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**Table S1 Information of software and R package**

Characteristic	Version	Function	Reference
<b>R package</b>			
"GEOquery"	2.68.0	Data extraction from GEO datasets	Davis S & Meltzer P S. GEOquery: a bridge between the Gene Expression Omnibus (GEO) and BioConductor. <i>Bioinformatics</i> . 2007; 23(14):1846-1847.
"limma"	3.56.2	Differentially expressed genes analysis	Ritchie M E, Phipson B, Wu D, et al. limma powers differential expression analyses for RNA-sequencing and microarray studies. <i>Nucleic Acids Res</i> . 2015; 43(7):e47.
"ggplot2"	3.4.2	Volcano plot visualization	Wickham H. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York. 2016.
"ieugwasr"	0.1.5	Linkage disequilibrium clumping	G H. ieugwasr: R Interface to the OpenGWAS Database API_. R package version 0.1.5, < <a href="https://github.com/MRCIEU/ieugwasr">https://github.com/MRCIEU/ieugwasr</a> >. 2023.
"TwoSampleMR"	0.5.6	Two sample mendelian randomization analysis	Hemani G, Zheng J, Elsworth B, et al. The MR-Base platform supports systematic causal inference across the human phenome. <i>Elife</i> . 2018; 7.
"forestploter"	1.1.0	Forest plots visualization	A D. forestploter: Create Flexible Forest Plot_. R package version 1.1.0, < <a href="https://CRAN.R-project.org/package=forestploter">https://CRAN.R-project.org/package=forestploter</a> >. 2023.
"coloc"	5.2	Bayesian co-localization analysis	Giambartolomei C, Vukcevic D, Schadt E E, et al. Bayesian test for colocalisation between pairs of genetic association studies using summary statistics. <i>PLoS Genet</i> . 2014; 10(5):e1004383.
"phenoscanner"	1.0	Phenotype scanning	PhenoScanner. phenoscanner: R package to query PhenoScanner from R_. R package version 1.0. 2023.
"meta"	6.5-0	Meta-analysis	Balduzzi S, R�cker G & Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. <i>Evid Based Ment Health</i> . 2019; 22(4):153-160.
<b>Software</b>			
R software	4.3.1	R analysis	Team R C. _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria. < <a href="https://www.R-project.org/">https://www.R-project.org/</a> >. 2023.
SMR software	1.03	Summary data-based mendelian randomization analysis	Zhu Z, Zhang F, Hu H, et al. Integration of summary data from GWAS and eQTL studies predicts complex trait gene targets. <i>Nat Genet</i> . 2016; 48(5):481-487.
AutoDockTools	1.5.6	Preparation of receptor molecules and ligands	Morris G M, Huey R, Lindstrom W, et al. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. <i>J Comput Chem</i> . 2009; 30(16):2785-2791.
AutoDock Vina	1.1.2	Blind docking screenings	Trott O & Olson A J. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. <i>J Comput Chem</i> . 2010; 31(2):455-461.
PyMOL	2.4.0	Molecular docking visualization	Gaudreault F, Morency L P & Najmanovich R J. NRGsuite: a PyMOL plugin to perform docking simulations in real time using FlexAID. <i>Bioinformatics</i> . 2015; 31(23):3856-3858.
<b>Database</b>			
Open Targets database	NA	Druggability annotations	Ochoa D, Hercules A, Carmona M, et al. The next-generation Open Targets Platform: reimaged, redesigned, rebuilt. <i>Nucleic Acids Res</i> . 2023; 51(D1):D1353-d1359.
AlphaFold Database	NA	obtaining protein structures ( <a href="https://alphafold.ebi.ac.uk/">https://alphafold.ebi.ac.uk/</a> )	1. Jumper J, Evans R, Pritzel A, et al. Highly accurate protein structure prediction with AlphaFold. <i>Nature</i> . 2021; 596(7873):583-589. 2. Varadi M, Anyango S, Deshpande M, et al. AlphaFold Protein Structure Database: massively expanding the structural coverage of protein-sequence space with high-accuracy models. <i>Nucleic Acids Res</i> . 2022; 50(D1):D439-d444.

**Table S2 Information of GEO, QTL, and asthma GWAS dataset**

Characteristic	Resource	Sample size	Population ancestry	Reference	Data download
<b>GEO dataset</b>					
GSE69683 (The largest whole blood asthma dataset currently available in GEO)	GEO	Whole blood: Number of cases: 80 Number of controls: 371	European	1.Barrett T, Wilhite S E, Ledoux P, et al. NCBI GEO: archive for functional genomics data sets--update. Nucleic Acids Res. 2013; 41(Database issue):D991-995. 2. Bigler J, Boedigheimer M, Schofield JPR, et al; U-BIOPRED Study Group I. A Severe Asthma Disease Signature from Gene Expression Profiling of Peripheral Blood from U-BIOPRED Cohorts. Am J Respir Crit Care Med. 2017 May 15;195(10):1311-1320.	<a href="https://www.ncbi.nlm.nih.gov/geo/">https://www.ncbi.nlm.nih.gov/geo/</a>
<b>eQTL dataset</b>					
eQTL: Discovery sample (The largest eQTL dataset currently)	eQTLGen Consortium	Whole blood: 31,684	Predominantly European	Võsa U, Claringbould A, Westra H J, et al. Large-scale cis- and trans-eQTL analyses identify thousands of genetic loci and polygenic scores that regulate blood gene expression. Nat Genet. 2021; 53(9):1300-1310.	<a href="https://www.eqtngen.org/cis-eqtls.html">https://www.eqtngen.org/cis-eqtls.html</a>
eQTL: Replication sample	GTEXV8	Whole blood: 670	Predominantly European	The GTEx Consortium atlas of genetic regulatory effects across human tissues. Science. 2020; 369(6509):1318-1330.	<a href="https://yanglab.westlake.edu.cn/software/smr/#DataResource">https://yanglab.westlake.edu.cn/software/smr/#DataResource</a>
eQTL: lung tissues	GTEXV8	lung tissues: 515	Predominantly European	The GTEx Consortium atlas of genetic regulatory effects across human tissues. Science. 2020; 369(6509):1318-1330.	<a href="https://yanglab.westlake.edu.cn/software/smr/#DataResource">https://yanglab.westlake.edu.cn/software/smr/#DataResource</a>
<b>mQTL dataset</b>					
mQTL: Discovery sample (The largest mQTL dataset currently)	GoDMC	Whole blood: 27,750	European	Min J L, Hemani G, Hannon E, et al. Genomic and phenotypic insights from an atlas of genetic effects on DNA methylation. Nat Genet. 2021; 53(9):1311-1321.	<a href="http://mqtl.db.godmc.org.uk/index">http://mqtl.db.godmc.org.uk/index</a>
mQTL: Replication sample	FSH	Whole blood: 4,170	European	Huan T, Joehanes R, Song C, et al. Genome-wide identification of DNA methylation QTLs in whole blood highlights pathways for cardiovascular disease. Nat Commun. 2019; 10(1):4267.	<a href="https://ftp.ncbi.nlm.nih.gov/eqtl/">https://ftp.ncbi.nlm.nih.gov/eqtl/</a>
<b>asthma GWAS dataset</b>					
UKB:Discovery sample (GCST90014325)	GWAS Catlog	Number of cases: 56,167 Number of controls: 352,255	European	1.Sollis E, Mosaku A, Abid A, et al. The NHGRI-EBI GWAS Catalog: knowledgebase and deposition resource. Nucleic Acids Res. 2023; 51(D1):D977-d985 2.Valette K, Li Z, Bon-Baret V, et al. Prioritization of candidate causal genes for asthma in susceptibility loci derived from UK Biobank. Commun Biol. 2021; 12:1-12.	<a href="https://www.ebi.ac.uk/gwas/">https://www.ebi.ac.uk/gwas/</a>
TAGC: Replication sample (GCST006862)	GWAS Catlog	Number of cases: 19,954 Number of controls: 107,715	European	1.Sollis E, Mosaku A, Abid A, et al. The NHGRI-EBI GWAS Catalog: knowledgebase and deposition resource. Nucleic Acids Res. 2023; 51(D1):D977-d985 2.Demenais F, Margariite-Jeannin P, Barnes K C, et al. Multiancestry association study identifies new asthma risk loci that colocalize with immune-cell enhancer marks. Nat Genet. 2018; 50(11):1669-1679.	<a href="https://www.ebi.ac.uk/gwas/">https://www.ebi.ac.uk/gwas/</a>
J10_ASTHMA: Replication sample	FinnGen, R7 release	Number of cases: 32,351 Number of controls: 180,942	European	Kurki M I, Karjalainen J, Palta P, et al. FinnGen provides genetic insights from a well-phenotyped isolated population. Nature. 2023; 613(7944):508-518.	<a href="https://www.finngen.fi/en">https://www.finngen.fi/en</a>

eQTL, expression quantitative trait loci; mQTL, DNA methylation quantitative trait loci; UKB, the UK Biobank; TAGC, Trans-National Asthma Genetic Consortium.

**Table S3 Parameters for Virtual Screening Pocket**

Molecular	center_x	center_y	center_z	size_x	size_y	size_z
CEP95	-25.615	-1.964	15.301	241.2	120.6	270.9
ETS1	-13.238	1.755	-10.017	149.4	94.5	105.3
ITPKB	-8.483	-8.483	-5.428	126	126	126
RBM6	0.193	-18.476	6.295	6.295	173.25	173.25

**Table S4 Differential expressed genes in blood of asthma patients**

Gene.symbol	FC	expression	pval	adj.pval
XIST	3.139	up	2.73E-04	3.30E-03
TSIX	2.253	up	1.03E-03	8.73E-03
OLFM4	1.940	up	3.68E-05	7.56E-04
DEFA4	1.926	up	7.78E-06	2.38E-04
CEACAM8	1.843	up	6.36E-06	2.05E-04
CCL23	1.807	up	7.64E-07	4.47E-05
LTF	1.797	up	5.72E-06	1.91E-04
RNASE3	1.774	up	3.89E-07	2.77E-05
MMP8	1.733	up	1.66E-05	4.22E-04
ARG1	1.715	up	3.75E-06	1.41E-04
CRISP3	1.700	up	2.31E-06	9.84E-05
HP	1.665	up	3.59E-09	1.05E-06
ANXA3	1.658	up	2.70E-10	2.08E-07
LCN2	1.622	up	3.12E-05	6.68E-04
CEACAM6	1.614	up	1.69E-05	4.26E-04
CD24	1.604	up	6.61E-09	1.59E-06
BPI	1.598	up	4.20E-05	8.35E-04
LINC00537	1.571	up	1.56E-12	1.07E-08
SLPI	1.555	up	1.40E-09	6.33E-07
CD177	1.538	up	4.77E-04	4.98E-03
RNASE2	1.523	up	5.24E-08	6.45E-06
F5	1.522	up	2.73E-13	2.98E-09
CLEC4D	1.510	up	2.80E-05	6.16E-04
IL5RA	1.488	up	2.47E-05	5.63E-04
ORM1	1.486	up	1.19E-04	1.82E-03
MS4A3	1.484	up	7.60E-05	1.30E-03
ANKRD22	1.482	up	1.88E-06	8.56E-05
PRSS33	1.477	up	5.58E-04	5.60E-03
SH3GL3	1.475	up	2.75E-03	1.76E-02
INSC	1.473	up	5.11E-08	6.31E-06
SLC26A8	1.435	up	1.92E-06	8.67E-05
CAMP	1.434	up	1.88E-06	8.57E-05
POM121L9P	1.432	up	6.99E-03	3.45E-02
BCL2A1	1.426	up	1.67E-05	4.23E-04
ADORA3	1.426	up	7.70E-07	4.48E-05
CEBPE	1.419	up	7.69E-08	8.41E-06
FOLR3	1.415	up	6.50E-04	6.25E-03
S100A12	1.414	up	4.24E-08	5.64E-06
CLC	1.408	up	1.21E-06	6.23E-05
OLIG2	1.405	up	3.24E-04	3.75E-03
NRG1	1.400	up	2.74E-04	3.31E-03
EVI2A	1.398	up	2.07E-04	2.72E-03
DSG2-AS1	1.397	up	1.20E-03	9.75E-03
CTSG	1.396	up	8.82E-04	7.82E-03
MCEMP1	1.395	up	5.32E-09	1.37E-06
COX7B	1.393	up	6.25E-04	6.10E-03
OLAH	1.392	up	6.08E-04	5.97E-03
CARD16	1.392	up	1.32E-08	2.50E-06
FCGR1A	1.391	up	2.42E-06	1.02E-04
FCGR1B	1.388	up	3.83E-07	2.73E-05
NFE4	1.380	up	2.07E-07	1.73E-05
MCTP2	1.375	up	1.12E-08	2.24E-06
DAPK2	1.375	up	2.09E-07	1.74E-05
VSTM1	1.370	up	7.00E-07	4.20E-05
SHOX2	1.368	up	2.28E-03	1.54E-02
LOC105377458	1.361	up	9.25E-03	4.20E-02
ABCC13	1.360	up	9.40E-03	4.24E-02
DACH1	1.359	up	1.50E-05	3.94E-04
ACOT11	1.356	up	2.19E-08	3.59E-06
TIMM8A	1.353	up	5.86E-03	3.05E-02
KREMEN1	1.353	up	2.88E-05	6.30E-04
HCAR3	1.352	up	4.25E-11	6.11E-08
SLC8A1	1.352	up	6.85E-06	2.17E-04
CYP1B1-AS1	1.351	up	2.14E-06	9.38E-05
CASP5	1.349	up	2.31E-06	9.84E-05
IDO1	1.347	up	4.85E-04	5.04E-03
LOC100129488	1.346	up	4.24E-03	2.42E-02
ALOX15	1.342	up	5.61E-03	2.96E-02
ANKRD28	1.339	up	5.07E-03	2.75E-02
TCN1	1.339	up	5.92E-05	1.07E-03
LOC100288781	1.336	up	1.45E-06	7.10E-05
DSC2	1.335	up	2.60E-04	3.18E-03
TRPM6	1.334	up	3.27E-08	4.71E-06
LINC01410	1.332	up	4.88E-08	6.24E-06
SAMSN1	1.329	up	1.27E-05	3.47E-04
CACNA1E	1.328	up	5.96E-05	1.08E-03

