell receptor signaling pathway	5	5.83E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, GATA3, PDE4D</i>
Regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	5	8.29E-4	<i>HLA-DRB1, HLA-DQB1, HLA-C, IL33, IL1RL1</i>
Cellular response to interferon-gamma	5	8.48E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Negative regulation of immune response	5	8.48E-4	<i>HLA-DRB1, HLA-A, IL33, IL1RL1, MICA</i>
Regulation of adaptive immune response	5	1.02E-3	<i>HLA-DRB1, HLA-A, IL33, IL1RL1, HLA-DQB1</i>
Positive regulation of cell adhesion	7	1.23E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, GATA3, SMAD3, ABI3BP</i>
Regulation of leukocyte mediated cytotoxicity	4	1.24E-3	<i>HLA-DRB1, HLA-DQB1, HLA-C, MICA</i>

Negative regulation of defense response	5	1.24E-3	<i>HLA-DRB1, HLA-A, GATA3, SMAD3, MICA</i>
Antigen receptor-mediated signaling pathway	5	1.24E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, GATA3, PDE4D</i>
Response to interferon-gamma	5	1.29E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	5	1.29E-3	<i>HLA-DRB1, HLA-DQB1, GATA3, IL18R1, MICA</i>
Positive regulation of interferon-gamma production	4	1.34E-3	<i>HLA-DPB1, HLA-A, IL18R1, PDE4D</i>
Regulation of cell killing	4	1.61E-3	<i>HLA-BRB1, HLA-DQB1, MICA</i>
Regulation of immune response	9	2.55E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, IL33, IL1RL1, GATA3, SMAD3, PDE4D, MICA</i>
Regulation of response to external stimulus	8	3.67E-3	<i>HLA-DRB1, HLA-A, IL33, IL1RL1, GATA3, SMAD3, RNF5, IL6R</i>
Adaptive immune response	5	3.67E-3	<i>HLA-DRB1, HLA-DQB1, GATA3, IL18R1, MICA</i>
Regulation of interleukin-4 production	3	3.67E-3	<i>HLA-DRB1, IL33, GATA3</i>
Response to other organism	8	3.67E-3	<i>HLA-DRB1, HLA-A, GATA3, SMAD3, RNF5, PDE4D, IL6R, MICA</i>
Positive regulation of T cell mediated cytotoxicity	3	3.67E-3	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Leukocyte mediated immunity	5	3.67E-3	<i>HLA-DRB1, HLA-DQB1, GATA3, IL6R, MICA</i>
Antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway, TAP-independent	2	3.67E-3	<i>HLA-A, HLA-C</i>
Antigen processing and presentation of exogenous peptide antigen	5	4.60E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, HLA-C</i>
Response to biotic stimulus	8	4.60E-3	<i>HLA-DRB1, HLA-A, RNF5, GATA3, SMAD3, PDE4D, MICA, IL6R</i>
Regulation of cytokine production	7	4.75E-3	<i>HLA-DPB1, HLA-DRB1, HLA-A, IL1RL1, IL18R1, PDE4D, IL6R</i>
Regulation of T cell mediated cytotoxicity	3	4.75E-3	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Antigen processing and presentation of exogenous antigen	5	4.96E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Positive regulation of T cell activation	5	4.96E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, GATA3</i>
Positive regulation of leukocyte cell-cell adhesion	5	5.11E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, GATA3</i>
Positive regulation of homotypic cell-cell adhesion	5	5.13E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, GATA3</i>
Negative regulation of cytokine production	5	5.73E-3	<i>HLA-DRB1, IL33, IL1RL1, GATA3, IL6R</i>
Regulation of lymphocyte activation	6	6.80E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, IKZF3, MICA</i>

Regulation of lymphocyte mediated immunity	4	9.17E-3	<i>HLA-DRB1, HLA-DQB1, HLA-C, MICA</i>
Positive regulation of cell-cell adhesion	5	9.91E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, GATA3</i>
Positive regulation of T cell mediated immunity	3	1.05E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Positive regulation of immune response	7	1.05E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, IL33, GATA3, PDE4D</i>
Positive regulation of chemokine production	3	1.16E-2	<i>IL33, IL1RL1, IL6R</i>
Positive regulation of leukocyte mediated cytotoxicity	3	1.16E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Negative regulation of T-helper 1 type immune response	2	1.21E-2	<i>IL33, IL1RL1</i>
Antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway	2	1.21E-2	<i>HLA-C, HLA-A</i>
Positive regulation of immune system process	8	1.29E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, IL1RL1, GATA3, PDE4D, IL6R</i>
Regulation of cytokine secretion	4	1.33E-2	<i>HLA-DRB1, IL33, IL1RL1, GATA3</i>
Positive regulation of lymphocyte activation	5	1.35E-2	<i>HLA-DPB1, HLA-DRBQ, HLA-DQB1, HLA-A, GATA3</i>
Regulation of defense response	7	1.35E-2	<i>HLA-DRB1, HLA-A, IL33, IL1RL1, GATA3, SMAD3, MICA</i>
Lymphocyte mediated immunity	4	1.35E-2	<i>HLA-DRB1, HLA-DQB1, GATA3, MICA</i>
Regulation of inflammatory response	5	1.36E-2	<i>HLA-DRB1, IL33, IL1RL1, GATA3, SMAD3</i>
Positive regulation of cell killing	3	1.43E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Cellular response to organic substance	11	1.44E-2	<i>HLA-DPB1, HLA-DRBQ, HLA-DQB1, HLA-A, HLA-C, IL1RL1, GATA3, IL18R1, IL2RB, RNF5, ATP6V1G2</i>
Immune effector process	6	1.60E-2	<i>HLA-DRB1, HLA-DQB1, GATA3, IL1RL1, IL6R, MICA</i>
Response to bacterium	6	1.75E-2	<i>HLA-DRB1, HLA-A, RNF5, PDE4D, IL6R, MICA</i>
Regulation of T cell mediated immunity	3	1.75E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Positive regulation of chemokine secretion	2	1.75E-2	<i>IL33, IL1RL1</i>
Negative regulation of natural killer cell mediated immunity	2	1.75E-2	<i>HLA-A, MICA</i>
Positive regulation of interleukin-13 production	2	1.75E-2	<i>IL33, GATA3</i>
Negative regulation of natural killer cell mediated cytotoxicity	2	1.75E-2	<i>HLA-A, MICA</i>
Regulation of leukocyte mediated immunity	4	1.81E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C, MICA</i>
Regulation of chemokine production	3	2.03E-2	<i>IL33-IL1RL1, IL6R</i>
Humoral immune response	4	2.03E-2	<i>HLA-DRB1, HLA-DQB1, HLA-A, GATA3</i>

Positive regulation of immune effector process	4	2.04E-2	<i>HLA-DRB1, HLA-DQB1, HLA-A, IL33</i>
Regulation of chemokine secretion	2	2.04E-2	<i>IL33, IL1RL1</i>
Type 2 immune response	2	2.04E-2	<i>IL33, GATA3</i>
Antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent	2	2.04E-2	<i>HLA-A, HLA-C</i>
Regulation of immune effector process	5	2.07E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C, IL33, MICA</i>
Immune response-activating cell surface receptor signaling pathway	5	2.08E-2	<i>HLA-DRB1, HLA-DRB1, HLA-DQB1, GATA3, PDE4D</i>
Regulation of immune system process	9	2.31E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, IL1RL1, SMAD3, IKZF3, PDE4D, IL6R, MICA</i>
Positive regulation of macrophage activation	2	2.39E-2	<i>IL33, IL1RL1</i>
Negative regulation of leukocyte mediated cytotoxicity	2	2.39E-2	<i>HLA-A, MICA</i>
Antigen processing and presentation of endogenous peptide antigen via MHC class I	2	2.88E-2	<i>HLA-C, HLA-A</i>
Lymphocyte activation	5	2.91E-2	<i>GATA3, SMAD3, IL18R1, IKZF3, MICA</i>
Negative regulation of immune system process	5	3.29E-2	<i>HLA-DRB1, HLA-A, IL33, IL1RL1, MICA</i>
Negative regulation of cell killing	2	3.29E-2	<i>HLA-A, MICA</i>
Antigen processing and presentation of endogenous peptide antigen	2	3.29E-2	<i>HLA-C, HLA-A</i>
Regulation of lymphocyte proliferation	4	3.67E-2	<i>HLA-DPB1, HLA-DRB1, HLA-A, IKZF3</i>
Regulation of mononuclear cell proliferation	4	3.71E-2	<i>HLA-DPB1, HLA-DRB1, HLA-A, IKZF3</i>
Regulation of interleukin-13 production	2	3.75E-2	<i>IL33, GATA3</i>
Positive regulation of lymphocyte mediated immunity	3	3.97E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Regulation of leukocyte proliferation	4	4.05E-2	<i>HLA-DPB1, HLA-DRB1, HLA-A, IKZF3</i>
Positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	3	4.05E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Antigen processing and presentation of endogenous antigen	2	4.05E-2	<i>HLA-C, HLA-A</i>
T-helper 1 type immune response	2	4.05E-2	<i>HLA-DRB1, IL18R1</i>
Detection of bacterium	2	4.05E-2	<i>HLA-DRB1, HLA-A</i>
Regulation of response to wounding	5	4.05E-2	<i>HLA-DRB1, IL33, IL1RL1, GATA3, SMAD3</i>
Positive regulation of adaptive immune response	3	4.35E-2	<i>HLA-DRB1, HLA-DQB1, HLA-C</i>
Positive regulation of cytokine secretion	3	4.46E-2	<i>IL33, IL1RL1, GATA3</i>
Regulation of cell adhesion	6	4.46E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-A, SMAD3, ABI3BP</i>
Detection of other organism	2	4.47E-2	<i>HLA-DRB1, HLA-A</i>