ACSL1	1.325	up	2.17E-11	4.29E-08
C11orf58	1.321	up	1.21E-03	9.80E-03
LIN7A	1.321	up	1.95E-06	8.75E-05
SIGLEC8	1.320	up	3.66E-03	2.18E-02
DOCK4	1.320	up	6.34E-04	6.15E-03
KIF1B	1.318	up	1.61E-07	1.45E-05
LINC01094	1.317	up	6.04E-08	7.18E-06
PPBP	1.316	up	2.08E-05	4.99E-04
LY96	1.315	up	9.42E-04	8.21E-03
ITGA2B	1.315	up	2.41E-04	3.02E-03
ABCA1	1.314	up	2.82E-05	6.19E-04
IGHA1	1.313	up	1.52E-06	7.34E-05
FAM200B	1.312	up	6.34E-05	1.13E-03
MMP9	1.309	up	1.11E-03	9.26E-03
STOX2	1.309	up	2.57E-04	3.16E-03
TSNAX	1.305	up	1.58E-08	2.88E-06
SYCP1	1.304	up	1.68E-04	2.34E-03
ASPH	1.303	up	6.90E-04	6.53E-03
MOCS1	1.303	up	2.73E-03	1.75E-02
GPR84	1.302	up	3.57E-07	2.60E-05
SMPD3	1.302	up	5.85E-05	1.07E-03
ZNF321P	1.301	up	5.08E-05	9.64E-04
CLEC5A	1.299	up	1.69E-05	4.26E-04
PNPLA1	1.299	up	3.11E-07	2.33E-05
LOC101929497	1.297	up	6.24E-03	3.19E-02
APOBEC3A	1.297	up	2.36E-07	1.91E-05
CR1	1.296	up	1.48E-10	1.42E-07
COMMD8	1.295	up	3.00E-03	1.88E-02
ANKRD12	1.293	up	5.78E-09	1.45E-06
CYP4F2	1.292	up	1.71E-06	8.02E-05
TRIQQ	1.292	up	1.80E-03	1.30E-02
SPTLC3	1.288	up	2.87E-03	1.82E-02
SNORD89	1.288	up	9.57E-08	9.96E-06
PGLYRP1	1.287	up	6.35E-05	1.13E-03
CYP11B1	1.287	up	1.78E-03	1.29E-02
NUDT16P1	1.287	up	1.15E-07	1.12E-05
SLC37A3	1.286	up	3.11E-05	6.66E-04
APOBR	1.286	up	7.09E-05	1.23E-03
FAM120A	1.286	up	2.21E-07	1.81E-05
GAPT	1.286	up	8.91E-09	1.91E-06
BMX	1.285	up	6.00E-05	1.09E-03
EPAS1	1.285	up	4.60E-05	8.95E-04
PGM5	1.284	up	7.02E-03	3.46E-02
IPMK	1.284	up	2.99E-03	1.88E-02
RPUSD3	1.284	up	4.79E-05	9.21E-04
TPST1	1.284	up	2.76E-03	1.77E-02
CNTNAP3B	1.284	up	1.18E-02	4.96E-02
IL1R2	1.284	up	2.93E-04	3.47E-03
HES1	1.283	up	9.19E-07	5.11E-05
ASTN2	1.281	up	2.86E-03	1.81E-02
ABCA13	1.278	up	2.36E-03	1.58E-02
MRVII	1.278	up	1.92E-06	8.65E-05
RPS3A	1.277	up	2.30E-03	1.55E-02
MGC70870	1.276	up	6.32E-08	7.45E-06
JAK2	1.276	up	1.01E-04	1.60E-03
OLR1	1.274	up	4.23E-04	4.56E-03
KCNJ15	1.274	up	8.12E-05	1.35E-03
LOC101929713	1.273	up	9.75E-03	4.35E-02
SLC22A4	1.272	up	2.92E-07	2.23E-05
NDUFB3	1.271	up	1.21E-06	6.20E-05
TLR5	1.270	up	1.80E-07	1.57E-05
GRB10	1.269	up	2.92E-03	1.84E-02
DHRS9	1.268	up	1.61E-04	2.27E-03
ACTA2	1.267	up	5.37E-05	1.00E-03
THSD4	1.267	up	1.08E-02	4.67E-02
IQGAP3	1.266	up	2.56E-04	3.14E-03
LIMK2	1.266	up	2.12E-06	9.33E-05
LILRA5	1.266	up	6.05E-05	1.09E-03
ZNF267	1.265	up	5.96E-03	3.08E-02
DUBR	1.265	up	9.35E-03	4.23E-02
ENTPD1	1.265	up	3.56E-05	7.38E-04
LPAR4	1.264	up	9.14E-04	8.04E-03
CHST15	1.264	up	2.08E-04	2.72E-03
NFIL3	1.264	up	6.22E-08	7.35E-06
FAM186A	1.262	up	2.97E-03	1.87E-02
PLIN5	1.261	up	6.05E-07	3.80E-05
LTB4R	1.260	up	1.24E-06	6.33E-05
ELAVL3	1.260	up	6.31E-04	6.13E-03

LILRB2	1.260	up	3.50E-07	2.55E-05
PMP22	1.259	up	1.10E-02	4.73E-02
OVOL2	1.259	up	1.85E-03	1.33E-02
PFKFB2	1.259	up	3.07E-03	1.91E-02
HIST1H3E	1.258	up	1.92E-03	1.37E-02
C10orf128	1.257	up	1.62E-06	7.70E-05
PRUNE2	1.256	up	2.23E-03	1.52E-02
CREB5	1.256	up	5.99E-08	7.16E-06
TMEM88	1.256	up	3.83E-05	7.78E-04
KCTD21	1.255	up	3.09E-09	9.54E-07
WDFY3	1.255	up	2.68E-06	1.10E-04
PLOD2	1.255	up	1.79E-04	2.44E-03
SCAMP1	1.255	up	6.04E-03	3.11E-02
SLC29A1	1.254	up	4.46E-06	1.59E-04
RAB33B	1.254	up	2.13E-03	1.47E-02
SYNE1	1.254	up	1.89E-04	2.54E-03
THBS1	1.253	up	1.55E-04	2.20E-03
GPR34	1.253	up	3.30E-04	3.81E-03
ADGRG3	1.252	up	5.16E-05	9.75E-04
RPS27L	1.252	up	1.96E-03	1.38E-02
ARSB	1.252	up	2.12E-07	1.75E-05
IL18RAP	1.251	up	6.12E-04	6.00E-03
PADI4	1.249	up	1.12E-04	1.73E-03
CES1	1.249	up	2.01E-03	1.41E-02
COL1A1	1.249	up	1.43E-03	1.10E-02
DYSF	1.248	up	1.27E-05	3.47E-04
SLC5A9	1.248	up	2.52E-04	3.12E-03
CYSTM1	1.248	up	5.10E-06	1.76E-04
ACSL4	1.248	up	1.17E-04	1.79E-03
ST3GAL4-AS1	1.247	up	6.21E-05	1.11E-03
GALNT14	1.246	up	1.28E-04	1.91E-03
CCPG1	1.246	up	2.88E-05	6.30E-04
PAQR6	1.246	up	2.30E-04	2.92E-03
S100A8	1.246	up	3.45E-08	4.86E-06
CEACAM1	1.246	up	1.15E-05	3.22E-04
FAR2	1.245	up	1.38E-04	2.02E-03
CCDC126	1.245	up	6.33E-03	3.21E-02
STXBP5	1.245	up	8.46E-07	4.81E-05
BCL6	1.245	up	1.06E-04	1.67E-03
SRGAP1	1.244	up	1.56E-03	1.18E-02
GRIN2B	1.244	up	6.51E-05	1.15E-03
PRICKLE2-AS3	1.243	up	4.72E-05	9.12E-04
POLR2K	1.243	up	1.73E-03	1.27E-02
ADAM8	1.243	up	1.25E-07	1.19E-05
TIMP2	1.242	up	9.29E-05	1.50E-03
F11R	1.242	up	1.98E-05	4.79E-04
ST3GAL6	1.241	up	1.81E-05	4.48E-04
MPO	1.241	up	1.49E-03	1.14E-02
PYGL	1.241	up	6.11E-09	1.51E-06
SGMS1	1.241	up	4.28E-03	2.44E-02
ECHDC3	1.240	up	4.80E-03	2.64E-02
CSTA	1.240	up	3.47E-05	7.23E-04
ST6GALNAC3	1.239	up	2.74E-04	3.31E-03
DRAM1	1.239	up	6.69E-09	1.59E-06
HTATSF1P2	1.239	up	6.31E-03	3.21E-02
LOC100128737	1.238	up	2.48E-06	1.04E-04
CYP4F12	1.238	up	1.34E-06	6.73E-05
OSBPL1A	1.238	up	1.27E-05	3.47E-04
HIST1H2BC	1.237	up	6.15E-05	1.11E-03
JAG1	1.237	up	2.49E-05	5.67E-04
ZNF467	1.237	up	1.37E-04	2.01E-03
LINC00323	1.236	up	1.46E-03	1.12E-02
CNIH4	1.236	up	6.18E-05	1.11E-03
ALPL	1.236	up	3.22E-04	3.73E-03
RRAGD	1.236	up	1.05E-07	1.05E-05
FAS	1.235	up	2.95E-04	3.49E-03
PI3	1.235	up	5.35E-04	5.44E-03
IL4R	1.234	up	2.62E-06	1.08E-04
HRASLS5	1.234	up	1.31E-05	3.54E-04
HRH4	1.233	up	1.88E-03	1.34E-02
FLJ1455	1.233	up	2.14E-03	1.47E-02
CEP350	1.232	up	9.24E-07	5.12E-05
QKI	1.232	up	6.37E-04	6.17E-03
LRG1	1.231	up	2.47E-04	3.07E-03
C18orf32	1.230	up	8.76E-04	7.78E-03
ACKR4	1.230	up	5.76E-03	3.01E-02
HK3	1.230	up	1.25E-06	6.35E-05
MARC1	1.230	up	1.41E-04	2.06E-03

CKLF	1.230	up	6.45E-10	3.73E-07
HSDL2	1.229	up	6.81E-05	1.19E-03
GLRX	1.229	up	4.27E-05	8.45E-04
LOC728323	1.229	up	1.83E-03	1.32E-02
SULT1B1	1.229	up	8.22E-04	7.41E-03
NFIB	1.229	up	1.07E-02	4.64E-02
KCNV1	1.228	up	1.35E-03	1.06E-02
FOXA2	1.228	up	1.98E-03	1.39E-02
LOC55338	1.227	up	2.75E-03	1.76E-02
PLBD1	1.227	up	9.87E-06	2.87E-04
MSRB3	1.227	up	7.59E-04	6.98E-03
HIST1H2BD	1.227	up	6.53E-04	6.28E-03
MEIOC	1.226	up	3.38E-04	3.87E-03
TPTEP1	1.226	up	1.22E-06	6.28E-05
NQO2	1.226	up	8.11E-05	1.35E-03
FIGN	1.226	up	1.75E-04	2.40E-03
PDK4	1.225	up	1.09E-02	4.71E-02
ROPN1L	1.224	up	7.14E-05	1.23E-03
RPL15	1.224	up	3.39E-05	7.10E-04
RNF175	1.224	up	4.13E-06	1.51E-04
LOC283075	1.224	up	1.86E-03	1.33E-02
ITPR2	1.224	up	3.96E-04	4.34E-03
ZNF354A	1.224	up	2.98E-03	1.87E-02
EPPIN	1.223	up	4.02E-05	8.09E-04
SHOX	1.223	up	6.19E-03	3.17E-02
HIF3A	1.223	up	1.63E-03	1.22E-02
RGPD5	1.223	up	1.81E-03	1.31E-02
C9orf66	1.222	up	1.05E-05	3.01E-04
SSFA2	1.222	up	1.79E-03	1.30E-02
RETN	1.222	up	5.09E-04	5.22E-03
TLR4	1.222	up	7.84E-04	7.16E-03
B3GNT5	1.221	up	1.20E-03	9.76E-03
HECW2	1.221	up	1.28E-03	1.02E-02
ZNF608	1.221	up	2.16E-04	2.79E-03
SIGLEC5	1.221	up	4.54E-04	4.81E-03
HIST2H2AA3	1.220	up	2.14E-04	2.77E-03
C2orf76	1.220	up	2.71E-04	3.28E-03
C9orf84	1.220	up	4.87E-04	5.05E-03
SORT1	1.219	up	8.28E-06	2.51E-04
PIK3R6	1.219	up	1.92E-04	2.57E-03
ARHGAP29	1.219	up	2.71E-04	3.28E-03
KLHL6	1.219	up	1.63E-05	4.16E-04
ADGRE2	1.218	up	1.25E-04	1.87E-03
DAPP1	1.217	up	2.12E-11	4.29E-08
ARHGAP26	1.217	up	1.58E-06	7.55E-05
FAM133A	1.217	up	6.28E-03	3.20E-02
TMEM67	1.216	up	1.40E-04	2.03E-03
C3AR1	1.215	up	6.11E-06	1.99E-04
LRRN1	1.215	up	8.49E-03	3.95E-02
C14orf2	1.215	up	1.55E-03	1.17E-02
ARAP3	1.215	up	1.13E-04	1.75E-03
FAM106A	1.215	up	5.86E-05	1.07E-03
TXN	1.215	up	3.13E-06	1.23E-04
KRCC1	1.215	up	1.78E-03	1.29E-02
NAIP	1.215	up	5.38E-06	1.83E-04
PLXDC2	1.214	up	7.37E-04	6.85E-03
TLR2	1.213	up	1.28E-05	3.50E-04
TP53I11	1.213	up	1.57E-04	2.23E-03
AQP9	1.213	up	1.76E-09	7.24E-07
RHOQ	1.212	up	1.55E-05	4.03E-04
NT5C2	1.212	up	6.19E-11	7.52E-08
DPH3	1.212	up	1.46E-06	7.13E-05
LPCAT2	1.212	up	1.09E-03	9.14E-03
LINC00619	1.212	up	1.61E-04	2.28E-03
IRAK3	1.211	up	1.22E-04	1.85E-03
HEBP2	1.211	up	3.77E-09	1.09E-06
NCF4	1.211	up	6.63E-07	4.05E-05
C9orf72	1.211	up	9.94E-03	4.41E-02
HNMT	1.211	up	5.08E-03	2.76E-02
HIPK3	1.211	up	3.12E-04	3.64E-03
FAM63A	1.211	up	5.90E-06	1.95E-04
ANTXR2	1.210	up	4.79E-06	1.68E-04
RRP12	1.210	up	4.55E-05	8.88E-04
LGALS12	1.210	up	9.95E-04	8.53E-03
IL1RL1	1.210	up	9.44E-03	4.25E-02
PIK3CG	1.209	up	3.60E-07	2.61E-05
CHST13	1.209	up	1.26E-03	1.01E-02
NEGR1-IT1	1.208	up	1.56E-04	2.21E-03



LOC101929243	1.208	up	6.23E-06	2.02E-04
CD163	1.208	up	1.10E-04	1.71E-03
LTBR	1.208	up	2.00E-04	2.65E-03
MYCT1	1.208	up	3.32E-04	3.81E-03
SH3GLB1	1.207	up	2.10E-07	1.74E-05
LINC01191	1.206	up	4.70E-06	1.66E-04
RAB32	1.206	up	1.22E-08	2.38E-06
NHSL2	1.206	up	3.97E-07	2.79E-05
RAB13	1.206	up	2.54E-05	5.74E-04
CPT1A	1.206	up	8.72E-06	2.61E-04
PLXNC1	1.206	up	1.88E-07	1.62E-05
FLJ31958	1.206	up	2.35E-04	2.96E-03
DEFT1P	1.205	up	9.19E-05	1.49E-03
UBE2J1	1.205	up	1.59E-07	1.43E-05
ASAP1	1.204	up	1.12E-06	5.88E-05
CHURC1	1.204	up	1.21E-04	1.83E-03
MEGF9	1.204	up	8.95E-06	2.67E-04
ALOX5	1.204	up	6.03E-09	1.50E-06
NAMPT	1.204	up	6.01E-03	3.11E-02
MYL9	1.204	up	8.71E-03	4.03E-02
EFCAB6	1.204	up	3.47E-05	7.24E-04
ZNF578	1.203	up	7.32E-05	1.26E-03
UBL5	1.203	up	7.01E-07	4.20E-05
CA4	1.203	up	1.23E-03	9.91E-03
NDFIP2	1.203	up	9.12E-04	8.02E-03
IKBIP	1.202	up	8.67E-04	7.72E-03
MTMR6	1.202	up	1.21E-03	9.84E-03
DGAT2	1.202	up	1.29E-04	1.93E-03
RPS17P5	1.201	up	2.90E-04	3.45E-03
CCDC58P3	1.201	up	1.82E-04	2.47E-03
DNAJC3-AS1	1.201	up	4.32E-04	4.63E-03
TOPORS-AS1	1.201	up	1.92E-05	4.69E-04
MRC1	1.201	up	2.43E-04	3.04E-03
NDUFA1	1.200	up	2.73E-06	1.12E-04
COL9A2	1.200	up	4.10E-03	2.36E-02
SLC39A14	1.200	up	5.89E-08	7.07E-06
ANKH	1.200	down	8.29E-05	1.37E-03
LOC100507281	1.200	down	1.10E-04	1.70E-03
ZCCHC7	1.200	down	7.76E-06	2.38E-04
IMPDH2	1.201	down	6.31E-10	3.71E-07
CAPRN1	1.201	down	3.26E-04	3.77E-03
RBM19	1.201	down	2.14E-07	1.77E-05
RORC	1.201	down	8.16E-05	1.36E-03
RTN4IP1	1.201	down	2.63E-06	1.09E-04
LOC100287024	1.201	down	7.02E-08	7.97E-06
POLR2J2	1.201	down	4.45E-05	8.74E-04
SIKE1	1.201	down	3.70E-07	2.66E-05
NKTR	1.201	down	6.36E-03	3.23E-02
TAOK1	1.202	down	5.48E-04	5.53E-03
PNPO	1.202	down	2.67E-09	8.79E-07
SNX29	1.202	down	3.54E-06	1.35E-04
XPO7	1.202	down	2.54E-07	2.01E-05
PGM5-AS1	1.202	down	8.64E-06	2.59E-04
TRIO	1.202	down	4.22E-06	1.53E-04
NNT-AS1	1.202	down	1.74E-04	2.39E-03
RIMKLB	1.202	down	1.95E-06	8.75E-05
PSME4	1.202	down	3.74E-08	5.18E-06
SRR	1.202	down	1.89E-05	4.64E-04
KDSR	1.203	down	1.29E-08	2.45E-06
GPAT2	1.203	down	1.05E-02	4.58E-02
SPAG16	1.203	down	3.70E-03	2.20E-02
GNAS	1.203	down	7.63E-05	1.30E-03
BLK	1.203	down	7.52E-05	1.28E-03
FAM226B	1.203	down	1.75E-04	2.40E-03
INTS2	1.203	down	1.22E-03	9.86E-03
STK38	1.203	down	3.86E-06	1.44E-04
RNASEH2B	1.203	down	1.15E-04	1.77E-03
PEX5	1.203	down	1.08E-04	1.68E-03
ARHGEF7	1.203	down	1.10E-03	9.19E-03
CNOT4	1.203	down	8.61E-07	4.89E-05
FOXO1	1.203	down	4.62E-07	3.14E-05
TNFSF4	1.203	down	5.87E-04	5.82E-03
NME7	1.203	down	1.39E-05	3.72E-04
ABHD18	1.203	down	8.76E-08	9.22E-06
INTS10	1.204	down	5.88E-04	5.82E-03
HIVEP3	1.204	down	1.50E-04	2.15E-03
ZNF326	1.204	down	3.65E-07	2.64E-05
ZNF519	1.204	down	1.72E-06	8.04E-05

XRCC5	1.204	down	1.45E-08	2.70E-06
RBM39	1.204	down	8.90E-05	1.45E-03
FTX	1.204	down	7.13E-03	3.50E-02
PATZ1	1.205	down	5.43E-11	6.91E-08
RASGRP3	1.205	down	1.57E-03	1.18E-02
UTP20	1.205	down	2.13E-06	9.34E-05
TAF11	1.205	down	1.24E-06	6.31E-05
LOC105371967	1.205	down	2.77E-05	6.13E-04
ZNF37A	1.205	down	7.86E-10	4.22E-07
LOC102724814	1.205	down	6.46E-07	3.99E-05
SLC25A39	1.206	down	6.17E-03	3.16E-02
CLPTM1L	1.206	down	1.15E-08	2.30E-06
PMS2P2	1.206	down	2.11E-08	3.49E-06
TBRG1	1.206	down	4.58E-07	3.12E-05
CASK	1.206	down	9.06E-05	1.47E-03
ZNF830	1.206	down	1.14E-07	1.12E-05
LINC01278	1.206	down	1.72E-06	8.05E-05
DNASE1	1.206	down	5.19E-06	1.78E-04
DGUOK	1.206	down	3.33E-05	7.00E-04
PHF7	1.206	down	5.72E-09	1.44E-06
TEX10	1.206	down	4.65E-10	3.03E-07
GPATCH4	1.206	down	4.75E-07	3.20E-05
AGPAT3	1.207	down	1.57E-06	7.54E-05
MAN1A2	1.207	down	4.46E-04	4.74E-03
PCMTD2	1.207	down	2.20E-04	2.82E-03
AGK	1.207	down	1.33E-07	1.24E-05
PRR5	1.207	down	1.99E-05	4.80E-04
C11orf31	1.207	down	1.83E-05	4.53E-04
RNASET2	1.207	down	6.13E-06	1.99E-04
BCL7A	1.207	down	1.69E-06	7.94E-05
POLH	1.207	down	3.63E-07	2.63E-05
CAPN7	1.207	down	2.60E-05	5.83E-04
DNAJC30	1.207	down	6.63E-07	4.05E-05
ZBTB4	1.208	down	6.53E-09	1.59E-06
KIAA0754	1.208	down	3.88E-06	1.45E-04
ZNF587	1.208	down	3.71E-06	1.40E-04
RBM6	1.208	down	1.25E-04	1.87E-03
CRTC3	1.208	down	1.68E-05	4.24E-04
CNOT7	1.208	down	2.17E-08	3.58E-06
LCMT1-AS2	1.208	down	2.24E-08	3.65E-06
PELP1	1.208	down	8.35E-09	1.84E-06
TSEN2	1.208	down	1.55E-04	2.20E-03
P2RX5	1.208	down	4.70E-04	4.93E-03
ZNF346	1.209	down	3.20E-08	4.70E-06
ZMYND8	1.209	down	9.08E-09	1.92E-06
SEPT11	1.209	down	7.64E-06	2.35E-04
TRD	1.209	down	4.66E-09	1.26E-06
MBNL1	1.209	down	2.76E-04	3.32E-03
KRR1	1.209	down	2.65E-08	4.09E-06
METTL3	1.209	down	1.35E-06	6.76E-05
ZBTB43	1.210	down	5.63E-09	1.43E-06
GPATCH2	1.210	down	7.19E-07	4.28E-05
NFATC2IP	1.210	down	2.81E-07	2.16E-05
XPO1	1.210	down	2.60E-07	2.04E-05
NFATC3	1.210	down	7.96E-06	2.44E-04
LOC100293705	1.210	down	7.88E-04	7.18E-03
VAPB	1.210	down	1.15E-05	3.22E-04
ING5	1.210	down	1.42E-04	2.07E-03
KLRG1	1.210	down	7.22E-04	6.76E-03
APLP2	1.210	down	1.21E-03	9.84E-03
DDHD2	1.211	down	6.82E-05	1.19E-03
HELB	1.211	down	4.00E-04	4.37E-03
CDC14A	1.211	down	2.28E-06	9.74E-05
NDUFA5	1.211	down	5.51E-05	1.02E-03
ZNF285	1.211	down	6.81E-04	6.47E-03
SYNJ2BP	1.211	down	5.70E-07	3.62E-05
BCOR	1.211	down	2.96E-07	2.25E-05
MGC24103	1.211	down	4.46E-03	2.51E-02
AFAP1L2	1.212	down	6.92E-06	2.18E-04
SUZ12P1	1.212	down	3.27E-03	2.00E-02
SLC20A1	1.212	down	1.22E-07	1.18E-05
BCL11B	1.212	down	1.39E-07	1.28E-05
AMIGO1	1.212	down	1.59E-05	4.09E-04
CD1C	1.212	down	9.34E-06	2.75E-04
LOC100293440	1.212	down	6.39E-03	3.24E-02
DNAJC16	1.212	down	8.16E-11	9.11E-08
NFIX	1.212	down	7.39E-03	3.59E-02
SART3	1.212	down	7.86E-08	8.54E-06

METTL6	1.213	down	1.39E-05	3.71E-04
HMCES	1.213	down	4.81E-11	6.41E-08
BTLA	1.213	down	2.57E-04	3.16E-03
MAP4K4	1.213	down	2.65E-07	2.07E-05
TNRC6A	1.213	down	1.30E-07	1.22E-05
SMC1A	1.213	down	1.47E-04	2.13E-03
EWSR1	1.213	down	5.75E-04	5.73E-03
GPBP1L1	1.213	down	1.67E-03	1.24E-02
BCLAF1	1.213	down	1.29E-05	3.52E-04
FBRSL1	1.213	down	2.21E-08	3.62E-06
NLK	1.214	down	7.70E-06	2.37E-04
THRAP3	1.214	down	1.23E-06	6.31E-05
GOSR2	1.214	down	4.55E-04	4.81E-03
MED13	1.214	down	6.42E-06	2.07E-04
ZFP82	1.214	down	4.83E-05	9.28E-04
ZNF202	1.215	down	5.00E-08	6.26E-06
YLPM1	1.215	down	6.10E-07	3.82E-05
NOLC1	1.215	down	3.64E-06	1.38E-04
SDC2	1.215	down	3.05E-04	3.57E-03
SEPT8	1.215	down	5.51E-05	1.02E-03
CUL4A	1.215	down	4.75E-07	3.20E-05
SFSWAP	1.215	down	1.02E-09	5.06E-07
DIP2C	1.216	down	2.89E-04	3.45E-03
DUSP5	1.216	down	2.18E-04	2.81E-03
RABGAP1	1.216	down	6.34E-08	7.45E-06
NMT2	1.216	down	2.69E-04	3.27E-03
CD47	1.216	down	3.24E-04	3.75E-03
TXLNG	1.216	down	9.57E-08	9.96E-06
NMNAT3	1.217	down	2.24E-05	5.26E-04
MRAS	1.217	down	3.64E-04	4.08E-03
BANK1	1.217	down	7.46E-05	1.28E-03
KLHL10	1.217	down	4.70E-08	6.08E-06
HSPH1	1.217	down	3.32E-08	4.76E-06
G3BP1	1.217	down	7.55E-07	4.42E-05
KLHL14	1.217	down	4.75E-03	2.63E-02
NOL9	1.217	down	5.00E-08	6.26E-06
CYB561	1.218	down	2.70E-05	6.00E-04
PIK3IP1	1.218	down	5.97E-08	7.15E-06
DIEXF	1.218	down	9.53E-05	1.53E-03
MIS18A	1.218	down	1.49E-04	2.14E-03
GPALPP1	1.219	down	1.35E-06	6.77E-05
ZC3H12B	1.219	down	5.19E-04	5.31E-03
CLIC3	1.219	down	1.74E-05	4.35E-04
NME9	1.219	down	2.19E-06	9.52E-05
ZNF747	1.219	down	3.09E-11	5.46E-08
LRRC1	1.219	down	6.58E-04	6.31E-03
ACSS1	1.220	down	2.34E-05	5.43E-04
PTPRS	1.220	down	9.41E-06	2.76E-04
KIAA1147	1.220	down	8.72E-06	2.61E-04
DDX42	1.220	down	1.84E-05	4.55E-04
LOC100288944	1.220	down	1.95E-05	4.75E-04
KLHL3	1.220	down	3.65E-05	7.52E-04
SCD5	1.220	down	1.01E-02	4.47E-02
G2E3	1.220	down	1.94E-04	2.59E-03
C21orf116	1.220	down	5.22E-05	9.82E-04
TPD52	1.220	down	2.15E-03	1.47E-02
SMAD5	1.220	down	4.77E-04	4.98E-03
SLFN5	1.221	down	2.35E-04	2.96E-03
POU2F2	1.221	down	2.72E-06	1.12E-04
PTGDR	1.221	down	1.87E-05	4.59E-04
NOP14-AS1	1.221	down	8.95E-09	1.91E-06
GPR18	1.221	down	5.88E-07	3.72E-05
FO XK1	1.222	down	7.12E-09	1.65E-06
SUN1	1.222	down	1.45E-05	3.85E-04
SREK1	1.222	down	9.10E-06	2.70E-04
NOP14	1.222	down	2.09E-08	3.48E-06
MMP19	1.222	down	5.60E-07	3.57E-05
SEC62	1.222	down	2.61E-04	3.19E-03
ZNF551	1.222	down	9.94E-08	1.02E-05
CCDC88C	1.222	down	4.14E-08	5.55E-06
MSI2	1.222	down	2.61E-05	5.85E-04
FOSB	1.222	down	2.73E-05	6.06E-04
RUNX1-IT1	1.222	down	1.38E-06	6.89E-05
RHOA	1.223	down	9.59E-05	1.54E-03
ZNF764	1.223	down	3.73E-06	1.40E-04
ZNF831	1.223	down	5.74E-06	1.92E-04
BLOC1S5	1.223	down	1.96E-05	4.77E-04
PCSK7	1.224	down	3.24E-09	9.73E-07