T cell costimulation	3	4.70E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Lymphocyte costimulation	3	4.84E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Positive regulation of interleukin-4 production	2	4.96E-2	<i>IL33, GATA3</i>
Cellular response to chemical stimulus	11	5.16E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A, IL18R1, IL2RB, RNF5, IL1RL1, GATA3, ATP6V1G2</i>

\*P-values are FDR corrected

## B:

Kegg pathway	Number of genes	P-value*	Gene
Allograft rejection	5	7.59E-7	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Graft-versus-host disease	5	7.59E-7	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Type I diabetes mellitus	5	8.78E-7	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Autoimmune thyroid disease	5	1.89E-6	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Viral myocarditis	5	2.73E-6	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Inflammatory bowel disease (IBD)	5	4.20E-6	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, GATA3, IL18R1</i>
Antigen processing and presentation	5	4.94E-6	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Phagosome	6	7.03E-6	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A, TUBB</i>
Cell adhesion molecules (CAMs)	5	1.41E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
HTLV-I infection	6	1.52E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A, IL2RB</i>
Herpes simplex infection	5	3.83E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Asthma	3	4.14E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Epstein-Barr virus infection	5	4.83E-4	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, HLA-C, HLA-A</i>
Intestinal immune network for IgA production	3	1.41E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Staphylococcus aureus infection	3	2.04E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Influenza A	4	4.02E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1, IL33</i>

Leishmaniasis	3	4.44E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Rheumatoid arthritis	3	7.74E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Systemic lupus erythematosus	3	9.85E-3	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Toxoplasmosis	3	1.56E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>
Cytokine-cytokine receptor interaction	4	1.65E-2	<i>IL18R1, IL2RB, TSLP, IL6R</i>
Natural killer cell mediated cytotoxicity	3	1.85E-2	<i>HLA-C, HLA-A, MICA</i>
Jak-STAT signaling pathway	3	3.36E-2	<i>IL2RB, TSLP, IL6R</i>
Tuberculosis	3	4.26E-2	<i>HLA-DPB1, HLA-DRB1, HLA-DQB1</i>

\*P-values are FDR corrected

**Supplementary table E12:** All asthma associated SNPs ( $p \leq 10^{-4}$  fixed effects) in the DAG cohort and meta-analysis. P; p-value fixed effect, P(R); p-value random effect, OR; Odds Ratio fixed effect, OR(R); Odds ratio random effect, I;  $I^2$  statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance

CHR	BP	SNP	A1	DAG Cohort					Meta-analysis					
				P	P(R)	OR	OR(R)	I	Included cohorts (n)	P	P(R)	OR	OR(R)	I
1	30258715	rs374904	T	4.23E-04	4.23E-04	0.68	0.68	0	3	1.22E-02	1.85E-01	0.80	0.80	70
1	30409346	rs12142410	G	9.93E-05	1.73E-03	0.72	0.72	35	3	1.81E-05	3.68E-05	0.75	0.75	7
1	43539725	rs7527092	A	8.02E-04	3.66E-02	1.25	1.25	62	3	2.91E-04	3.74E-03	1.21	1.21	37
1	47837606	rs12742768	G	4.56E-04	4.56E-04	1.47	1.47	0	3	5.48E-03	6.67E-02	1.27	1.28	58
1	48466846	rs764656	C	5.72E-04	5.72E-04	1.33	1.33	0	3	9.49E-03	1.08E-01	1.19	1.19	63
1	55746074	rs1695941	A	6.69E-04	6.69E-04	1.29	1.29	0	3	8.22E-03	7.29E-02	1.17	1.17	57
1	63867699	rs855314	G	5.85E-05	3.47E-04	0.69	0.69	21	3	2.68E-03	1.25E-01	0.80	0.79	76
1	81429313	rs4120877	T	7.04E-04	7.04E-04	1.33	1.33	0	3	5.82E-04	5.89E-04	1.26	1.26	0
1	81440903	rs2225966	G	5.27E-04	5.27E-04	1.27	1.27	0	3	6.53E-04	6.53E-04	1.20	1.20	0
1	99222557	rs12084355	C	3.10E-04	3.26E-02	0.75	0.74	67	3	4.03E-04	1.71E-02	0.79	0.79	57
1	188918156	rs10753952	T	9.79E-04	9.79E-04	0.79	0.79	0	3	9.52E-03	7.80E-02	0.86	0.86	56
1	188930912	rs10920778	T	8.13E-04	8.13E-04	0.79	0.79	0	3	7.70E-03	7.43E-02	0.86	0.85	57
1	233827440	rs10926189	T	4.90E-04	1.18E-03	0.78	0.78	14	3	2.87E-02	2.75E-01	0.88	0.87	79
2	15812394	rs10204448	A	5.97E-04	5.97E-04	0.62	0.62	0	3	4.42E-03	4.72E-02	0.73	0.73	52
2	20600243	rs10167494	T	8.32E-05	8.06E-04	0.76	0.76	27	3	1.55E-04	5.13E-03	0.82	0.81	47
2	24917697	rs2241759	G	1.32E-04	1.32E-04	0.78	0.78	0	3	1.26E-02	2.26E-01	0.88	0.87	79
2	43756570	rs3828297	A	7.31E-04	7.31E-04	1.28	1.28	0	3	1.57E-03	4.17E-03	1.20	1.20	19
2	50128278	rs1037426	C	4.86E-04	4.86E-04	0.79	0.79	0	5	1.15E-03	6.24E-03	0.88	0.88	37
2	50128582	rs3861561	G	3.28E-04	3.28E-04	0.78	0.78	0	3	3.40E-05	3.40E-05	0.80	0.80	0
2	76235569	rs12618337	C	3.01E-04	3.01E-04	1.58	1.58	0	3	1.78E-02	2.04E-01	1.26	1.30	77
2	76259467	rs1608590	T	1.59E-04	1.59E-04	1.56	1.56	0	3	6.01E-03	1.41E-01	1.29	1.32	75
2	76407585	rs1526611	A	1.54E-04	1.54E-04	1.49	1.49	0	3	5.49E-03	1.21E-01	1.27	1.28	71

2	106806735	rs7607147	C	7.38E-04	7.38E-04	0.64	0.64	0	3	8.92E-03	8.89E-02	0.76	0.76	57
2	106874134	rs6709151	C	6.25E-04	6.25E-04	0.71	0.71	0	3	6.31E-03	7.30E-02	0.80	0.80	60
2	126996061	rs1440049	T	4.16E-04	4.16E-04	1.40	1.40	0	3	6.86E-05	6.86E-05	1.35	1.35	0
2	127173938	rs17014263	G	5.86E-04	9.95E-03	1.49	1.49	44	3	9.73E-03	1.18E-01	1.25	1.29	71
2	128975785	rs7583856	G	7.85E-04	7.85E-04	1.34	1.34	0	3	1.02E-03	1.02E-03	1.25	1.25	0
2	141289053	rs6749275	C	6.27E-05	6.27E-05	1.30	1.30	0	3	6.68E-04	2.55E-02	1.20	1.20	59
2	167793103	rs7602119	T	2.29E-04	2.29E-04	0.72	0.72	0	3	9.63E-04	8.61E-03	0.79	0.79	37
2	167807984	rs10497323	C	5.29E-04	5.29E-04	0.73	0.73	0	3	1.17E-03	2.16E-03	0.79	0.79	11
2	173767653	rs3769165	C	8.10E-04	8.10E-04	1.31	1.31	0	3	3.02E-03	1.28E-02	1.21	1.21	30
2	205524087	rs6435265	T	3.10E-04	3.10E-04	1.28	1.28	0	3	5.11E-05	5.11E-05	1.25	1.25	0
2	210940277	rs10932328	C	1.96E-04	1.96E-04	1.34	1.34	0	3	1.49E-03	2.29E-02	1.22	1.23	50
2	215247415	rs6727011	T	5.49E-04	1.51E-02	0.62	0.63	45	3	2.54E-01	8.78E-01	0.87	0.94	91
2	217132354	rs12463731	T	6.20E-04	6.20E-04	0.79	0.79	0	3	2.12E-02	1.71E-01	0.88	0.87	70
2	217530158	rs1921987	A	5.33E-04	5.33E-04	0.79	0.79	0	3	9.19E-04	9.19E-04	0.84	0.84	0
2	221931479	rs1897121	A	6.87E-04	6.87E-04	1.27	1.27	0	3	8.47E-02	4.27E-01	1.10	1.11	82
2	226190916	rs1431086	A	1.98E-04	1.98E-04	1.48	1.48	0	3	9.26E-03	1.48E-01	1.24	1.26	73
2	226225481	rs4641920	C	9.83E-04	9.83E-04	1.32	1.32	0	3	5.61E-02	3.01E-01	1.14	1.15	77
2	239995931	rs843451	G	6.55E-04	1.23E-02	0.78	0.78	46	3	3.89E-03	6.47E-02	0.84	0.84	62
3	2689759	rs10510237	A	9.83E-04	9.83E-04	1.44	1.44	0	3	2.38E-02	1.88E-01	1.21	1.23	71
3	13165384	rs9864101	C	3.00E-04	2.94E-02	0.78	0.78	64	3	1.88E-03	7.09E-02	0.85	0.84	69
3	22457093	rs10510529	T	3.52E-04	3.52E-04	1.39	1.39	0	3	3.60E-02	3.22E-01	1.16	1.18	80
3	31900672	rs4438696	A	6.78E-04	6.78E-04	1.27	1.27	0	3	2.93E-02	2.29E-01	1.13	1.14	74
3	43358645	rs7621298	A	4.95E-04	4.95E-04	1.26	1.26	0	3	3.33E-02	2.72E-01	1.12	1.13	77
3	43643180	rs9852783	T	6.92E-04	1.87E-02	1.26	1.25	51	3	3.12E-02	2.96E-01	1.12	1.13	79
3	43801826	rs4682696	C	7.90E-04	7.90E-04	0.80	0.80	0	3	5.35E-02	3.21E-01	0.90	0.89	78
3	54441305	rs9818236	C	5.25E-04	9.28E-04	0.75	0.75	9	3	3.78E-03	5.37E-02	0.83	0.82	58
3	56771220	rs9825368	T	6.90E-04	6.90E-04	0.70	0.70	0	5	4.01E-03	3.65E-02	0.84	0.81	59
3	59517436	rs958241	C	7.47E-04	7.47E-04	1.30	1.30	0	3	6.00E-02	3.68E-01	1.12	1.13	80
3	67177936	rs13086581	T	8.79E-04	8.79E-04	0.67	0.67	0	3	4.72E-02	3.02E-01	0.83	0.82	77



3	68204481	rs6548962	C	3.51E-04	3.51E-04	1.27	1.27	0	3	3.65E-04	3.65E-04	1.21	1.21	0
3	68206421	rs7610023	C	4.62E-05	8.97E-05	1.32	1.32	8	3	1.32E-04	5.97E-03	1.23	1.23	51
3	68231965	rs6548984	C	2.22E-04	2.22E-04	1.28	1.28	0	3	1.47E-04	1.56E-04	1.22	1.22	1
3	68267702	rs6768632	T	1.11E-05	1.11E-05	1.34	1.34	0	3	3.46E-05	1.58E-03	1.25	1.25	43
3	68270600	rs6776172	G	2.23E-05	2.23E-05	1.38	1.38	0	3	2.39E-03	1.39E-01	1.20	1.21	78
3	79572661	rs4535189	G	9.64E-04	9.64E-04	0.81	0.81	0	3	5.86E-03	3.05E-02	0.87	0.86	40
3	96078762	rs7613024	A	9.66E-04	2.91E-03	1.61	1.62	19	3	8.72E-03	8.30E-02	1.34	1.38	62
3	96346161	rs4407407	C	3.29E-04	4.02E-02	1.65	1.67	69	3	1.15E-03	4.87E-02	1.43	1.46	67
3	96475398	rs6806336	A	6.60E-04	4.27E-02	1.61	1.62	66	3	1.28E-03	3.30E-02	1.43	1.45	59
3	102098240	rs2245556	T	3.51E-04	3.51E-04	0.70	0.70	0	3	2.54E-03	2.30E-02	0.79	0.78	48
3	102114269	rs2252229	C	1.83E-04	1.83E-04	0.78	0.78	0	3	1.63E-02	2.25E-01	0.88	0.87	78
3	102172552	rs10511181	G	8.43E-04	8.43E-04	0.71	0.71	0	3	6.75E-03	4.07E-02	0.81	0.80	48
3	102212341	rs1449302	C	2.91E-04	2.91E-04	0.79	0.79	0	5	1.56E-05	1.57E-04	0.88	0.87	28
3	102220701	rs13091963	A	1.95E-04	1.40E-01	0.76	0.76	85	5	1.77E-05	2.90E-03	0.87	0.85	58
3	105681807	rs2263357	G	8.46E-04	2.35E-02	0.75	0.75	53	3	4.78E-02	3.22E-01	0.88	0.86	81
3	128745447	rs2594210	A	9.88E-06	9.88E-06	0.74	0.74	0	3	1.74E-04	2.36E-02	0.82	0.81	66
3	128775478	rs4974445	C	1.45E-05	1.45E-05	0.72	0.72	0	3	8.64E-04	7.81E-02	0.82	0.81	74
3	128834182	rs13082666	T	4.58E-06	4.58E-06	0.73	0.73	0	3	9.17E-04	1.35E-01	0.83	0.83	81
3	168159533	rs7613166	G	4.57E-04	8.55E-04	0.75	0.75	10	3	5.63E-03	8.73E-02	0.83	0.83	65
3	179671802	rs13075114	G	4.56E-04	4.56E-04	1.33	1.33	0	3	2.64E-04	2.64E-04	1.27	1.27	0
4	5614097	rs13113867	A	8.84E-04	8.84E-04	1.26	1.26	0	3	5.01E-03	4.36E-02	1.16	1.17	52
4	7413908	rs10937807	A	1.60E-06	1.66E-04	0.72	0.72	38	3	1.20E-06	5.06E-04	0.77	0.77	50
4	16199686	rs11945652	A	9.11E-04	3.78E-03	1.29	1.29	23	3	4.37E-03	4.88E-02	1.19	1.19	53
4	17890573	rs10488992	A	8.83E-04	7.54E-03	1.32	1.32	34	3	2.28E-03	2.44E-02	1.23	1.23	46
4	66459835	rs7660970	G	5.50E-04	5.50E-04	0.78	0.78	0	3	6.43E-02	3.65E-01	0.90	0.89	81
4	70627379	rs2292092	T	3.47E-04	3.47E-04	0.78	0.78	0	3	1.48E-03	1.85E-02	0.84	0.84	47
4	70633662	rs1847366	T	3.47E-04	3.47E-04	0.78	0.78	0	3	1.76E-03	2.43E-02	0.84	0.84	50
4	77793218	rs7656480	G	3.57E-04	3.57E-04	1.30	1.30	0	3	6.53E-03	1.09E-01	1.17	1.18	67
4	77797774	rs903044	G	7.37E-04	7.37E-04	1.29	1.29	0	3	1.75E-02	1.82E-01	1.15	1.16	71