ILF3	1.224	down	6.91E-07	4.16E-05
ZMYM2	1.224	down	1.78E-08	3.12E-06
RUFY2	1.224	down	3.17E-04	3.68E-03
VPREB3	1.224	down	1.85E-03	1.33E-02
GSPT1	1.224	down	3.80E-07	2.72E-05
FRG1JP	1.224	down	1.21E-03	9.81E-03
FAM98A	1.224	down	3.45E-05	7.21E-04
CAMTA1	1.225	down	1.02E-02	4.50E-02
GPR180	1.225	down	3.60E-04	4.05E-03
THUMPD3	1.225	down	7.44E-08	8.25E-06
THEM4	1.225	down	1.23E-05	3.38E-04
URB1	1.225	down	9.69E-08	1.00E-05
ST6GALNAC4	1.226	down	5.57E-05	1.03E-03
SEL1L3	1.226	down	2.82E-05	6.20E-04
NUCKS1	1.226	down	1.11E-06	5.84E-05
EP400	1.226	down	1.07E-05	3.05E-04
PEX3	1.226	down	2.85E-07	2.19E-05
ZFAND6	1.226	down	5.35E-09	1.37E-06
NELL2	1.226	down	1.34E-03	1.05E-02
SNCA	1.226	down	7.82E-03	3.73E-02
CCDC91	1.226	down	6.56E-05	1.16E-03
RGP1	1.227	down	6.31E-09	1.55E-06
SPATS2	1.227	down	4.23E-07	2.93E-05
SCFD1	1.228	down	2.35E-06	9.95E-05
FMNL3	1.228	down	3.22E-04	3.73E-03
ZNF330	1.228	down	1.75E-06	8.12E-05
MAP2K7	1.228	down	6.62E-08	7.61E-06
DDI2	1.228	down	9.16E-09	1.94E-06
WDR61	1.229	down	1.68E-07	1.49E-05
RAD51C	1.229	down	1.47E-06	7.17E-05
SNX9	1.229	down	2.46E-09	8.55E-07
USP40	1.229	down	8.98E-08	9.42E-06
CXXC5	1.229	down	2.00E-09	7.58E-07
PCBP2	1.230	down	2.87E-09	9.18E-07
TSPYL5	1.230	down	5.74E-04	5.72E-03
TSR2	1.230	down	1.11E-11	2.63E-08
NUP107	1.230	down	5.81E-06	1.93E-04
GTF3A	1.230	down	1.40E-07	1.28E-05
TASP1	1.230	down	1.06E-03	8.93E-03
LRCH3	1.230	down	8.95E-06	2.67E-04
ESCO1	1.230	down	2.09E-04	2.72E-03
BCORP1	1.230	down	4.71E-03	2.61E-02
DDHD1	1.231	down	1.11E-05	3.14E-04
FCMR	1.231	down	6.93E-08	7.88E-06
CD27	1.231	down	1.09E-05	3.10E-04
TBC1D31	1.231	down	4.61E-06	1.64E-04
CHRM3-AS2	1.231	down	5.36E-03	2.87E-02
RBM17	1.231	down	1.74E-09	7.24E-07
N4BP2L1	1.231	down	1.67E-05	4.24E-04
SUPV3L1	1.232	down	9.17E-12	2.39E-08
HNRNPR	1.232	down	1.33E-06	6.70E-05
THNSL1	1.232	down	1.34E-03	1.06E-02
RAPH1	1.232	down	1.40E-05	3.73E-04
ATXN2L	1.232	down	2.96E-07	2.25E-05
PIK3C2B	1.232	down	1.73E-05	4.34E-04
KLF12	1.232	down	1.76E-05	4.40E-04
PLEKHA2	1.233	down	1.70E-04	2.36E-03
EGOT	1.233	down	4.05E-05	8.14E-04
DPF3	1.233	down	2.56E-04	3.14E-03
LOC101927027	1.233	down	7.95E-05	1.34E-03
RANBP10	1.233	down	7.44E-07	4.39E-05
MYEF2	1.233	down	6.40E-05	1.14E-03
C5orf63	1.234	down	2.95E-07	2.25E-05
OPN3	1.234	down	4.40E-06	1.58E-04
TGIF2	1.234	down	2.44E-09	8.55E-07
CCNC	1.234	down	2.19E-05	5.17E-04
DOCK9	1.234	down	3.23E-03	1.99E-02
TCF12	1.234	down	3.55E-07	2.59E-05
NBAS	1.234	down	2.25E-08	3.65E-06
TTC3	1.235	down	8.18E-08	8.81E-06
EIF4A1	1.235	down	1.80E-07	1.57E-05
ZNF83	1.235	down	8.64E-06	2.59E-04
LILRA4	1.235	down	7.62E-06	2.35E-04
CLK4	1.235	down	1.47E-03	1.13E-02
NAP1L4	1.236	down	4.66E-09	1.26E-06
ATP8B1	1.236	down	5.42E-11	6.91E-08
QSOX2	1.236	down	4.09E-08	5.52E-06
ESYT2	1.236	down	4.78E-07	3.21E-05

ZNF160	1.236	down	1.60E-05	4.11E-04
PRICKLE1	1.236	down	9.35E-07	5.16E-05
SLC38A10	1.237	down	3.42E-08	4.86E-06
HIST1H2AE	1.237	down	3.62E-05	7.50E-04
PSPC1	1.237	down	6.78E-09	1.59E-06
KMO	1.237	down	3.66E-05	7.54E-04
MORC4	1.237	down	7.62E-08	8.36E-06
ZEB2	1.237	down	5.30E-04	5.39E-03
YBX1	1.237	down	2.01E-07	1.69E-05
EXOSC7	1.238	down	8.08E-10	4.29E-07
DOCK10	1.238	down	1.57E-06	7.53E-05
QSER1	1.238	down	4.23E-06	1.53E-04
FOXP1	1.239	down	4.74E-05	9.14E-04
NAPSB	1.239	down	1.99E-03	1.40E-02
PAX5	1.239	down	5.56E-04	5.59E-03
NSUN6	1.239	down	2.29E-09	8.44E-07
LOXL1-AS1	1.239	down	1.33E-04	1.96E-03
TAF15	1.239	down	1.40E-06	6.93E-05
C2CD2	1.239	down	3.81E-08	5.24E-06
ELP2	1.239	down	1.35E-08	2.56E-06
WHSC1	1.239	down	2.65E-08	4.09E-06
TMPO	1.239	down	5.12E-03	2.77E-02
DCAF8	1.240	down	3.08E-10	2.31E-07
HOXB-AS1	1.240	down	4.23E-04	4.55E-03
NBPF10	1.240	down	5.01E-06	1.73E-04
MTERF4	1.240	down	1.15E-07	1.12E-05
AK5	1.241	down	1.90E-04	2.56E-03
EPB41	1.241	down	2.18E-03	1.49E-02
TEKT4P2	1.241	down	2.06E-04	2.70E-03
IPO9	1.241	down	2.06E-06	9.12E-05
SRGAP2	1.241	down	3.88E-04	4.27E-03
ZBTB20	1.241	down	1.70E-10	1.58E-07
SF1	1.242	down	7.37E-05	1.26E-03
ZDHHC2	1.242	down	2.18E-08	3.59E-06
CAMK2D	1.242	down	6.19E-06	2.01E-04
ATF7IP2	1.242	down	2.35E-07	1.91E-05
SOX6	1.242	down	3.72E-07	2.67E-05
TCEA1	1.242	down	1.71E-05	4.30E-04
METAP1D	1.243	down	1.18E-06	6.10E-05
UNG	1.243	down	3.08E-09	9.54E-07
ALKBH7	1.243	down	2.17E-06	9.46E-05
RGCC	1.243	down	1.24E-04	1.87E-03
TRA	1.243	down	2.32E-05	5.40E-04
GSAP	1.243	down	1.57E-08	2.86E-06
ATP6V1H	1.243	down	6.61E-08	7.61E-06
CCNK	1.243	down	1.77E-04	2.42E-03
ZNF703	1.244	down	1.12E-04	1.73E-03
RGS12	1.244	down	6.77E-09	1.59E-06
ZNF141	1.245	down	7.71E-10	4.17E-07
LIX1	1.246	down	6.00E-05	1.08E-03
CEP104	1.246	down	1.21E-09	5.75E-07
XKR6	1.246	down	8.28E-06	2.51E-04
ATP1A1	1.247	down	1.33E-07	1.24E-05
SCOC-AS1	1.247	down	2.53E-05	5.73E-04
MMD	1.247	down	1.58E-07	1.43E-05
PER3	1.247	down	8.86E-05	1.44E-03
GTPBP4	1.247	down	2.45E-06	1.03E-04
VPS13C	1.247	down	8.20E-08	8.82E-06
NGDN	1.247	down	2.48E-09	8.55E-07
HEMGN	1.247	down	4.46E-03	2.51E-02
COA7	1.247	down	1.54E-06	7.41E-05
LOC283713	1.248	down	6.79E-04	6.46E-03
SHISA4	1.248	down	1.22E-05	3.36E-04
KIAA0368	1.248	down	1.70E-07	1.50E-05
KCNA3	1.249	down	1.04E-05	3.00E-04
BCCIP	1.249	down	8.87E-07	4.99E-05
SEMA6A	1.249	down	1.52E-06	7.34E-05
SLC3A1	1.249	down	3.38E-05	7.08E-04
NRCAM	1.249	down	4.73E-06	1.66E-04
ZDHHC21	1.250	down	2.04E-06	9.06E-05
FLJ10038	1.250	down	6.76E-07	4.10E-05
TRAF3IP1	1.250	down	5.80E-05	1.06E-03
HNRNPA1	1.251	down	6.46E-07	3.99E-05
CAMK4	1.251	down	4.75E-04	4.97E-03
ANAPC5	1.251	down	1.29E-07	1.22E-05
DGCR8	1.251	down	1.53E-09	6.62E-07
EVL	1.252	down	8.11E-08	8.75E-06
LOC286272	1.253	down	3.28E-07	2.44E-05

PRR3	1.253	down	5.24E-08	6.45E-06
RBM14	1.254	down	9.88E-07	5.39E-05
CHD6	1.254	down	3.25E-09	9.73E-07
MATR3	1.254	down	1.86E-06	8.50E-05
TGFBR1	1.254	down	1.97E-09	7.58E-07
SNX1	1.254	down	4.63E-07	3.14E-05
SPIB	1.254	down	3.17E-06	1.24E-04
LUC7L	1.254	down	4.14E-09	1.16E-06
SWAP70	1.255	down	3.01E-05	6.52E-04
LINC00494	1.255	down	1.80E-05	4.46E-04
GAR1	1.255	down	4.36E-11	6.11E-08
SPG7	1.255	down	1.11E-10	1.16E-07
YTHDC1	1.255	down	2.36E-05	5.46E-04
ZMYM6	1.255	down	2.51E-07	1.99E-05
CAMSAP1	1.255	down	1.95E-07	1.66E-05
PSMG4	1.256	down	9.11E-07	5.08E-05
GCOM1	1.256	down	1.29E-04	1.92E-03
DDX39B	1.256	down	1.02E-08	2.09E-06
IL21R	1.256	down	2.86E-08	4.33E-06
NXT1	1.257	down	4.13E-08	5.55E-06
CDK9	1.257	down	3.95E-07	2.78E-05
FAM213A	1.257	down	7.95E-08	8.60E-06
CD40	1.257	down	3.85E-06	1.44E-04
CD79B	1.258	down	7.52E-06	2.32E-04
LOC728613	1.258	down	7.24E-04	6.76E-03
MS4A7	1.258	down	2.55E-05	5.75E-04
WASF2	1.258	down	5.08E-05	9.64E-04
ITPKB	1.259	down	1.04E-07	1.05E-05
ZNRD1ASP	1.259	down	2.47E-04	3.07E-03
HIST1H3H	1.259	down	4.02E-05	8.10E-04
AHSA2	1.260	down	1.26E-03	1.01E-02
PIGL	1.260	down	3.34E-05	7.02E-04
ZNF785	1.260	down	3.53E-11	5.85E-08
EIF3B	1.261	down	7.48E-07	4.40E-05
CDKN1C	1.261	down	6.21E-05	1.11E-03
CBX3	1.261	down	1.17E-05	3.25E-04
ZBTB38	1.261	down	4.28E-08	5.66E-06
RPAIN	1.261	down	1.34E-03	1.06E-02
ATM	1.261	down	1.80E-07	1.57E-05
PTPRK	1.262	down	3.52E-06	1.34E-04
CCNL1	1.262	down	9.36E-04	8.16E-03
NAF1	1.263	down	1.67E-08	2.98E-06
IGHG1	1.263	down	4.44E-03	2.51E-02
WDR60	1.263	down	2.32E-08	3.75E-06
CIAPIN1	1.263	down	1.61E-07	1.45E-05
SEMA4C	1.263	down	1.73E-05	4.34E-04
TADA2A	1.263	down	2.11E-04	2.75E-03
SLC15A2	1.264	down	2.53E-03	1.66E-02
NPAT	1.264	down	6.33E-07	3.92E-05
FYN	1.265	down	3.99E-08	5.43E-06
LMLN	1.266	down	9.74E-09	2.03E-06
MUM1	1.266	down	2.85E-08	4.33E-06
LRIG2	1.266	down	7.24E-07	4.30E-05
GOLGA8A	1.266	down	3.27E-08	4.71E-06
PPAT	1.266	down	3.28E-04	3.78E-03
SIK1	1.266	down	8.96E-07	5.01E-05
KLHL42	1.267	down	1.10E-06	5.84E-05
CBX5	1.267	down	1.07E-08	2.16E-06
TTC9	1.267	down	2.65E-05	5.91E-04
SERBP1	1.268	down	5.90E-12	1.93E-08
SHMT2	1.268	down	1.55E-09	6.62E-07
SNX19	1.268	down	6.23E-07	3.89E-05
PRMT2	1.269	down	1.08E-05	3.07E-04
FCRL5	1.269	down	1.34E-03	1.06E-02
AUTS2	1.269	down	1.92E-06	8.67E-05
LINC01550	1.270	down	4.69E-07	3.17E-05
MZB1	1.270	down	4.71E-04	4.93E-03
TRABD2A	1.270	down	3.29E-05	6.93E-04
KATNBL1	1.270	down	1.30E-03	1.03E-02
ZNF512B	1.270	down	2.03E-07	1.71E-05
KDM4B	1.270	down	4.46E-04	4.74E-03
DTWD1	1.271	down	3.63E-08	5.06E-06
FBXO21	1.271	down	1.96E-10	1.65E-07
LINC00996	1.271	down	4.35E-05	8.57E-04
ZMYND11	1.272	down	6.59E-07	4.04E-05
SERPINB9	1.273	down	1.77E-06	8.18E-05
CARD11	1.273	down	5.87E-09	1.47E-06
PDE9A	1.273	down	2.51E-06	1.05E-04