4	77808983	rs7691621	G	7.05E-04	7.05E-04	1.29	1.29	0	3	1.51E-02	1.49E-01	1.16	1.16	67
4	113537032	rs2351458	C	8.06E-04	2.76E-02	0.80	0.80	57	3	1.60E-02	2.13E-01	0.88	0.88	75
4	125125707	rs908822	T	5.80E-04	5.80E-04	0.60	0.60	0	3	1.77E-04	1.77E-04	0.65	0.65	0
4	151450821	rs1813134	T	2.44E-04	1.16E-03	0.77	0.77	22	3	7.40E-04	1.39E-02	0.83	0.83	48
4	151457886	rs962626	T	1.83E-04	3.94E-04	0.77	0.77	10	3	7.08E-04	1.59E-02	0.83	0.82	50
4	164177106	rs4132177	A	1.27E-04	1.36E-03	1.79	1.79	30	4	1.37E-05	1.47E-03	1.45	1.47	42
4	182564832	rs724658	A	9.27E-04	9.27E-04	1.30	1.30	0	3	8.63E-03	6.30E-02	1.18	1.18	51
5	3182592	rs17551573	A	7.52E-05	2.43E-02	0.64	0.64	66	3	1.90E-02	3.11E-01	0.82	0.79	86
5	4830480	rs10069581	A	8.03E-04	8.03E-04	0.68	0.68	0	3	2.43E-03	1.33E-02	0.75	0.75	34
5	7938959	rs162036	G	6.79E-04	6.79E-04	1.42	1.42	0	3	2.88E-02	2.57E-01	1.20	1.21	76
5	28061691	rs7710236	T	3.28E-04	3.28E-04	1.32	1.32	0	3	4.93E-03	8.11E-02	1.19	1.19	63
5	29285301	rs7717683	G	3.01E-04	3.01E-04	0.72	0.72	0	3	6.37E-04	2.24E-03	0.78	0.77	21
5	29403231	rs7717780	T	1.51E-04	1.79E-03	0.76	0.76	32	3	2.13E-03	7.67E-02	0.84	0.83	69
5	41608479	rs589757	A	8.80E-04	2.32E-02	0.76	0.76	54	3	1.06E-04	3.77E-04	0.78	0.78	16
5	62499530	rs601429	C	8.22E-04	8.22E-04	1.26	1.26	0	3	5.37E-02	3.30E-01	1.11	1.12	78
5	71723979	rs13158670	A	7.20E-04	7.20E-04	1.25	1.25	0	3	1.97E-02	1.70E-01	1.13	1.14	69
5	82983972	rs2045380	G	7.54E-04	7.54E-04	0.73	0.73	0	3	2.23E-02	2.65E-01	0.84	0.85	73
5	96559225	rs1000083	T	2.45E-04	2.45E-04	0.63	0.63	0	3	2.67E-03	5.69E-02	0.75	0.74	62
5	96766902	rs291805	A	2.18E-04	2.18E-04	0.58	0.58	0	3	2.86E-03	4.86E-02	0.72	0.70	62
5	115212349	rs26529	C	4.19E-04	4.19E-04	0.78	0.78	0	3	2.35E-03	1.73E-02	0.84	0.84	40
5	127028777	rs711363	C	4.50E-04	2.25E-03	1.30	1.30	25	3	1.40E-04	1.44E-04	1.25	1.25	0
5	127076410	rs1213745	G	2.71E-04	4.96E-03	1.32	1.32	41	3	1.89E-04	2.01E-03	1.25	1.25	33
5	127163508	rs1616107	G	2.42E-04	2.42E-04	1.32	1.32	0	3	3.03E-05	3.03E-05	1.28	1.28	0
5	127175702	rs790479	C	9.91E-04	9.91E-04	1.27	1.27	0	3	1.51E-04	1.51E-04	1.25	1.25	0
5	145700624	rs891970	T	3.44E-04	3.44E-04	0.76	0.76	0	3	3.72E-03	5.59E-02	0.83	0.83	58
5	155007766	rs2552979	C	5.25E-04	1.51E-02	0.76	0.76	52	3	1.03E-02	1.54E-01	0.85	0.84	74
5	170167299	rs10063254	T	8.62E-04	8.62E-04	1.29	1.29	0	3	9.09E-02	4.21E-01	1.11	1.12	82
5	172075156	rs12657303	A	2.99E-04	2.99E-04	0.78	0.78	0	3	1.90E-02	2.19E-01	0.88	0.87	76
6	6674737	rs6924289	C	1.71E-04	1.74E-02	1.44	1.44	60	3	2.64E-05	6.40E-04	1.38	1.38	35

6	6675511	rs201061	A	9.77E-04	8.95E-02	1.24	1.24	73	3	4.40E-03	1.11E-01	1.16	1.16	70
6	18180845	rs10456820	T	8.43E-04	1.11E-02	0.76	0.76	42	3	1.92E-02	2.08E-01	0.86	0.85	74
6	20345022	rs717208	A	8.92E-04	8.92E-04	0.80	0.80	0	3	1.11E-02	9.79E-02	0.88	0.87	61
6	20632361	rs761154	A	1.34E-05	6.85E-04	0.75	0.75	39	5	3.63E-03	1.12E-01	0.90	0.89	75
6	20641141	rs6909467	T	4.88E-04	4.88E-04	0.78	0.78	0	3	4.29E-03	4.17E-02	0.85	0.84	52
6	20674435	rs6918457	G	1.13E-04	1.13E-04	0.73	0.73	0	3	4.28E-03	1.09E-01	0.84	0.82	73
6	24202119	rs2176933	A	6.81E-04	5.76E-02	1.45	1.45	69	3	2.83E-02	3.27E-01	1.21	1.22	81
6	31463297	rs2596560	C	7.41E-04	7.41E-04	1.27	1.27	0	5	2.13E-05	2.13E-05	1.20	1.20	0
6	32255739	rs3134943	T	9.93E-04	9.93E-04	0.74	0.74	0	3	1.97E-03	1.97E-03	0.79	0.79	0
6	32295001	rs394657	G	3.01E-04	3.01E-04	1.27	1.27	0	5	1.40E-03	9.69E-03	1.10	1.13	60
6	32296361	rs422951	C	9.50E-04	9.50E-04	1.24	1.24	0	3	3.57E-04	3.57E-04	1.20	1.20	0
6	32298006	rs3132946	A	9.36E-04	9.36E-04	0.73	0.73	0	3	2.13E-03	2.13E-03	0.79	0.79	0
6	45651316	rs2280229	T	2.80E-04	2.80E-04	0.78	0.78	0	3	7.18E-03	1.11E-01	0.86	0.86	68
6	45671713	rs7742046	A	7.46E-04	1.51E-01	1.32	1.32	82	3	1.08E-04	2.19E-02	1.28	1.28	65
6	66898096	rs9354380	A	8.88E-04	8.88E-04	1.33	1.33	0	3	3.09E-04	3.09E-04	1.28	1.28	0
6	75114909	rs6936857	G	4.26E-04	6.52E-04	0.77	0.77	6	3	2.42E-02	2.46E-01	0.88	0.87	78
6	88031086	rs9353470	A	8.07E-05	8.68E-02	0.66	0.68	78	3	2.26E-04	6.37E-02	0.73	0.74	72
6	113823263	rs6568783	T	2.84E-06	1.21E-02	0.59	0.58	72	3	1.05E-03	1.69E-01	0.75	0.72	87
6	113862599	rs909543	A	3.57E-06	3.57E-06	0.63	0.63	0	3	3.35E-04	7.74E-02	0.76	0.74	79
6	140232551	rs9484321	T	9.39E-04	5.82E-03	1.25	1.25	31	3	4.06E-03	4.34E-02	1.16	1.17	54
6	140243368	rs7760148	A	2.12E-04	2.12E-04	1.29	1.29	0	3	1.45E-02	1.99E-01	1.14	1.16	77
6	144066988	rs7739094	T	9.75E-04	9.75E-04	1.26	1.26	0	3	7.43E-03	4.36E-02	1.16	1.16	47
6	144078630	rs761627	G	2.81E-04	1.96E-03	1.27	1.27	27	3	1.07E-02	1.76E-01	1.14	1.15	76
6	157503677	rs1007250	A	3.97E-04	2.66E-03	0.74	0.74	28	3	1.75E-02	2.00E-01	0.86	0.84	77
6	158281887	rs912879	C	9.43E-04	9.43E-04	0.77	0.77	0	3	1.00E-01	4.28E-01	0.90	0.89	82
6	161481246	rs1807426	T	5.71E-04	1.12E-02	1.66	1.69	48	3	6.26E-02	2.98E-01	1.23	1.33	83
7	19443464	rs7811056	G	9.22E-04	9.22E-04	1.24	1.24	0	3	4.82E-03	2.20E-02	1.16	1.16	36
7	55105882	rs10488140	T	2.71E-04	2.71E-04	1.34	1.34	0	3	3.38E-02	3.37E-01	1.15	1.16	82
7	57474574	rs9642239	T	9.09E-04	9.09E-04	0.79	0.79	0	3	5.43E-03	2.91E-02	0.85	0.85	41

7	76679195	rs10488500	G	4.25E-04	4.25E-04	1.47	1.47	0	3	8.40E-03	8.51E-02	1.25	1.27	64
7	86891086	rs31667	A	2.72E-04	2.70E-03	1.44	1.44	33	3	2.78E-02	2.66E-01	1.19	1.22	82
7	97974246	rs817921	C	5.56E-04	6.23E-02	0.78	0.78	72	3	1.04E-04	5.08E-03	0.80	0.80	49
7	103153828	rs563264	G	1.79E-04	1.79E-04	0.70	0.70	0	3	1.03E-03	1.31E-02	0.78	0.78	43
7	105124158	rs2075114	T	3.51E-04	3.51E-04	0.60	0.60	0	3	6.03E-02	3.75E-01	0.81	0.79	83
7	106232810	rs10262903	A	4.02E-04	4.02E-04	1.29	1.29	0	3	2.59E-02	2.19E-01	1.13	1.15	76
7	124168925	rs1544452	C	4.83E-04	4.83E-04	1.30	1.30	0	3	8.51E-03	1.03E-01	1.17	1.17	64
7	128157600	rs750464	T	7.85E-04	8.24E-03	1.74	1.73	37	3	3.22E-02	2.34E-01	1.31	1.37	77
7	150051637	rs3735078	G	8.02E-04	8.02E-04	0.67	0.67	0	3	7.31E-04	7.31E-04	0.73	0.73	0
7	151851010	rs10248875	T	7.44E-04	7.44E-04	0.80	0.80	0	3	3.31E-02	2.37E-01	0.89	0.89	74
7	152382419	rs2037929	G	7.83E-04	7.83E-04	0.76	0.76	0	3	2.56E-02	1.86E-01	0.87	0.86	70
7	152405485	rs626190	G	8.13E-04	1.09E-03	0.71	0.71	5	3	2.95E-02	2.27E-01	0.84	0.82	75
8	17134884	rs2904698	G	8.31E-04	8.31E-04	1.38	1.38	0	3	1.97E-02	1.89E-01	1.20	1.20	70
8	17156132	rs7834656	C	5.73E-04	5.73E-04	1.39	1.39	0	3	6.43E-03	6.52E-02	1.23	1.24	57
8	21287480	rs17497685	T	8.72E-04	8.72E-04	0.67	0.67	0	3	7.38E-02	3.50E-01	0.85	0.82	80
8	54294966	rs966247	G	6.22E-05	6.22E-05	0.65	0.65	0	3	2.23E-04	8.10E-03	0.73	0.73	51
8	117017347	rs760297	C	5.76E-04	5.76E-04	0.73	0.73	0	3	7.09E-03	8.18E-02	0.83	0.82	63
8	129508233	rs6470627	T	9.48E-04	9.48E-04	0.63	0.63	0	3	1.63E-01	5.77E-01	0.85	0.85	86
8	133227223	rs1864773	A	9.74E-04	4.39E-03	0.73	0.73	26	3	2.56E-02	2.34E-01	0.84	0.84	74
8	141529043	rs7841423	C	2.24E-04	2.24E-04	1.53	1.53	0	3	6.37E-03	1.23E-01	1.29	1.30	71
8	142185324	rs925358	A	5.56E-04	9.16E-03	0.73	0.73	43	3	3.24E-02	2.79E-01	0.86	0.84	80
9	5382199	rs3739636	A	3.52E-04	3.52E-04	0.79	0.79	0	3	2.90E-03	3.33E-02	0.86	0.85	51
9	5402546	rs10815211	T	7.80E-04	1.15E-01	0.76	0.75	79	3	3.10E-03	1.09E-01	0.83	0.82	73
9	6118897	rs340908	T	9.17E-04	9.17E-04	0.74	0.74	0	3	1.24E-03	1.42E-03	0.79	0.79	3
9	6180076	rs1342326	C	6.88E-04	6.88E-04	1.36	1.36	0	3	1.37E-03	3.09E-03	1.25	1.26	16
9	15576534	rs10810402	T	9.01E-04	9.01E-04	0.80	0.80	0	3	1.59E-03	6.89E-03	0.85	0.85	28
9	15594746	rs10481557	G	7.65E-04	1.21E-01	0.80	0.80	79	3	1.25E-03	6.67E-02	0.84	0.84	69
9	15660445	rs6474944	C	7.12E-04	1.02E-01	0.80	0.80	77	3	9.06E-04	4.78E-02	0.84	0.84	66
9	15695479	rs1396708	A	5.11E-04	9.39E-02	0.79	0.79	77	3	8.59E-04	5.27E-02	0.84	0.83	68

9	15743411	rs4740624	C	7.49E-04	5.41E-02	0.80	0.80	68	3	2.04E-03	5.37E-02	0.85	0.85	63
9	15774631	rs1539172	A	5.04E-04	1.11E-01	0.80	0.79	80	3	6.45E-03	1.84E-01	0.87	0.86	79
9	15813667	rs7019205	C	3.41E-04	1.11E-02	1.27	1.27	50	3	6.36E-03	1.38E-01	1.15	1.16	73
9	15815230	rs1009468	G	2.22E-04	1.71E-02	1.28	1.28	59	3	4.92E-03	1.43E-01	1.16	1.17	76
9	15831937	rs2066292	C	1.45E-04	4.95E-03	1.29	1.29	46	3	9.54E-04	4.15E-02	1.19	1.20	64
9	15836112	rs4741546	T	1.05E-04	3.35E-02	0.77	0.77	70	3	8.16E-04	7.26E-02	0.84	0.83	73
9	15851885	rs770191	C	7.13E-04	7.13E-04	1.25	1.25	0	3	1.43E-03	3.88E-03	1.18	1.19	19
9	15888553	rs1984246	A	3.36E-04	1.17E-03	0.79	0.79	18	3	2.31E-03	4.54E-02	0.85	0.85	59
9	15890771	rs1891212	A	2.87E-04	1.48E-03	0.78	0.78	23	3	2.16E-03	4.88E-02	0.85	0.84	61
9	15976487	rs1927699	G	8.78E-04	8.78E-04	1.25	1.25	0	3	3.13E-03	1.20E-02	1.17	1.17	30
9	16013469	rs1328273	A	1.09E-04	3.50E-02	0.77	0.77	70	3	5.58E-04	5.45E-02	0.83	0.83	71
9	16020606	rs1328279	G	9.55E-06	5.02E-02	0.75	0.75	80	5	1.03E-04	2.09E-02	0.87	0.86	69
9	16020960	rs4247294	A	5.80E-06	3.80E-02	0.74	0.74	79	3	2.17E-05	3.40E-02	0.80	0.80	76
9	16038844	rs10810528	A	6.14E-04	5.09E-02	0.80	0.80	67	3	1.04E-02	1.85E-01	0.88	0.87	76
9	20645564	rs13290184	T	5.50E-04	5.50E-04	0.56	0.56	0	3	3.33E-02	2.60E-01	0.75	0.73	76
9	21951866	rs7041637	A	4.35E-04	4.35E-04	0.76	0.76	0	3	3.07E-03	2.48E-02	0.84	0.83	47
9	27810493	rs7020269	G	2.30E-05	1.06E-03	0.76	0.76	40	5	7.12E-03	9.40E-02	0.91	0.88	74
9	33614429	rs855523	C	9.22E-04	9.22E-04	0.73	0.73	0	3	4.80E-03	2.76E-02	0.79	0.80	34
9	84749764	rs7029717	C	9.42E-04	1.21E-02	1.42	1.43	44	3	6.41E-03	8.08E-02	1.26	1.27	62
9	91902306	rs4744096	T	9.14E-04	9.14E-04	0.73	0.73	0	3	8.58E-04	8.58E-04	0.77	0.77	0
9	101886451	rs16918878	T	2.35E-04	1.48E-02	1.31	1.31	57	3	1.48E-02	2.42E-01	1.15	1.17	81
9	106726226	rs2487052	T	6.96E-04	6.96E-04	1.31	1.31	0	3	1.36E-01	5.17E-01	1.10	1.11	85
9	116394764	rs2274595	G	2.11E-04	2.11E-04	0.57	0.57	0	3	1.16E-04	1.16E-04	0.64	0.64	0
9	117002347	rs4978627	C	4.98E-04	4.98E-04	0.78	0.78	0	3	1.32E-03	3.08E-03	0.84	0.84	16
9	121074859	rs17534	C	7.72E-04	7.72E-04	1.27	1.27	0	3	8.35E-03	6.99E-02	1.16	1.16	55
10	6826051	rs353201	T	1.22E-04	1.81E-02	0.48	0.47	64	3	8.69E-04	5.08E-02	0.61	0.58	70
10	8685729	rs10905417	C	5.83E-04	6.19E-03	0.80	0.79	37	3	1.72E-02	1.98E-01	0.88	0.87	75
10	42751362	rs12572458	T	7.74E-04	7.74E-04	0.67	0.67	0	3	3.37E-02	2.42E-01	0.82	0.80	74
10	49438438	rs2120910	T	1.64E-04	1.64E-04	0.72	0.72	0	3	8.70E-03	1.43E-01	0.84	0.82	74