ABLIM1	1.274	down	2.56E-08	4.04E-06
CARM1	1.274	down	8.68E-05	1.42E-03
GART	1.274	down	1.46E-11	3.33E-08
CAND1	1.275	down	9.67E-07	5.30E-05
HAUS5	1.275	down	4.77E-07	3.20E-05
PHRF1	1.275	down	4.03E-06	1.48E-04
MBNL2	1.276	down	1.71E-08	3.02E-06
LOC728163	1.276	down	1.27E-07	1.21E-05
SLC16A10	1.276	down	2.28E-04	2.90E-03
CELSR3	1.276	down	9.24E-07	5.12E-05
LOC100131541	1.276	down	1.83E-06	8.40E-05
U2SURP	1.277	down	4.01E-09	1.14E-06
CNN3	1.277	down	1.29E-03	1.03E-02
WASL	1.277	down	7.30E-06	2.27E-04
IKZF3	1.277	down	5.31E-07	3.48E-05
YIPF2	1.278	down	2.69E-05	5.98E-04
FAM210B	1.278	down	2.04E-03	1.43E-02
KDM4C	1.279	down	5.51E-06	1.86E-04
MTUS1	1.279	down	6.64E-06	2.12E-04
KCNQ1OT1	1.279	down	7.96E-05	1.34E-03
TRIB2	1.280	down	2.48E-09	8.55E-07
GATAD1	1.280	down	5.52E-07	3.54E-05
MLLT3	1.281	down	1.20E-05	3.33E-04
FBXO34	1.282	down	1.85E-05	4.57E-04
FUS	1.283	down	5.39E-07	3.49E-05
STAP1	1.284	down	5.37E-05	1.00E-03
ACKR3	1.284	down	5.57E-07	3.56E-05
HSP90AB1	1.284	down	8.47E-09	1.85E-06
C11orf80	1.284	down	2.26E-05	5.30E-04
SNRPA1	1.284	down	7.23E-08	8.09E-06
ATAD5	1.285	down	4.56E-11	6.24E-08
TMEM97	1.285	down	2.00E-09	7.58E-07
CD72	1.285	down	2.18E-05	5.16E-04
SNRPN	1.287	down	5.35E-07	3.48E-05
HLA-DOB	1.287	down	5.62E-05	1.04E-03
MAF	1.288	down	6.29E-07	3.90E-05
CEP95	1.288	down	7.23E-07	4.30E-05
LRPPRC	1.289	down	1.64E-08	2.93E-06
TNIP1	1.289	down	3.23E-05	6.85E-04
LOC100507557	1.290	down	1.22E-04	1.85E-03
ARMC8	1.290	down	1.45E-06	7.09E-05
IFNLR1	1.290	down	5.44E-06	1.84E-04
HTATSF1	1.293	down	1.68E-05	4.24E-04
PCNP	1.293	down	2.53E-06	1.05E-04
PZP	1.294	down	6.12E-07	3.83E-05
SLC6A8	1.294	down	3.87E-03	2.26E-02
HBS1L	1.294	down	2.61E-07	2.05E-05
COBLL1	1.295	down	8.40E-05	1.39E-03
GIMAP5	1.296	down	5.83E-06	1.93E-04
AKT3	1.296	down	3.78E-10	2.60E-07
RCL1	1.297	down	4.81E-10	3.10E-07
SCML1	1.298	down	1.78E-06	8.23E-05
LOC644450	1.299	down	8.68E-03	4.02E-02
ETS1	1.299	down	8.00E-11	9.11E-08
KRT77	1.299	down	1.71E-03	1.26E-02
FAM171A1	1.300	down	8.85E-07	4.99E-05
DKC1	1.300	down	8.52E-10	4.48E-07
SLFNL1	1.300	down	1.23E-08	2.38E-06
PRKXP1	1.300	down	2.02E-04	2.66E-03
TARSL2	1.301	down	7.79E-07	4.52E-05
NAA25	1.302	down	5.50E-10	3.38E-07
FAM208B	1.304	down	5.54E-07	3.56E-05
A2M-AS1	1.304	down	1.23E-04	1.85E-03
PMEP A1	1.305	down	1.06E-06	5.67E-05
CLN8	1.306	down	2.78E-12	1.32E-08
CAND2	1.307	down	7.44E-07	4.39E-05
NAPEPLD	1.307	down	7.45E-08	8.25E-06
PRKCQ-AS1	1.307	down	5.55E-05	1.03E-03
HLA-DOA	1.307	down	2.99E-06	1.19E-04
ZNF131	1.308	down	2.50E-08	3.97E-06
LEF1-AS1	1.308	down	3.32E-04	3.81E-03
RAB30	1.308	down	4.03E-07	2.82E-05
HLA-DPA1	1.310	down	1.19E-04	1.82E-03
SYMPK	1.311	down	3.08E-07	2.31E-05
RBBP4	1.311	down	3.48E-06	1.33E-04
WDR11	1.312	down	6.60E-06	2.11E-04
AQP3	1.313	down	9.79E-09	2.03E-06
CR2	1.313	down	3.80E-06	1.42E-04

PCDH9	1.314	down	1.52E-05	3.97E-04
CLDN23	1.315	down	4.65E-06	1.64E-04
ZNF709	1.315	down	3.56E-05	7.40E-04
APBA2	1.316	down	8.53E-08	9.11E-06
ZCCHC18	1.322	down	4.78E-06	1.67E-04
HACD3	1.323	down	2.07E-09	7.81E-07
CCR6	1.324	down	4.06E-08	5.50E-06
PARP14	1.324	down	3.84E-04	4.24E-03
APOOL	1.324	down	5.28E-07	3.47E-05
EPPK1	1.325	down	2.01E-06	8.93E-05
MAP2K5	1.326	down	4.74E-09	1.28E-06
LARGE1	1.327	down	3.63E-05	7.51E-04
HACD2	1.328	down	1.80E-06	8.30E-05
HNRNPH1	1.329	down	2.88E-07	2.21E-05
NUP62	1.329	down	7.08E-09	1.65E-06
LEF1	1.329	down	4.26E-08	5.64E-06
TTN	1.330	down	8.76E-08	9.22E-06
ZNF275	1.332	down	5.99E-12	1.93E-08
ZNF662	1.333	down	2.40E-06	1.01E-04
LARGE-AS1	1.333	down	1.63E-08	2.93E-06
WDR4	1.335	down	5.06E-06	1.75E-04
CD79A	1.336	down	1.23E-05	3.38E-04
TRAF3IP2	1.336	down	1.28E-07	1.21E-05
FAM129C	1.337	down	7.87E-07	4.55E-05
RORA	1.338	down	1.43E-06	7.03E-05
OSBPL10	1.338	down	4.16E-05	8.29E-04
FCRL1	1.339	down	6.61E-04	6.34E-03
CD22	1.340	down	3.55E-05	7.38E-04
ABCB4	1.341	down	9.78E-06	2.85E-04
SCAF4	1.342	down	3.36E-07	2.48E-05
DDX17	1.342	down	5.02E-05	9.56E-04
NASP	1.343	down	9.54E-07	5.26E-05
FBNP4	1.345	down	1.96E-07	1.66E-05
ZNF496	1.347	down	5.52E-09	1.41E-06
POU6F1	1.347	down	2.76E-07	2.14E-05
SLC16A7	1.348	down	1.69E-06	7.94E-05
HIST1H1D	1.349	down	8.56E-06	2.58E-04
CCDC50	1.350	down	8.38E-06	2.53E-04
TSPAN3	1.352	down	3.62E-10	2.59E-07
LINC00926	1.352	down	4.56E-05	8.90E-04
FOLR1	1.353	down	6.42E-05	1.14E-03
SPON1	1.354	down	4.44E-08	5.85E-06
CUX2	1.354	down	5.55E-07	3.56E-05
LRRN3	1.354	down	1.65E-03	1.22E-02
TNFRSF21	1.354	down	5.07E-08	6.29E-06
EPT1	1.355	down	1.40E-08	2.63E-06
FCRLA	1.356	down	4.70E-05	9.10E-04
COL5A3	1.356	down	2.79E-04	3.35E-03
LOC389834	1.356	down	1.52E-03	1.16E-02
RCAN3	1.356	down	6.31E-07	3.92E-05
POU2AF1	1.356	down	6.09E-07	3.81E-05
LINC00342	1.358	down	4.83E-06	1.69E-04
AAK1	1.358	down	3.63E-09	1.05E-06
SRRM2	1.359	down	2.56E-09	8.67E-07
ACAT1	1.359	down	4.76E-08	6.14E-06
LARS	1.362	down	1.82E-11	3.99E-08
BLNK	1.368	down	1.43E-06	7.03E-05
PLEKHG1	1.374	down	1.15E-05	3.22E-04
GATM	1.375	down	4.05E-05	8.14E-04
TCF4	1.375	down	5.17E-12	1.89E-08
UR11	1.376	down	1.14E-10	1.17E-07
LOC100288282	1.376	down	4.23E-07	2.93E-05
CHD1L	1.379	down	6.65E-10	3.73E-07
HNRNPD	1.379	down	6.14E-10	3.65E-07
BCL11A	1.382	down	5.32E-10	3.31E-07
BACH2	1.382	down	1.20E-07	1.15E-05
LOC100190986	1.384	down	4.17E-08	5.58E-06
GPM6B	1.385	down	7.55E-12	2.18E-08
COL4A3	1.385	down	1.04E-06	5.60E-05
LINC01184	1.388	down	1.96E-09	7.58E-07
PDE7A	1.388	down	1.76E-12	1.07E-08
IKZF1	1.389	down	3.90E-10	2.64E-07
IL6ST	1.392	down	1.83E-09	7.33E-07
PRKY	1.395	down	1.17E-04	1.79E-03
MAN1C1	1.396	down	6.76E-09	1.59E-06
USP10	1.398	down	3.40E-08	4.85E-06
MS4A1	1.400	down	1.90E-06	8.60E-05
PLEKHA1	1.404	down	3.82E-09	1.09E-06



IGHM	1.407	down	8.07E-06	2.46E-04
RAB11FIP3	1.409	down	2.19E-11	4.29E-08
ZFY	1.411	down	1.10E-02	4.72E-02
STRBP	1.415	down	9.37E-09	1.97E-06
PPM1K	1.418	down	1.55E-09	6.62E-07
THRA1/BTR	1.425	down	9.87E-09	2.04E-06
AFF3	1.427	down	1.76E-06	8.16E-05
IGHD	1.436	down	1.72E-04	2.37E-03
TTY10	1.449	down	1.94E-04	2.59E-03
TCL1A	1.519	down	3.26E-05	6.90E-04
NOG	1.537	down	8.38E-07	4.78E-05
TSPAN13	1.555	down	4.91E-08	6.25E-06
UTY	1.637	down	3.84E-03	2.25E-02
EBF1	1.675	down	3.52E-09	1.03E-06
TXLNGY	2.055	down	3.38E-04	3.87E-03
DDX3Y	2.142	down	6.93E-04	6.55E-03
EIF1AY	2.310	down	2.00E-03	1.40E-02
USP9Y	2.432	down	2.95E-04	3.49E-03
KDM5D	2.583	down	6.61E-04	6.34E-03
RPS4Y1	2.737	down	1.23E-03	9.91E-03

**Table S5 Summary-based Mendelian Randomization (SMR) analysis of blood gene expression on asthma in discovery phase (FDR < 0.05, p\_HEIDI > 0.01)**

Source exposure	Gene exposure	Outcome	ID.outcome	topSNP	A1	A2	Freq	b_SMR	se_SMR	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI
eQTLGen	ADORA3	Asthma	UKB	rs2032006	C	T	0.442	-0.064	0.017	1.22E-04	5.45E-03	0.265	20
eQTLGen	BACH2	Asthma	UKB	rs72928038	A	G	0.180	0.344	0.040	3.22E-18	7.67E-16	0.016	20
eQTLGen	CEP95	Asthma	UKB	rs1991401	G	A	0.359	-0.063	0.015	2.75E-05	1.37E-03	0.485	13
eQTLGen	ELP2	Asthma	UKB	rs1785930	G	A	0.376	-0.036	0.010	3.21E-04	1.09E-02	0.034	20
eQTLGen	ETS1	Asthma	UKB	rs55836957	A	C	0.192	0.484	0.116	2.89E-05	1.37E-03	0.028	10
eQTLGen	HOXB-AS1	Asthma	UKB	rs7214534	C	T	0.516	0.050	0.010	2.01E-06	1.30E-04	0.050	20
eQTLGen	ING5	Asthma	UKB	rs6437282	C	G	0.371	-0.082	0.016	1.32E-07	1.05E-05	0.113	20
eQTLGen	ITPKB	Asthma	UKB	rs6694031	A	G	0.463	-0.194	0.057	6.93E-04	2.25E-02	0.114	20
eQTLGen	JAK2	Asthma	UKB	rs6476941	T	C	0.500	0.122	0.033	2.55E-04	9.57E-03	0.318	20
eQTLGen	NAP1L4	Asthma	UKB	rs12363575	G	A	0.207	0.102	0.031	9.96E-04	3.09E-02	0.157	20
eQTLGen	NFATC3	Asthma	UKB	rs7204192	G	A	0.150	-0.146	0.038	1.34E-04	5.64E-03	0.052	20
eQTLGen	RBM6	Asthma	UKB	rs2245365	A	C	0.478	-0.032	0.009	2.47E-04	9.57E-03	0.256	20
eQTLGen	RORC	Asthma	UKB	rs4845604	A	G	0.135	-0.404	0.084	1.69E-06	1.20E-04	0.407	8
eQTLGen	SLFN5	Asthma	UKB	rs12945522	C	A	0.401	-0.038	0.012	1.08E-03	3.21E-02	0.904	20
eQTLGen	TGFBR1	Asthma	UKB	rs41283642	T	C	0.035	-0.287	0.045	2.94E-10	5.25E-08	0.748	6
eQTLGen	TP53I11	Asthma	UKB	rs11604720	C	T	0.306	-0.130	0.041	1.50E-03	3.97E-02	0.046	20
eQTLGen	ZBTB38	Asthma	UKB	rs1344674	G	A	0.427	0.088	0.027	1.31E-03	3.68E-02	0.615	20

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs.

**Table S6 Two-Sample Mendelian Randomization (TSMR) analysis of blood gene expression on asthma in the discovery phase**

Source exposure	Gene exposure	OutcomeID.outcome	Method	n SNP	b	se	pval	FDR	lo_ci	up_ci	or	or_lci95	or_uci95	hetero_pval	ple_pval
eQTLGen	BACH2	Asthma UKB	IVW	2	0.345	0.035	3.29E-23	5.59E-22	0.277	0.413	1.412	1.319	1.511	0.959	-
eQTLGen	CEP95	Asthma UKB	IVW	2	-0.061	0.014	2.07E-05	5.83E-05	-0.090	-0.033	0.940	0.914	0.967	0.656	-
eQTLGen	ELP2	Asthma UKB	IVW	4	-0.034	0.009	3.35E-04	6.34E-04	-0.052	-0.015	0.967	0.949	0.985	0.686	0.643
eQTLGen	ETS1	Asthma UKB	IVW	2	0.463	0.079	5.22E-09	2.96E-08	0.308	0.618	1.589	1.360	1.856	0.731	-
eQTLGen	HOXB-AS1	Asthma UKB	IVW	2	0.048	0.011	2.40E-05	5.83E-05	0.026	0.070	1.049	1.026	1.073	0.533	-
eQTLGen	ING5	Asthma UKB	IVW	3	-0.083	0.039	3.43E-02	4.17E-02	-0.161	-0.006	0.920	0.852	0.994	0.003	0.629
eQTLGen	ITPKB	Asthma UKB	Wald ratio	1	-0.194	0.056	4.92E-04	8.37E-04	-0.303	-0.085	0.824	0.738	0.919	-	-
eQTLGen	JAK2	Asthma UKB	IVW	2	0.131	0.029	6.70E-06	2.28E-05	0.074	0.188	1.140	1.077	1.207	0.547	-
eQTLGen	NFATC3	Asthma UKB	IVW	2	-0.131	0.032	4.93E-05	1.05E-04	-0.195	-0.068	0.877	0.823	0.934	0.450	-
eQTLGen	RBM6	Asthma UKB	IVW	7	-0.028	0.011	9.65E-03	1.26E-02	-0.049	-0.007	0.973	0.953	0.993	0.429	0.522
eQTLGen	RORC	Asthma UKB	Wald ratio	1	-0.404	0.075	8.58E-08	3.65E-07	-0.552	-0.256	0.668	0.576	0.774	-	-
eQTLGen	SLFN5	Asthma UKB	IVW	2	-0.042	0.013	1.39E-03	1.96E-03	-0.067	-0.016	0.959	0.935	0.984	0.440	-
eQTLGen	TGFBR1	Asthma UKB	IVW	2	-0.278	0.037	7.43E-14	6.32E-13	-0.351	-0.205	0.757	0.704	0.814	0.663	-
eQTLGen	ZBTB38	Asthma UKB	Wald ratio	1	0.088	0.027	1.21E-03	1.87E-03	0.035	0.142	1.092	1.035	1.152	-	-
eQTLGen	ADORA3	Asthma UKB	IVW	3	-0.032	0.025	2.05E-01	2.05E-01	-0.082	0.018	0.968	0.922	1.018	0.950	0.810
eQTLGen	NAP1L4	Asthma UKB	IVW	2	0.081	0.041	5.00E-02	5.67E-02	0.000	0.163	1.085	1.000	1.177	0.132	-
eQTLGen	TP53I11	Asthma UKB	IVW	2	-0.099	0.061	1.04E-01	1.11E-01	-0.218	0.020	0.906	0.804	1.021	0.091	-

nSNP, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results.