10	49452423	rs10491040	C	7.14E-04	7.14E-04	0.71	0.71	0	3	1.60E-03	2.80E-03	0.79	0.78	11
10	72194347	rs2688768	G	5.67E-04	5.67E-04	0.75	0.75	0	3	1.49E-04	1.49E-04	0.77	0.77	0
10	73190834	rs3747868	T	1.51E-04	1.51E-04	1.33	1.33	0	3	8.53E-05	8.53E-05	1.27	1.27	0
10	78434534	rs1907718	G	5.59E-04	5.59E-04	0.69	0.69	0	3	2.04E-02	1.92E-01	0.82	0.81	72
10	80478533	rs10824709	T	7.75E-04	7.75E-04	0.79	0.79	0	3	2.57E-02	2.09E-01	0.88	0.88	71
10	80488288	rs1961130	A	1.67E-04	1.67E-04	0.78	0.78	0	3	5.29E-03	1.08E-01	0.86	0.86	69
10	80495455	rs1370562	A	1.51E-04	1.51E-04	0.72	0.72	0	3	7.48E-03	1.29E-01	0.84	0.82	73
10	96698216	rs10509679	A	8.86E-04	8.86E-04	0.75	0.75	0	3	2.92E-02	2.26E-01	0.86	0.85	71
10	102498567	rs4244341	T	6.68E-04	7.52E-03	1.33	1.32	38	3	3.46E-02	2.96E-01	1.15	1.16	79
10	124755847	rs9328842	T	1.05E-04	1.01E-02	0.75	0.75	56	3	2.02E-03	9.33E-02	0.84	0.82	74
10	134579752	rs7096936	G	1.05E-04	1.05E-04	1.30	1.30	0	3	1.37E-03	5.07E-02	1.19	1.19	63
10	134682390	rs7071996	G	9.22E-05	9.22E-05	1.30	1.30	0	3	1.97E-03	5.79E-02	1.18	1.19	65
11	11453829	rs3741409	G	4.76E-04	1.24E-02	0.77	0.77	50	3	9.57E-04	1.77E-02	0.83	0.82	51
11	11464491	rs2403515	C	1.25E-04	1.25E-04	0.68	0.68	0	3	2.99E-05	2.99E-05	0.72	0.72	0
11	35510369	rs1144589	A	3.73E-04	3.73E-04	1.29	1.29	0	3	4.18E-03	5.39E-02	1.18	1.18	58
11	37089996	rs7946463	C	5.42E-04	5.42E-04	0.78	0.78	0	5	2.96E-02	1.64E-01	0.91	0.90	70
11	40713036	rs11036050	A	8.85E-04	8.85E-04	0.80	0.80	0	3	9.80E-04	9.80E-04	0.84	0.84	0
11	44737501	rs1665150	G	6.12E-04	6.12E-04	0.75	0.75	0	3	4.47E-03	4.95E-02	0.83	0.82	57
11	83115362	rs7111226	T	7.04E-04	7.04E-04	1.29	1.29	0	3	2.77E-03	1.12E-02	1.19	1.20	30
11	85036902	rs2290823	G	9.48E-04	9.48E-04	0.69	0.69	0	3	4.18E-02	2.35E-01	0.84	0.81	74
11	94027733	rs11020874	T	2.59E-04	2.59E-04	1.30	1.30	0	3	4.56E-04	6.72E-04	1.22	1.22	6
11	98834366	rs1910710	G	2.41E-04	2.41E-04	1.28	1.28	0	3	8.44E-03	1.30E-01	1.15	1.16	71
11	98888063	rs11220245	G	7.92E-04	7.92E-04	1.29	1.29	0	3	1.02E-02	8.41E-02	1.17	1.17	58
11	111511149	rs243908	G	7.16E-04	7.16E-04	1.26	1.26	0	3	4.05E-02	3.14E-01	1.12	1.13	79
11	114239611	rs2462169	A	4.89E-04	1.24E-03	0.80	0.80	14	3	1.14E-02	1.78E-01	0.87	0.87	72
11	114246392	rs7104748	G	3.24E-04	2.33E-03	0.79	0.79	28	3	1.15E-02	2.15E-01	0.88	0.88	76
11	124242492	rs7102701	C	8.82E-04	8.82E-04	1.25	1.25	0	3	1.37E-02	1.10E-01	1.14	1.15	61
12	3564728	rs758637	A	4.38E-04	4.38E-04	0.78	0.78	0	3	2.75E-02	2.58E-01	0.89	0.88	78
12	4303650	rs3885283	A	5.04E-04	1.51E-03	1.29	1.29	17	3	1.74E-02	1.93E-01	1.15	1.16	75

12	9705286	rs1108453	G	5.88E-04	5.88E-04	0.73	0.73	0	3	6.35E-04	6.35E-04	0.78	0.78	0
12	9738400	rs10492164	T	7.64E-04	7.64E-04	0.72	0.72	0	3	1.75E-03	3.46E-03	0.79	0.79	14
12	14182567	rs11055792	T	3.56E-05	3.56E-05	1.32	1.32	0	3	2.89E-04	1.49E-02	1.21	1.22	57
12	26364744	rs11614526	C	7.14E-04	1.09E-02	0.79	0.79	43	3	3.32E-03	5.15E-02	0.85	0.85	58
12	40232806	rs285584	A	8.60E-04	8.60E-04	0.74	0.74	0	3	2.22E-02	1.68E-01	0.85	0.84	68
12	46630305	rs1015390	T	4.85E-04	4.85E-04	1.43	1.43	0	3	2.61E-02	2.33E-01	1.20	1.21	75
12	55775976	rs1059513	C	9.83E-04	9.83E-04	0.68	0.68	0	3	2.65E-03	4.84E-03	0.76	0.76	13
12	72965321	rs1554486	C	9.12E-04	2.17E-03	1.26	1.26	14	3	4.64E-03	4.65E-02	1.17	1.17	53
12	72968165	rs10128762	G	6.94E-04	8.82E-03	1.26	1.26	40	3	1.06E-02	1.41E-01	1.15	1.16	70
12	75847095	rs773488	G	3.64E-04	3.64E-04	0.79	0.79	0	3	6.65E-03	9.19E-02	0.87	0.86	65
12	97027466	rs1811264	C	2.28E-04	2.28E-04	0.76	0.76	0	3	2.89E-03	4.48E-02	0.84	0.83	59
12	104772017	rs10507202	C	9.61E-04	9.61E-04	1.29	1.29	0	3	2.82E-03	6.64E-03	1.19	1.20	19
12	118144240	rs1346227	T	7.01E-04	1.28E-01	0.71	0.69	83	3	3.05E-03	1.11E-01	0.80	0.77	77
13	26421026	rs2149219	A	5.14E-04	1.11E-03	0.74	0.74	12	3	2.38E-02	2.27E-01	0.86	0.84	77
13	26935566	rs1475221	G	7.78E-04	7.78E-04	0.77	0.77	0	3	2.42E-03	5.91E-03	0.83	0.83	19
13	71512876	rs2612813	A	5.77E-04	8.06E-03	1.28	1.28	40	3	3.26E-02	3.35E-01	1.13	1.14	80
13	71517526	rs2706411	T	8.94E-04	5.25E-03	1.27	1.27	29	3	4.18E-02	3.41E-01	1.13	1.13	79
13	72887581	rs2325510	G	7.30E-04	7.30E-04	1.52	1.52	0	3	1.37E-03	4.68E-03	1.37	1.37	23
13	76985266	rs1323619	A	3.42E-04	3.42E-04	1.27	1.27	0	3	2.06E-03	3.33E-02	1.18	1.18	54
13	77078772	rs2274015	C	2.23E-04	2.23E-04	0.78	0.78	0	3	2.69E-03	4.20E-02	0.86	0.85	58
13	77255783	rs1144383	T	4.65E-04	4.65E-04	1.37	1.37	0	3	1.25E-01	4.95E-01	1.12	1.14	86
13	84187773	rs6563411	C	7.92E-04	7.92E-04	0.80	0.80	0	3	3.65E-02	2.71E-01	0.90	0.89	75
13	93718257	rs959390	C	5.88E-04	5.88E-04	1.30	1.30	0	3	1.55E-02	1.56E-01	1.15	1.17	71
13	105726015	rs9301126	G	3.70E-04	3.97E-04	0.71	0.71	1	3	6.23E-05	6.23E-05	0.74	0.74	0
13	109697956	rs4145072	C	8.37E-05	3.60E-04	1.29	1.29	18	3	8.20E-03	2.18E-01	1.15	1.16	81
14	25758820	rs8012418	G	2.96E-04	2.96E-04	1.27	1.27	0	3	3.97E-04	3.97E-04	1.21	1.21	0
14	25780111	rs1950857	T	7.21E-04	7.21E-04	0.78	0.78	0	3	5.56E-04	5.56E-04	0.82	0.82	0
14	29054049	rs977122	A	3.15E-04	3.15E-04	1.42	1.42	0	3	6.96E-03	1.09E-01	1.24	1.24	66
14	43320843	rs1957260	A	1.47E-04	1.47E-04	1.44	1.44	0	3	9.24E-03	1.81E-01	1.22	1.24	76

14	43936603	rs12436502	T	4.97E-05	1.50E-01	1.93	1.76	82	3	2.63E-05	4.04E-02	1.83	1.70	67
14	51522324	rs1253676	G	4.05E-04	4.05E-04	1.30	1.30	0	3	1.33E-02	1.51E-01	1.15	1.17	71
14	72537512	rs12880210	C	8.88E-04	8.88E-04	0.75	0.75	0	3	2.41E-01	6.11E-01	0.92	0.91	87
14	83897200	rs12432589	A	7.45E-05	7.45E-05	1.30	1.30	0	3	1.39E-03	4.57E-02	1.18	1.19	64
14	83969190	rs10138991	G	2.87E-04	2.18E-03	1.28	1.28	29	3	2.48E-03	5.57E-02	1.18	1.19	64
14	84007010	rs1449104	G	4.62E-04	8.91E-02	0.79	0.79	78	3	8.79E-03	2.18E-01	0.87	0.86	80
14	89230591	rs8007740	A	1.37E-04	5.10E-02	1.52	1.54	75	3	3.34E-03	1.59E-01	1.29	1.32	80
15	20499445	rs12594495	G	8.88E-04	8.88E-04	1.27	1.27	0	3	3.13E-03	1.16E-02	1.19	1.19	28
15	29467308	rs8042404	A	4.53E-04	4.53E-04	1.29	1.29	0	3	2.01E-04	2.01E-04	1.24	1.24	0
15	58823842	rs9920962	G	6.98E-04	4.69E-02	0.70	0.70	64	3	5.02E-03	1.05E-01	0.79	0.79	69
15	69323596	rs961577	G	3.62E-04	3.62E-04	0.79	0.79	0	3	2.18E-03	3.31E-02	0.85	0.85	52
15	69331029	rs4776542	C	2.82E-04	2.82E-04	0.79	0.79	0	3	3.25E-03	7.01E-02	0.86	0.85	63
15	69332571	rs10518937	T	8.27E-04	8.27E-04	1.25	1.25	0	3	1.80E-03	2.30E-03	1.18	1.18	5
15	69335278	rs1561884	C	3.12E-05	3.12E-05	1.31	1.31	0	3	4.05E-04	2.93E-02	1.20	1.21	63
15	69351194	rs10518942	G	3.60E-04	3.60E-04	1.27	1.27	0	3	2.12E-03	1.94E-02	1.18	1.18	44
15	69358022	rs7173870	T	5.34E-04	5.34E-04	0.80	0.80	0	3	3.96E-03	3.51E-02	0.86	0.86	49
15	69378393	rs4777363	T	2.35E-04	2.35E-04	1.28	1.28	0	3	3.17E-03	5.01E-02	1.17	1.18	59
15	69477995	rs10518959	T	8.95E-04	8.95E-04	1.25	1.25	0	3	1.40E-02	1.11E-01	1.14	1.15	61
15	90522481	rs10520705	G	5.38E-04	5.38E-04	1.59	1.59	0	3	2.71E-02	1.86E-01	1.25	1.30	74
16	4037223	rs917522	C	4.38E-04	4.38E-04	1.40	1.40	0	3	1.77E-02	2.12E-01	1.20	1.21	74
16	5743925	rs11866983	A	1.88E-05	1.88E-05	0.74	0.74	0	3	2.29E-04	2.55E-02	0.81	0.80	65
16	5771031	rs726239	T	8.52E-05	8.52E-05	0.75	0.75	0	3	2.13E-03	6.99E-02	0.83	0.83	68
16	5775439	rs11076969	T	3.59E-05	3.59E-05	0.74	0.74	0	3	2.65E-04	9.97E-03	0.81	0.81	52
16	5779288	rs2342735	A	4.59E-04	4.59E-04	0.77	0.77	0	3	1.35E-03	6.00E-03	0.83	0.83	28
16	5782092	rs4322667	T	9.43E-04	9.43E-04	0.78	0.78	0	3	4.43E-03	1.97E-02	0.84	0.84	34
16	11625762	rs6498232	C	6.28E-04	6.28E-04	1.36	1.36	0	3	6.62E-04	6.62E-04	1.28	1.28	0
16	27258188	rs3024530	G	6.14E-04	8.49E-02	1.25	1.25	75	3	1.60E-05	2.25E-03	1.25	1.25	50
16	30037994	rs11865086	A	7.24E-04	7.24E-04	0.80	0.80	0	3	6.10E-03	5.38E-02	0.86	0.86	54
16	49495030	rs1395605	T	4.19E-04	7.94E-04	1.26	1.26	10	3	1.13E-02	1.55E-01	1.14	1.15	73



16	51379138	rs1420258	G	9.06E-04	9.06E-04	0.80	0.80	0	3	3.19E-04	3.19E-04	0.83	0.83	0
16	51408972	rs2110830	T	9.36E-04	9.36E-04	0.80	0.80	0	3	1.15E-03	1.15E-03	0.84	0.84	0
16	51411008	rs2024446	A	9.07E-05	9.07E-05	0.77	0.77	0	3	1.36E-04	4.71E-04	0.82	0.81	17
16	54295157	rs42460	G	9.76E-04	8.37E-02	1.51	1.51	73	3	3.48E-02	2.68E-01	1.22	1.27	81
16	56247384	rs1376041	T	3.92E-05	1.61E-04	1.35	1.35	16	3	1.16E-05	4.38E-05	1.29	1.29	14
16	63319927	rs231053	C	1.62E-04	5.54E-04	1.41	1.41	16	3	2.25E-03	6.25E-02	1.24	1.26	67
16	63322771	rs231059	A	2.28E-04	7.69E-04	1.40	1.40	17	3	4.28E-03	9.14E-02	1.23	1.25	70
16	63380873	rs1364218	G	3.66E-04	3.66E-04	1.38	1.38	0	3	3.58E-03	4.93E-02	1.23	1.24	59
16	71644995	rs4788697	A	2.52E-04	2.52E-04	0.77	0.77	0	3	3.11E-03	6.00E-02	0.84	0.84	61
16	81008660	rs1025065	T	8.59E-04	8.59E-04	0.80	0.80	0	3	7.91E-03	5.82E-02	0.87	0.86	52
16	83261468	rs12596786	A	8.52E-04	8.52E-04	1.32	1.32	0	3	1.64E-03	2.02E-03	1.23	1.23	4
17	7959231	rs3027215	T	9.89E-04	5.57E-03	1.51	1.51	30	3	3.18E-03	2.91E-02	1.33	1.35	49
17	9649681	rs3843735	G	8.19E-04	8.19E-04	1.25	1.25	0	3	3.89E-02	2.49E-01	1.11	1.13	74
17	29973811	rs2009472	C	8.25E-04	8.25E-04	0.65	0.65	0	3	1.34E-02	1.02E-01	0.79	0.77	63
17	34472851	rs4795343	T	1.33E-04	1.33E-04	0.75	0.75	0	3	2.26E-03	6.52E-02	0.83	0.82	67
17	34483768	rs2091763	C	1.80E-04	3.05E-04	0.75	0.75	7	3	2.48E-03	6.49E-02	0.84	0.83	67
17	34488719	rs3744077	A	1.37E-04	1.37E-04	0.75	0.75	0	3	2.00E-03	5.72E-02	0.83	0.82	66
17	35229995	rs9303277	T	8.15E-04	8.15E-04	0.80	0.80	0	4	1.43E-14	1.53E-06	0.76	0.75	57
17	35282160	rs11557467	T	5.22E-04	5.22E-04	0.80	0.80	0	4	3.29E-15	2.14E-06	0.76	0.75	60
17	35304874	rs8067378	G	5.88E-04	5.88E-04	0.80	0.80	0	4	3.27E-15	6.15E-06	0.76	0.75	64
17	35315722	rs2305480	A	1.35E-04	1.35E-04	0.78	0.78	0	5	3.63E-17	1.47E-07	0.78	0.77	60
17	35319766	rs2290400	C	7.79E-05	7.79E-05	0.77	0.77	0	5	2.55E-20	1.47E-09	0.76	0.76	56
17	35323475	rs7216389	C	9.71E-05	9.71E-05	0.77	0.77	0	4	2.86E-16	7.79E-06	0.75	0.73	69
17	35341943	rs4795405	T	1.19E-04	1.19E-04	0.77	0.77	0	5	1.90E-15	1.05E-06	0.79	0.78	64
17	56778202	rs1990293	A	2.87E-04	2.87E-04	0.74	0.74	0	3	2.66E-03	4.28E-02	0.82	0.81	57
17	64177801	rs16973217	T	4.57E-06	5.81E-04	1.55	1.54	43	3	4.04E-06	9.07E-04	1.43	1.43	48
17	64178397	rs9915635	G	3.15E-05	3.15E-05	1.47	1.47	0	5	6.80E-05	1.39E-03	1.23	1.24	37
17	66891676	rs10512566	A	8.94E-04	8.94E-04	0.79	0.79	0	3	1.36E-02	1.06E-01	0.87	0.87	61
17	69131303	rs6501655	T	7.98E-04	7.98E-04	0.78	0.78	0	3	9.90E-02	4.49E-01	0.91	0.89	83