Table S7 SMR analysis of blood gene expression on asthma in replication phase

Group	Source exposure	Gene exposure	Outcome	ID.outcome	topSNP	A1	A2	b_SM	se_SM	p_SM	FDR_SM	p_HEIDI	nsp_HEIDI	I2	pval_Q
1	Gtex	CEP95	Asthma	TAGC	rs1991401	G	A	-0.073	0.099	4.62E-01	5.20E-01	0.754	3	-	-
1	Gtex	CEP95	Asthma	Finngen	rs1991401	G	A	-0.172	0.065	7.98E-03	2.82E-02	0.955	7	-	-
1	Gtex	CEP95	Asthma	F_T	-	-	-	-0.142	0.054	8.75E-03	2.84E-02	-	-	0.000	0.401
1	Gtex	ELP2	Asthma	TAGC	rs948416	G	A	-0.037	0.044	4.03E-01	5.20E-01	0.839	19	-	-
1	Gtex	ELP2	Asthma	Finngen	rs1785927	G	C	-0.033	0.031	2.81E-01	3.52E-01	0.785	20	-	-
1	Gtex	ELP2	Asthma	F_T	-	-	-	-0.035	0.025	1.73E-01	2.23E-01	-	-	0.000	0.942
1	Gtex	HOXB-AS1	Asthma	TAGC	rs1042815	A	G	0.017	0.038	6.62E-01	6.62E-01	0.442	20	-	-
1	Gtex	HOXB-AS1	Asthma	Finngen	rs1042815	A	G	0.056	0.027	3.70E-02	9.24E-02	0.087	20	-	-
1	Gtex	HOXB-AS1	Asthma	F_T	-	-	-	0.043	0.022	4.99E-02	8.99E-02	-	-	0.000	0.403
1	Gtex	ITPKB	Asthma	TAGC	rs708778	T	C	-0.193	0.138	1.62E-01	3.64E-01	0.045	13	-	-
1	Gtex	ITPKB	Asthma	Finngen	rs6694031	A	G	-0.180	0.095	5.98E-02	1.20E-01	0.243	19	-	-
1	Gtex	ITPKB	Asthma	F_T	-	-	-	-0.184	0.078	1.91E-02	4.30E-02	-	-	0.000	0.938
1	Gtex	NFATC3	Asthma	TAGC	rs3743733	C	T	-0.095	0.088	2.75E-01	4.96E-01	0.019	20	-	-
1	Gtex	NFATC3	Asthma	Finngen	rs3743733	C	T	0.044	0.057	4.43E-01	4.43E-01	0.073	20	-	-
1	Gtex	NFATC3	Asthma	F_T	-	-	-	0.002	0.048	9.64E-01	9.64E-01	-	-	0.437	0.183
1	Gtex	RBM6	Asthma	TAGC	rs7613875	A	C	-0.033	0.022	1.36E-01	3.64E-01	0.521	20	-	-
1	Gtex	RBM6	Asthma	Finngen	rs7613875	A	C	-0.050	0.015	7.71E-04	7.71E-03	0.064	20	-	-
1	Gtex	RBM6	Asthma	F_T	-	-	-	-0.045	0.012	2.90E-04	2.61E-03	-	-	0.000	0.529
1	Gtex	SLFN5	Asthma	TAGC	rs11653987	C	T	-0.032	0.041	4.40E-01	5.20E-01	0.383	20	-	-
1	Gtex	SLFN5	Asthma	Finngen	rs11653987	C	T	-0.077	0.029	8.47E-03	2.82E-02	0.547	20	-	-
1	Gtex	SLFN5	Asthma	F_T	-	-	-	-0.062	0.024	9.47E-03	2.84E-02	-	-	0.000	0.372
1	Gtex	TGFBR1	Asthma	TAGC	rs7034716	T	C	-0.196	0.101	5.32E-02	2.40E-01	0.102	11	-	-
1	Gtex	TGFBR1	Asthma	Finngen	rs7034716	T	C	0.108	0.070	1.24E-01	2.07E-01	0.010	17	-	-
1	Gtex	TGFBR1	Asthma	F_T	-	-	-	-0.035	0.152	8.17E-01	9.20E-01	-	-	0.835	0.014
1	Gtex	ZBTB38	Asthma	TAGC	rs724016	G	A	0.212	0.083	1.08E-02	9.69E-02	0.102	20	-	-
1	Gtex	ZBTB38	Asthma	Finngen	rs724016	G	A	0.051	0.055	3.52E-01	3.91E-01	0.925	20	-	-
1	Gtex	ZBTB38	Asthma	F_T	-	-	-	0.119	0.080	1.34E-01	2.01E-01	-	-	0.618	0.106
2	eQTLGen	BACH2	Asthma	TAGC_2	rs10944479	A	G	0.398	0.088	6.88E-06	3.44E-05	0.043	20	-	-
2	eQTLGen	BACH2	Asthma	Finngen_2	rs72928038	A	G	0.160	0.058	6.32E-03	1.05E-02	0.000	20	-	-
2	eQTLGen	BACH2	Asthma	F_T_2	-	-	-	0.269	0.119	2.33E-02	2.91E-02	-	-	0.802	0.025
2	eQTLGen	ETS1	Asthma	TAGC_2	rs1940378	A	G	0.407	0.213	5.62E-02	9.36E-02	0.001	8	-	-
2	eQTLGen	ETS1	Asthma	Finngen_2	rs55836957	A	C	0.337	0.134	1.17E-02	1.46E-02	0.271	10	-	-
2	eQTLGen	ETS1	Asthma	F_T_2	-	-	-	0.357	0.113	1.63E-03	4.08E-03	-	-	0.000	0.781
2	eQTLGen	ING5	Asthma	TAGC_2	rs10191556	T	C	-0.182	0.061	2.89E-03	7.21E-03	0.477	5	-	-
2	eQTLGen	ING5	Asthma	Finngen_2	rs6437282	C	G	-0.074	0.021	5.11E-04	2.56E-03	0.001	20	-	-
2	eQTLGen	ING5	Asthma	F_T_2	-	-	-	-0.113	0.052	3.00E-02	3.00E-02	-	-	0.643	0.094
2	eQTLGen	JAK2	Asthma	TAGC_2	rs2149556	T	C	0.081	0.065	2.13E-01	2.13E-01	0.310	20	-	-
2	eQTLGen	JAK2	Asthma	Finngen_2	rs6476941	T	C	0.135	0.043	1.88E-03	4.69E-03	0.234	20	-	-
2	eQTLGen	JAK2	Asthma	F_T_2	-	-	-	0.119	0.036	1.04E-03	4.08E-03	-	-	0.000	0.494
2	eQTLGen	RORC	Asthma	TAGC_2	rs4845604	A	G	-0.208	0.148	1.60E-01	2.00E-01	0.239	5	-	-
2	eQTLGen	RORC	Asthma	Finngen_2	rs11801866	A	T	-0.215	0.115	6.24E-02	6.24E-02	0.094	7	-	-
2	eQTLGen	RORC	Asthma	F_T_2	-	-	-	-0.213	0.091	1.96E-02	2.91E-02	-	-	0.000	0.971

HEIDI: heterogeneity in dependent instruments; nsp, the number of SNPs; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from Gtex and outcome from Finngen; TAGC, exposure from Gtex and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from Gtex→Finngen and Gtex→TAGC; Finngen\_2, exposure from eQTLGen and outcome from Finngen; TAGC\_2, exposure from eQTLGen and outcome from TAGC; F\_T\_2, meta-analysis of results from eQTLGen→Finngen and eQTLGen→TAGC.

**Table S8 TSMR analysis of blood gene expression on asthma in the replication phase**

Group	Source exposure	Gene exposure	Outcome	ID.outcome	Method	nsnp	b	se	pval	FDR	or	or_lci95	or_uci95	hetero_pval	ple_pval	I2	pval_Q
1	Gtex	CEP95	Asthma	TAGC	Wald ratio	1	-0.073	0.098	4.60E-01	5.18E-01	0.930	0.767	1.127	-	-	-	-
1	Gtex	CEP95	Asthma	Finngen	Wald ratio	1	-0.172	0.060	4.45E-03	2.23E-02	0.842	0.748	0.948	-	-	-	-
1	Gtex	CEP95	Asthma	F_T	-	-	-0.145	0.051	4.95E-03	2.23E-02	0.865	0.782	0.957	-	-	0.000	0.390
1	Gtex	ELP2	Asthma	TAGC	Wald ratio	1	-0.037	0.044	4.02E-01	5.18E-01	0.963	0.883	1.051	-	-	-	-
1	Gtex	ELP2	Asthma	Finngen	Wald ratio	1	-0.033	0.031	2.80E-01	3.50E-01	0.967	0.911	1.027	-	-	-	-
1	Gtex	ELP2	Asthma	F_T	-	-	-0.035	0.025	1.72E-01	2.21E-01	0.966	0.919	1.015	-	-	0.000	0.942
1	Gtex	HOXB-AS1	Asthma	TAGC	Wald ratio	1	0.017	0.038	6.62E-01	6.62E-01	1.017	0.944	1.096	-	-	-	-
1	Gtex	HOXB-AS1	Asthma	Finngen	Wald ratio	1	0.056	0.026	3.39E-02	8.47E-02	1.057	1.004	1.113	-	-	-	-
1	Gtex	HOXB-AS1	Asthma	F_T	-	-	0.043	0.022	4.60E-02	8.27E-02	1.044	1.001	1.089	-	-	0.000	0.400
1	Gtex	ITPKB	Asthma	TAGC	Wald ratio	1	-0.193	0.134	1.49E-01	3.35E-01	0.825	0.635	1.071	-	-	-	-
1	Gtex	ITPKB	Asthma	Finngen	Wald ratio	1	-0.180	0.091	4.75E-02	9.50E-02	0.836	0.700	0.998	-	-	-	-
1	Gtex	ITPKB	Asthma	F_T	-	-	-0.184	0.075	1.43E-02	3.21E-02	0.832	0.718	0.964	-	-	0.000	0.935
1	Gtex	NFATC3	Asthma	TAGC	Wald ratio	1	-0.095	0.087	2.70E-01	4.86E-01	0.909	0.767	1.077	-	-	-	-
1	Gtex	NFATC3	Asthma	Finngen	Wald ratio	1	0.044	0.057	4.41E-01	4.41E-01	1.045	0.935	1.168	-	-	-	-
1	Gtex	NFATC3	Asthma	F_T	-	-	0.002	0.048	9.69E-01	9.69E-01	1.002	0.913	1.100	-	-	0.447	0.179
1	Gtex	RBM6	Asthma	TAGC	Wald ratio	1	-0.033	0.022	1.36E-01	3.35E-01	0.967	0.926	1.010	-	-	-	-
1	Gtex	RBM6	Asthma	Finngen	Wald ratio	1	-0.050	0.015	6.84E-04	6.84E-03	0.951	0.924	0.979	-	-	-	-
1	Gtex	RBM6	Asthma	F_T	-	-	-0.045	0.012	2.57E-04	2.31E-03	0.956	0.934	0.979	-	-	0.000	0.527
1	Gtex	SLFN5	Asthma	TAGC	Wald ratio	1	-0.034	0.042	4.23E-01	5.18E-01	0.967	0.891	1.050	-	-	-	-
1	Gtex	SLFN5	Asthma	Finngen	Wald ratio	1	-0.075	0.029	9.08E-03	3.03E-02	0.928	0.877	0.982	-	-	-	-
1	Gtex	SLFN5	Asthma	F_T	-	-	-0.062	0.024	9.21E-03	2.76E-02	0.940	0.898	0.985	-	-	0.000	0.414
1	Gtex	TGFBR1	Asthma	TAGC	Wald ratio	1	-0.196	0.099	4.78E-02	2.15E-01	0.822	0.677	0.998	-	-	-	-
1	Gtex	TGFBR1	Asthma	Finngen	Wald ratio	1	0.108	0.069	1.19E-01	1.98E-01	1.114	0.973	1.276	-	-	-	-
1	Gtex	TGFBR1	Asthma	F_T	-	-	-0.036	0.152	8.15E-01	9.17E-01	0.965	0.717	1.299	-	-	0.842	0.012
1	Gtex	ZBTB38	Asthma	TAGC	Wald ratio	1	0.212	0.079	7.54E-03	6.78E-02	1.236	1.058	1.445	-	-	-	-
1	Gtex	ZBTB38	Asthma	Finngen	Wald ratio	1	0.051	0.054	3.49E-01	3.88E-01	1.052	0.946	1.171	-	-	-	-
1	Gtex	ZBTB38	Asthma	F_T	-	-	0.121	0.080	1.29E-01	1.94E-01	1.129	0.965	1.320	-	-	0.643	0.094
2	eQTLGen	BACH2	Asthma	TAGC_2	IVW	2	0.417	0.081	3.07E-07	1.54E-06	1.517	1.293	1.779	0.486	-	-	-
2	eQTLGen	BACH2	Asthma	Finngen_2	IVW	2	0.127	0.104	2.24E-01	2.79E-01	1.135	0.926	1.392	0.060	-	-	-
2	eQTLGen	BACH2	Asthma	F_T_2	-	-	0.279	0.145	5.43E-02	6.79E-02	1.322	0.995	1.756	-	-	0.793	0.028
2	eQTLGen	ETS1	Asthma	TAGC_2	Wald ratio	1	0.407	0.207	4.96E-02	1.24E-01	1.502	1.001	2.254	-	-	-	-
2	eQTLGen	ETS1	Asthma	Finngen_2	IVW	2	0.302	0.101	2.68E-03	6.70E-03	1.353	1.111	1.648	0.659	-	-	-
2	eQTLGen	ETS1	Asthma	F_T_2	-	-	0.322	0.091	3.73E-04	1.86E-03	1.380	1.156	1.648	-	-	0.000	0.651
2	eQTLGen	ING5	Asthma	TAGC_2	IVW	2	-0.132	0.120	2.69E-01	2.70E-01	0.876	0.693	1.108	0.033	-	-	-
2	eQTLGen	ING5	Asthma	Finngen_2	IVW	4	-0.030	0.037	4.20E-01	4.20E-01	0.970	0.902	1.044	0.083	0.687	-	-
2	eQTLGen	ING5	Asthma	F_T_2	-	-	-0.039	0.036	2.72E-01	2.72E-01	0.962	0.897	1.031	-	-	0.000	0.414
2	eQTLGen	JAK2	Asthma	TAGC_2	IVW	2	0.068	0.062	2.70E-01	2.70E-01	1.070	0.949	1.207	0.537	-	-	-
2	eQTLGen	JAK2	Asthma	Finngen_2	IVW	2	0.125	0.038	1.04E-03	5.22E-03	1.133	1.051	1.221	0.614	-	-	-
2	eQTLGen	JAK2	Asthma	F_T_2	-	-	0.109	0.032	7.57E-04	1.89E-03	1.115	1.047	1.188	-	-	0.000	0.431
2	eQTLGen	RORC	Asthma	TAGC_2	Wald ratio	1	-0.208	0.147	1.56E-01	2.61E-01	0.812	0.609	1.083	-	-	-	-
2	eQTLGen	RORC	Asthma	Finngen_2	Wald ratio	1	-0.215	0.113	5.68E-02	9.47E-02	0.806	0.646	1.006	-	-	-	-
2	eQTLGen	RORC	Asthma	F_T_2	-	-	-0.213	0.090	1.76E-02	2.93E-02	0.808	0.678	0.964	-	-	0.000	0.970