17	69137515	rs8080253	G	4.74E-05	4.74E-05	0.75	0.75	0	3	1.91E-02	3.14E-01	0.88	0.86	85
17	69142605	rs8064411	C	6.14E-05	6.14E-05	0.75	0.75	0	3	2.23E-02	3.20E-01	0.88	0.87	85
17	71297313	rs10221244	G	2.60E-04	2.60E-04	1.28	1.28	0	3	1.82E-02	2.39E-01	1.14	1.14	77
17	73759725	rs1109279	C	6.00E-04	6.91E-02	0.78	0.78	72	3	3.74E-03	1.10E-01	0.85	0.84	72
18	986719	rs789056	C	8.99E-04	8.99E-04	1.24	1.24	0	3	1.71E-03	1.71E-03	1.18	1.18	0
18	10475250	rs518978	G	8.85E-04	8.85E-04	1.24	1.24	0	3	1.70E-02	1.52E-01	1.13	1.14	68
18	10501302	rs559412	A	8.20E-04	8.20E-04	1.25	1.25	0	3	8.53E-03	6.52E-02	1.15	1.15	54
18	22703047	rs151245	G	2.14E-04	2.82E-04	1.29	1.29	4	3	9.72E-03	1.77E-01	1.15	1.16	76
18	27636700	rs567225	T	7.55E-04	1.64E-02	1.25	1.25	50	3	3.12E-02	2.97E-01	1.12	1.13	79
18	40543599	rs2614999	G	5.47E-04	1.10E-03	0.78	0.78	11	3	4.93E-04	1.54E-03	0.82	0.82	18
18	40554951	rs11082401	G	5.00E-04	5.00E-04	0.71	0.71	0	3	4.02E-03	3.30E-02	0.80	0.80	49
18	42389850	rs4581799	A	8.06E-04	2.11E-02	1.32	1.32	53	3	3.32E-02	2.97E-01	1.15	1.16	79
18	44050037	rs12455475	C	8.16E-04	3.55E-03	1.30	1.30	25	3	3.12E-02	2.37E-01	1.14	1.16	76
18	46017294	rs11082811	T	3.37E-04	3.37E-04	1.31	1.31	0	3	6.42E-02	3.63E-01	1.11	1.14	83
18	46023080	rs1790423	C	3.63E-04	3.63E-04	1.30	1.30	0	3	4.83E-02	3.19E-01	1.12	1.14	81
18	54142526	rs10503022	C	3.93E-04	3.93E-04	1.32	1.32	0	3	6.83E-04	4.23E-03	1.24	1.24	30
18	55369820	rs2851871	G	6.70E-04	6.70E-04	1.27	1.27	0	3	7.48E-04	7.48E-04	1.20	1.20	0
18	59736240	rs724558	C	4.17E-04	4.17E-04	1.35	1.35	0	3	3.66E-02	3.23E-01	1.15	1.16	81
18	69328006	rs2156186	A	6.39E-04	6.39E-04	1.26	1.26	0	3	3.08E-05	3.08E-05	1.25	1.25	0
18	69395672	rs12454180	G	7.51E-04	7.51E-04	1.25	1.25	0	3	1.05E-03	1.27E-03	1.19	1.19	3
18	69620647	rs1430540	C	7.00E-04	9.51E-02	0.80	0.80	76	3	2.81E-02	3.27E-01	0.89	0.88	83
19	15591767	rs8107048	A	7.43E-04	4.43E-02	1.32	1.32	64	3	2.21E-03	5.29E-02	1.22	1.23	61
19	17413306	rs11667945	G	3.86E-04	3.86E-04	1.27	1.27	0	3	6.88E-03	9.25E-02	1.16	1.16	63
20	3740226	rs2282128	T	7.48E-04	7.48E-04	1.25	1.25	0	3	4.22E-02	2.72E-01	1.11	1.13	76
20	51222125	rs2801008	G	8.57E-05	1.55E-02	1.33	1.33	61	3	8.05E-03	2.29E-01	1.16	1.18	83
20	52246231	rs2145827	A	9.06E-04	9.06E-04	0.78	0.78	0	3	9.15E-04	9.15E-04	0.82	0.82	0
21	23383873	rs2827841	C	4.32E-04	2.32E-02	1.27	1.26	58	3	3.46E-02	3.48E-01	1.12	1.13	83
21	23385645	rs1506002	T	1.01E-04	3.34E-02	0.75	0.75	70	3	7.10E-03	2.24E-01	0.86	0.85	83
21	23452912	rs198047	G	2.22E-04	2.22E-04	0.73	0.73	0	3	2.21E-04	2.21E-04	0.78	0.78	0

21	23460356	rs198052	T	7.79E-04	7.79E-04	0.75	0.75	0	3	1.11E-03	1.11E-03	0.80	0.80	0
21	23461389	rs2827944	G	7.79E-04	7.79E-04	0.75	0.75	0	3	9.97E-04	9.97E-04	0.79	0.79	0
21	42407904	rs2187240	A	6.68E-04	6.68E-04	0.67	0.67	0	3	2.39E-02	1.75E-01	0.82	0.80	71
22	25327482	rs2301440	T	7.06E-04	7.06E-04	0.80	0.80	0	3	3.01E-02	2.44E-01	0.89	0.89	75
22	25336189	rs2267103	A	9.47E-04	9.47E-04	0.79	0.79	0	3	1.77E-03	6.56E-03	0.84	0.84	26
22	31098551	rs5749412	T	4.34E-04	4.34E-04	0.69	0.69	0	3	1.06E-02	1.44E-01	0.81	0.80	68
22	31109227	rs2413113	T	8.51E-04	8.51E-04	1.25	1.25	0	3	9.22E-03	7.16E-02	1.15	1.15	55
22	31138355	rs2049948	A	7.01E-04	7.01E-04	1.27	1.27	0	3	3.84E-03	2.66E-02	1.18	1.18	44
22	31153071	rs1543320	G	1.58E-04	1.58E-04	0.78	0.78	0	3	2.74E-03	5.92E-02	0.85	0.85	62
22	31526693	rs9619311	C	8.74E-04	9.07E-03	1.27	1.27	39	3	9.25E-03	1.08E-01	1.16	1.17	66
22	31582041	rs1427378	G	3.94E-04	1.72E-03	1.32	1.32	22	3	9.75E-03	1.50E-01	1.17	1.18	73
22	31595922	rs1543803	T	2.48E-04	4.48E-03	1.32	1.32	40	3	4.74E-02	3.79E-01	1.12	1.14	85
22	31602699	rs5754322	C	9.42E-04	9.42E-04	1.31	1.31	0	3	8.63E-02	3.89E-01	1.12	1.13	81
22	33217654	rs130698	T	1.72E-05	1.72E-05	1.88	1.88	0	3	1.82E-04	1.41E-02	1.57	1.56	57
22	33500735	rs10483184	T	2.69E-04	2.69E-04	1.54	1.54	0	3	9.14E-03	1.23E-01	1.27	1.30	70
22	35754794	rs8141597	C	9.45E-04	9.45E-04	0.79	0.79	0	3	2.26E-03	3.23E-03	0.84	0.84	7
22	35758545	rs228129	A	6.77E-04	6.77E-04	0.80	0.80	0	3	3.63E-02	2.75E-01	0.90	0.89	76
22	43437912	rs136911	A	7.78E-04	7.78E-04	0.79	0.79	0	3	9.66E-03	9.95E-02	0.86	0.86	61

CHR: Chromosome; BP: Basepair position; SNP: Single Nucleotide Polymorphism; A1: Analysed allele; P: p-value (fixed effect); P(R): p-value (random effect)  
OR: Odds Ratio fixed effect; OR (R): Odds Ratio random effect; I: Heterogeneity

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