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochrane Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from Gtex and outcome from Finngen; TAGC, exposure from Gtex and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from Gtex→Finngen and Gtex→TAGC; Finngen\_2, exposure from eQTLGen and outcome from Finngen; TAGC\_2, exposure from eQTLGen and outcome from TAGC; F\_T\_2, meta-analysis of results from eQTLGen→Finngen and eQTLGen→TAGC.

**Table S9 Colocalization analysis between gene expression from eQTLGen and asthma from UKB**

Source exposure	Gene exposure	Outcome	ID.outcome	p1	p2	p12	PP.H0.abf	PP.H1.abf	PP.H2.abf	PP.H3.abf	PP.H4.abf
eQTLGen	ETS1	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.003	0.000	0.017	0.980
eQTLGen	CEP95	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.035	0.000	0.002	0.963
eQTLGen	HOXB-AS1	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.003	0.000	0.049	0.948
eQTLGen	RBM6	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.248	0.000	0.082	0.670
eQTLGen	ITPKB	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.304	0.000	0.033	0.664
eQTLGen	JAK2	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.188	0.000	0.240	0.571
eQTLGen	SLFN5	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.560	0.000	0.047	0.393
eQTLGen	BACH2	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.956	0.044
eQTLGen	RORC	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	1.000	0.000

p1, a prior probability for a SNP being associated with trait 1 only; p2, a prior probability for a SNP being associated with trait 2 only; p12, a prior probability for a SNP being associated with both traits.

**Table S10 SMR analysis of blood DNA methylation on asthma in discovery phase (FDR < 0.05, p\_HEIDI > 0.01)**

Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	topSNP	A1	A2	Freq	b_SMR	se_SMR	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI
GoDMC	ITPKB	cg04213163	Asthma	UKB	rs708772	C	T	0.417	-0.031	0.010	1.28E-03	7.44E-03	0.114	20
GoDMC	ITPKB	cg16265553	Asthma	UKB	rs835665	A	G	0.235	0.251	0.069	2.88E-04	3.87E-03	0.276	5
GoDMC	ITPKB	cg05306109	Asthma	UKB	rs708772	C	T	0.417	0.188	0.060	1.77E-03	7.88E-03	0.057	7
GoDMC	ITPKB	cg23717186	Asthma	UKB	rs3768410	T	C	0.426	0.136	0.034	5.42E-05	1.75E-03	0.127	16
GoDMC	RBM6	cg12257692	Asthma	UKB	rs6793528	C	A	0.446	0.030	0.010	2.92E-03	1.10E-02	0.013	20
GoDMC	RBM6	cg05635617	Asthma	UKB	rs2624822	T	C	0.446	0.048	0.016	2.90E-03	1.10E-02	0.015	20
GoDMC	RBM6	cg21729847	Asthma	UKB	rs6793528	C	A	0.446	0.072	0.024	3.02E-03	1.10E-02	0.026	20
GoDMC	JAK2	cg20394284	Asthma	UKB	rs10758669	C	A	0.353	0.043	0.011	9.05E-05	1.75E-03	0.247	20
GoDMC	JAK2	cg02405213	Asthma	UKB	rs7851556	T	C	0.273	-0.026	0.007	6.75E-05	1.75E-03	0.856	20
GoDMC	JAK2	cg13661497	Asthma	UKB	rs10491650	C	T	0.289	-0.323	0.102	1.58E-03	7.62E-03	0.152	9
GoDMC	ETS1	cg11760500	Asthma	UKB	rs11221335	C	T	0.245	-0.059	0.018	8.65E-04	6.27E-03	0.165	20
GoDMC	ETS1	cg14998713	Asthma	UKB	rs61907765	T	C	0.237	0.175	0.054	1.28E-03	7.44E-03	0.342	12
GoDMC	ETS1	cg09915500	Asthma	UKB	rs11221342	C	T	0.167	-0.115	0.045	1.12E-02	3.37E-02	0.129	10
GoDMC	ETS1	cg23774988	Asthma	UKB	rs4396302	A	G	0.428	-0.166	0.047	3.65E-04	3.87E-03	0.254	20
GoDMC	ETS1	cg01900413	Asthma	UKB	rs11221342	C	T	0.167	-0.135	0.054	1.15E-02	3.37E-02	0.147	8
GoDMC	ETS1	cg14718848	Asthma	UKB	rs4245079	A	C	0.433	0.023	0.007	4.32E-04	3.87E-03	0.182	20
GoDMC	ETS1	cg08458745	Asthma	UKB	rs4245079	A	C	0.433	-0.087	0.025	4.67E-04	3.87E-03	0.250	20

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs.

Table S11 TSMR analysis of blood DNA methylation on asthma in discovery phase

Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	Method	nsnp	b	se	pval	FDR	or	or_uci95	or_uci95	hetero_pval	ple_pval
GoDMC	ETS1	cg08458745	Asthma	UKB	Wald ratio	1	-0.087	0.025	4.30E-04	2.39E-03	0.916	0.873	0.962	-	-
GoDMC	ETS1	cg14998713	Asthma	UKB	Wald ratio	1	0.175	0.053	9.55E-04	2.70E-03	1.191	1.074	1.321	-	-
GoDMC	ETS1	cg23774988	Asthma	UKB	Wald ratio	1	-0.471	0.145	1.15E-03	2.80E-03	0.624	0.470	0.829	-	-
GoDMC	ETS1	cg14718848	Asthma	UKB	IVW	3	0.019	0.007	7.75E-03	1.20E-02	1.019	1.005	1.033	0.740	0.624
GoDMC	ETS1	cg09915500	Asthma	UKB	Wald ratio	1	-0.115	0.045	1.03E-02	1.34E-02	0.891	0.817	0.973	-	-
GoDMC	ETS1	cg01900413	Asthma	UKB	Wald ratio	1	-0.135	0.053	1.03E-02	1.34E-02	0.873	0.788	0.969	-	-
GoDMC	ETS1	cg11760500	Asthma	UKB	Wald ratio	1	-0.041	0.021	4.81E-02	5.11E-02	0.960	0.922	1.000	-	-
GoDMC	ITPKB	cg23717186	Asthma	UKB	Wald ratio	1	0.136	0.033	3.98E-05	6.77E-04	1.146	1.074	1.223	-	-
GoDMC	ITPKB	cg16265553	Asthma	UKB	Wald ratio	1	0.251	0.066	1.35E-04	1.15E-03	1.286	1.130	1.463	-	-
GoDMC	ITPKB	cg05306109	Asthma	UKB	Wald ratio	1	0.214	0.063	7.02E-04	2.39E-03	1.238	1.094	1.401	-	-
GoDMC	ITPKB	cg04213163	Asthma	UKB	IVW	4	-0.012	0.016	4.59E-01	4.59E-01	0.988	0.958	1.020	0.288	0.257
GoDMC	JAK2	cg13661497	Asthma	UKB	Wald ratio	1	-0.323	0.094	5.86E-04	2.39E-03	0.724	0.602	0.870	-	-
GoDMC	JAK2	cg20394284	Asthma	UKB	IVW	2	0.045	0.015	2.28E-03	4.85E-03	1.046	1.016	1.077	0.276	-
GoDMC	JAK2	cg02405213	Asthma	UKB	IVW	3	-0.025	0.010	1.60E-02	1.94E-02	0.975	0.956	0.995	0.107	0.854
GoDMC	RBM6	cg05635617	Asthma	UKB	Wald ratio	1	0.049	0.016	2.62E-03	4.94E-03	1.051	1.017	1.085	-	-
GoDMC	RBM6	cg12257692	Asthma	UKB	Wald ratio	1	0.030	0.010	2.99E-03	5.09E-03	1.030	1.010	1.051	-	-
GoDMC	RBM6	cg21729847	Asthma	UKB	IVW	2	0.083	0.040	3.93E-02	4.45E-02	1.087	1.004	1.177	0.725	-

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results.



Table S12 SMR analysis of blood DNA methylation on asthma in replication phase

Group	Source exposure	Gene exposur	ID.exposure	Outcome	ID.outcome	topSNP	A1	A2	b_SMR	se_SMR	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI	I2	pval_Q
1	FSH	ETS1	cg01900413	Asthma	TAGC	rs11221342	T	C	-7.470	3.978	6.04E-02	2.21E-01	0.678	6	-	-
1	FSH	ETS1	cg01900413	Asthma	Finngen	rs4396302	A	G	-5.504	2.214	1.29E-02	2.15E-02	0.554	10	-	-
1	FSH	ETS1	cg01900413	Asthma	F_T	-	-	-	-5.969	1.934	2.03E-03	7.08E-03	-	-	0.000	0.666
1	FSH	ETS1	cg08458745	Asthma	TAGC	rs4245079	A	C	-3.315	2.231	1.37E-01	2.52E-01	0.252	12	-	-
1	FSH	ETS1	cg08458745	Asthma	Finngen	rs4262739	A	G	-3.404	1.503	2.35E-02	2.57E-02	0.898	17	-	-
1	FSH	ETS1	cg08458745	Asthma	F_T	-	-	-	-3.376	1.247	6.76E-03	1.07E-02	-	-	0.000	0.974
1	FSH	ETS1	cg09915500	Asthma	TAGC	rs11221342	T	C	-8.598	4.558	5.92E-02	2.21E-01	0.793	4	-	-
1	FSH	ETS1	cg09915500	Asthma	Finngen	rs56075344	G	A	-1.924	2.668	4.71E-01	4.71E-01	0.064	5	-	-
1	FSH	ETS1	cg09915500	Asthma	F_T	-	-	-	-3.627	2.302	1.15E-01	1.15E-01	-	-	0.374	0.206
1	FSH	ETS1	cg14718848	Asthma	TAGC	rs4245079	A	C	0.310	0.207	1.35E-01	2.52E-01	0.120	20	-	-
1	FSH	ETS1	cg14718848	Asthma	Finngen	rs4262739	A	G	0.319	0.139	2.16E-02	2.57E-02	0.910	20	-	-
1	FSH	ETS1	cg14718848	Asthma	F_T	-	-	-	0.316	0.116	6.15E-03	1.07E-02	-	-	0.000	0.970
1	FSH	ETS1	cg23774988	Asthma	TAGC	rs4128561	C	T	-2.911	1.726	9.16E-02	2.52E-01	0.548	5	-	-
1	FSH	ETS1	cg23774988	Asthma	Finngen	rs4396302	A	G	-2.822	1.130	1.25E-02	2.15E-02	0.758	9	-	-
1	FSH	ETS1	cg23774988	Asthma	F_T	-	-	-	-2.849	0.945	2.58E-03	7.08E-03	-	-	0.000	0.966
1	FSH	ITPKB	cg23717186	Asthma	TAGC	rs3768414	G	A	2.826	2.395	2.38E-01	3.27E-01	0.320	5	-	-
1	FSH	ITPKB	cg23717186	Asthma	Finngen	rs3768410	C	T	3.588	1.465	1.43E-02	2.15E-02	0.918	8	-	-
1	FSH	ITPKB	cg23717186	Asthma	F_T	-	-	-	3.381	1.250	6.83E-03	1.07E-02	-	-	0.000	0.786
1	FSH	JAK2	cg02405213	Asthma	TAGC	rs10974922	C	T	-0.140	0.106	1.88E-01	2.95E-01	0.093	20	-	-
1	FSH	JAK2	cg02405213	Asthma	Finngen	rs57299248	C	G	-0.222	0.071	1.71E-03	5.13E-03	0.002	20	-	-
1	FSH	JAK2	cg02405213	Asthma	F_T	-	-	-	-0.196	0.059	8.36E-04	4.60E-03	-	-	0.000	0.521
1	FSH	JAK2	cg20394284	Asthma	TAGC	rs10758669	A	C	0.828	0.419	4.82E-02	2.21E-01	0.383	20	-	-
1	FSH	JAK2	cg20394284	Asthma	Finngen	rs1887428	C	G	0.744	0.267	5.28E-03	1.27E-02	0.295	20	-	-
1	FSH	JAK2	cg20394284	Asthma	F_T	-	-	-	0.768	0.225	6.40E-04	4.60E-03	-	-	0.000	0.866
1	FSH	RBM6	cg05635617	Asthma	TAGC	rs2624819	G	T	0.985	1.835	5.92E-01	6.15E-01	0.161	20	-	-
1	FSH	RBM6	cg05635617	Asthma	Finngen	rs2624819	G	T	4.669	1.308	3.56E-04	2.14E-03	0.134	20	-	-
1	FSH	RBM6	cg05635617	Asthma	F_T	-	-	-	3.052	1.828	9.51E-02	1.10E-01	-	-	0.626	0.102
1	FSH	RBM6	cg12257692	Asthma	TAGC	rs17657664	T	G	0.385	0.765	6.15E-01	6.15E-01	0.160	20	-	-
1	FSH	RBM6	cg12257692	Asthma	Finngen	rs13079006	G	T	1.913	0.532	3.20E-04	2.14E-03	0.177	20	-	-
1	FSH	RBM6	cg12257692	Asthma	F_T	-	-	-	1.248	0.758	9.96E-02	1.10E-01	-	-	0.629	0.101
1	FSH	RBM6	cg21729847	Asthma	TAGC	rs2624822	C	T	2.023	3.929	6.07E-01	6.15E-01	0.184	20	-	-
1	FSH	RBM6	cg21729847	Asthma	Finngen	rs2526749	G	A	9.722	2.811	5.44E-04	2.18E-03	0.252	20	-	-
1	FSH	RBM6	cg21729847	Asthma	F_T	-	-	-	6.362	3.818	9.57E-02	1.10E-01	-	-	0.606	0.111
2	GoDMC	ETS1	cg14998713	Asthma	TAGC_2	rs11221332	T	C	0.249	0.105	1.78E-02	3.16E-02	0.614	10	-	-
2	GoDMC	ETS1	cg14998713	Asthma	Finngen_2	rs61907765	T	C	0.100	0.068	1.38E-01	1.38E-01	0.065	12	-	-
2	GoDMC	ETS1	cg14998713	Asthma	F_T_2	-	-	-	0.144	0.057	1.14E-02	1.52E-02	-	-	0.293	0.234
2	GoDMC	ITPKB	cg05306109	Asthma	TAGC_2	rs708772	C	T	0.256	0.113	2.37E-02	3.16E-02	0.076	4	-	-
2	GoDMC	ITPKB	cg05306109	Asthma	Finngen_2	rs708772	C	T	0.129	0.080	1.08E-01	1.38E-01	0.607	7	-	-
2	GoDMC	ITPKB	cg05306109	Asthma	F_T_2	-	-	-	0.172	0.066	8.81E-03	1.52E-02	-	-	0.000	0.361
2	GoDMC	ITPKB	cg16265553	Asthma	TAGC_2	rs835673	T	C	0.304	0.129	1.82E-02	3.16E-02	0.831	3	-	-
2	GoDMC	ITPKB	cg16265553	Asthma	Finngen_2	rs835665	A	G	0.154	0.091	8.92E-02	1.38E-01	0.411	5	-	-
2	GoDMC	ITPKB	cg16265553	Asthma	F_T_2	-	-	-	0.204	0.074	5.96E-03	1.52E-02	-	-	0.000	0.341
2	GoDMC	JAK2	cg13661497	Asthma	TAGC_2	rs10491650	C	T	-0.059	0.178	7.42E-01	7.42E-01	0.034	8	-	-
2	GoDMC	JAK2	cg13661497	Asthma	Finngen_2	rs10491650	C	T	-0.208	0.117	7.70E-02	1.38E-01	0.005	9	-	-
2	GoDMC	JAK2	cg13661497	Asthma	F_T_2	-	-	-	-0.162	0.098	9.75E-02	9.75E-02	-	-	0.000	0.484
3	GoDMC	ETS1	cg08458745	Asthma	TAGC_2	rs4245079	A	C	-0.072	0.049	1.35E-01	2.03E-01	0.048	16	-	-
3	GoDMC	ETS1	cg08458745	Asthma	Finngen_2	rs4245079	A	C	-0.075	0.033	2.14E-02	2.14E-02	0.797	20	-	-
3	GoDMC	ETS1	cg08458745	Asthma	F_T_2	-	-	-	-0.074	0.027	6.08E-03	6.08E-03	-	-	0.000	0.967
3	GoDMC	ETS1	cg14718848	Asthma	TAGC_2	rs4245079	A	C	0.019	0.013	1.35E-01	2.03E-01	0.109	20	-	-
3	GoDMC	ETS1	cg14718848	Asthma	Finngen_2	rs4245079	A	C	0.020	0.009	2.10E-02	2.14E-02	0.902	20	-	-
3	GoDMC	ETS1	cg14718848	Asthma	F_T_2	-	-	-	0.019	0.007	5.98E-03	6.08E-03	-	-	0.000	0.967
3	GoDMC	ETS1	cg23774988	Asthma	TAGC_2	rs4128561	C	T	-0.165	0.097	8.86E-02	2.03E-01	0.244	14	-	-
3	GoDMC	ETS1	cg23774988	Asthma	Finngen_2	rs4396302	A	G	-0.154	0.060	1.07E-02	1.89E-02	0.744	20	-	-
3	GoDMC	ETS1	cg23774988	Asthma	F_T_2	-	-	-	-0.157	0.051	2.17E-03	4.33E-03	-	-	0.000	0.922
3	GoDMC	ITPKB	cg23717186	Asthma	TAGC_2	rs3768414	A	G	0.084	0.071	2.35E-01	2.35E-01	0.180	10	-	-
3	GoDMC	ITPKB	cg23717186	Asthma	Finngen_2	rs3768410	T	C	0.111	0.044	1.26E-02	1.89E-02	0.815	16	-	-

3	GoDMC	ITPKB	cg23717186	Asthma	F_T_2	-	-	-	0.103	0.038	6.06E-03	6.08E-03	-	-	0.000	0.751
3	GoDMC	JAK2	cg02405213	Asthma	TAGC_2	rs7851556	T	C	-0.016	0.013	1.93E-01	2.31E-01	0.123	20	-	-
3	GoDMC	JAK2	cg02405213	Asthma	Finngen_2	rs7851556	T	C	-0.023	0.008	3.97E-03	1.89E-02	0.005	20	-	-
3	GoDMC	JAK2	cg02405213	Asthma	F_T_2	-	-	-	-0.021	0.007	1.76E-03	4.33E-03	-	-	0.000	0.645
3	GoDMC	JAK2	cg20394284	Asthma	TAGC_2	rs10758669	C	A	0.043	0.022	4.78E-02	2.03E-01	0.550	20	-	-
3	GoDMC	JAK2	cg20394284	Asthma	Finngen_2	rs10758669	C	A	0.036	0.014	1.19E-02	1.89E-02	0.426	20	-	-
3	GoDMC	JAK2	cg20394284	Asthma	F_T_2	-	-	-	0.038	0.012	1.41E-03	4.33E-03	-	-	0.000	0.807

HEIDI: heterogeneity in dependent instruments; nsp, the number of SNPs; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from FSH and outcome from Finngen; TAGC, exposure from FSH and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from FSH→Finngen and FSH→TAGC; Finngen\_2, exposure from GoDMC and outcome from Finngen; TAGC, exposure from GoDMC and outcome from TAGC; F\_T\_2, meta-analysis of results from GoDMC→Finngen and GoDMC→TAGC.

Table S13 TSMR analysis of blood DNA methylation on asthma in replication phase

Group	Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	Method	nsp	b	se	pval	FDR	or	or_lci95	or_uci95	hetero_pval	ple_pval	I2	pval_Q
1	FSH	ETS1	cg01900413	Asthma	TAGC	Wald ratic	1	-7.470	3.889	5.48E-02	1.51E-01	0.001	0.000	1.166	-	-	-	-
1	FSH	ETS1	cg01900413	Asthma	Finngen	Wald ratic	1	-5.504	2.132	9.82E-03	1.54E-02	0.004	0.000	0.266	-	-	-	-
1	FSH	ETS1	cg01900413	Asthma	F_T	-	-	-5.958	1.869	1.44E-03	4.87E-03	0.003	0.000	0.101	-	-	0.000	0.658
1	FSH	ETS1	cg08458745	Asthma	TAGC	Wald ratic	1	-3.315	2.218	1.35E-01	2.27E-01	0.036	0.000	2.806	-	-	-	-
1	FSH	ETS1	cg08458745	Asthma	Finngen	Wald ratic	1	-3.404	1.482	2.16E-02	2.37E-02	0.033	0.002	0.606	-	-	-	-
1	FSH	ETS1	cg08458745	Asthma	F_T	-	-	-3.377	1.232	6.13E-03	9.63E-03	0.034	0.003	0.382	-	-	0.000	0.973
1	FSH	ETS1	cg09915500	Asthma	TAGC	Wald ratic	1	-8.598	4.477	5.48E-02	1.51E-01	0.000	0.000	1.193	-	-	-	-
1	FSH	ETS1	cg09915500	Asthma	Finngen	Wald ratic	1	-1.924	2.661	4.70E-01	4.70E-01	0.146	0.001	26.881	-	-	-	-
1	FSH	ETS1	cg09915500	Asthma	F_T	-	-	-3.667	2.288	1.09E-01	1.20E-01	0.026	0.000	2.263	-	-	0.391	0.200
1	FSH	ETS1	cg14718848	Asthma	TAGC	Wald ratic	1	0.548	0.269	4.17E-02	1.51E-01	1.729	1.021	2.928	-	-	-	-
1	FSH	ETS1	cg14718848	Asthma	Finngen	IVW	3	0.372	0.158	1.87E-02	2.28E-02	1.451	1.064	1.978	0.274	0.355	-	-
1	FSH	ETS1	cg14718848	Asthma	F_T	-	-	0.417	0.136	2.21E-03	4.87E-03	1.518	1.162	1.982	-	-	0.000	0.573
1	FSH	ETS1	cg23774988	Asthma	TAGC	Wald ratic	1	-2.911	1.699	8.67E-02	1.91E-01	0.054	0.002	1.521	-	-	-	-
1	FSH	ETS1	cg23774988	Asthma	Finngen	Wald ratic	1	-2.822	1.093	9.82E-03	1.54E-02	0.059	0.007	0.507	-	-	-	-
1	FSH	ETS1	cg23774988	Asthma	F_T	-	-	-2.848	0.919	1.95E-03	4.87E-03	0.058	0.010	0.351	-	-	0.000	0.965
1	FSH	ITPKB	cg23717186	Asthma	TAGC	Wald ratic	1	2.826	2.377	2.35E-01	3.23E-01	16.874	0.160	1781.955	-	-	-	-
1	FSH	ITPKB	cg23717186	Asthma	Finngen	Wald ratic	1	3.588	1.428	1.20E-02	1.65E-02	36.169	2.200	594.665	-	-	-	-
1	FSH	ITPKB	cg23717186	Asthma	F_T	-	-	3.386	1.224	5.69E-03	9.63E-03	29.546	2.681	325.648	-	-	0.000	0.783
1	FSH	JAK2	cg02405213	Asthma	TAGC	IVW	2	-0.268	0.184	1.45E-01	2.27E-01	0.765	0.533	1.097	0.684	-	-	-
1	FSH	JAK2	cg02405213	Asthma	Finngen	IVW	2	-0.227	0.074	2.21E-03	6.08E-03	0.797	0.689	0.922	0.778	-	-	-
1	FSH	JAK2	cg02405213	Asthma	F_T	-	-	-0.233	0.069	7.15E-04	4.87E-03	0.792	0.692	0.907	-	-	0.000	0.834
1	FSH	JAK2	cg20394284	Asthma	TAGC	IVW	2	0.797	0.404	4.88E-02	1.51E-01	2.218	1.004	4.901	0.769	-	-	-
1	FSH	JAK2	cg20394284	Asthma	Finngen	IVW	2	0.690	0.258	7.34E-03	1.54E-02	1.994	1.204	3.304	0.408	-	-	-
1	FSH	JAK2	cg20394284	Asthma	F_T	-	-	0.721	0.217	9.02E-04	4.87E-03	2.057	1.344	3.148	-	-	0.000	0.824
1	FSH	RBM6	cg05635617	Asthma	TAGC	Wald ratic	1	0.985	1.835	5.92E-01	6.19E-01	2.677	0.073	97.587	-	-	-	-
1	FSH	RBM6	cg05635617	Asthma	Finngen	Wald ratic	1	4.669	1.292	3.04E-04	1.33E-03	106.571	8.462	1342.202	-	-	-	-
1	FSH	RBM6	cg05635617	Asthma	F_T	-	-	3.057	1.828	9.44E-02	1.15E-01	21.260	0.591	764.366	-	-	0.629	0.101
1	FSH	RBM6	cg12257692	Asthma	TAGC	Wald ratic	1	0.381	0.766	6.19E-01	6.19E-01	1.464	0.326	6.567	-	-	-	-
1	FSH	RBM6	cg12257692	Asthma	Finngen	Wald ratic	1	2.254	0.584	1.14E-04	1.25E-03	9.530	3.032	29.950	-	-	-	-
1	FSH	RBM6	cg12257692	Asthma	F_T	-	-	1.383	0.935	1.39E-01	1.39E-01	3.987	0.639	24.896	-	-	0.736	0.052
1	FSH	RBM6	cg21729847	Asthma	TAGC	Wald ratic	1	2.023	3.926	6.06E-01	6.19E-01	7.565	0.003	16636.334	-	-	-	-
1	FSH	RBM6	cg21729847	Asthma	Finngen	Wald ratic	1	9.722	2.726	3.62E-04	1.33E-03	16685.043	79.746	3490950.573	-	-	-	-
1	FSH	RBM6	cg21729847	Asthma	F_T	-	-	6.391	3.814	9.38E-02	1.15E-01	596.721	0.338	1053192.420	-	-	0.614	0.107
2	GoDMC	ETS1	cg14998713	Asthma	TAGC_2	Wald ratic	1	0.249	0.103	1.62E-02	3.25E-02	1.282	1.047	1.570	-	-	-	-
2	GoDMC	ETS1	cg14998713	Asthma	Finngen_2	Wald ratic	1	0.100	0.067	1.36E-01	1.36E-01	1.105	0.969	1.261	-	-	-	-
2	GoDMC	ETS1	cg14998713	Asthma	F_T_2	-	-	0.144	0.056	1.05E-02	2.10E-02	1.155	1.034	1.290	-	-	0.309	0.229
2	GoDMC	ITPKB	cg05306109	Asthma	TAGC_2	Wald ratic	1	0.143	0.121	2.35E-01	3.13E-01	1.154	0.911	1.462	-	-	-	-
2	GoDMC	ITPKB	cg05306109	Asthma	Finngen_2	Wald ratic	1	0.175	0.084	3.70E-02	1.14E-01	1.191	1.011	1.403	-	-	-	-
2	GoDMC	ITPKB	cg05306109	Asthma	F_T_2	-	-	0.164	0.069	1.68E-02	2.24E-02	1.179	1.030	1.349	-	-	0.000	0.831
2	GoDMC	ITPKB	cg16265553	Asthma	TAGC_2	Wald ratic	1	0.304	0.126	1.58E-02	3.25E-02	1.355	1.059	1.735	-	-	-	-
2	GoDMC	ITPKB	cg16265553	Asthma	Finn_2	Wald ratic	1	0.154	0.090	8.57E-02	1.14E-01	1.167	0.979	1.391	-	-	-	-
2	GoDMC	ITPKB	cg16265553	Asthma	F_T	-	-	0.205	0.073	5.12E-03	2.05E-02	1.227	1.063	1.416	-	-	0.000	0.333
2	GoDMC	JAK2	cg13661497	Asthma	TAGC_2	Wald ratic	1	-0.059	0.177	7.41E-01	7.41E-01	0.943	0.666	1.335	-	-	-	-
2	GoDMC	JAK2	cg13661497	Asthma	Finngen_2	Wald ratic	1	-0.208	0.115	6.98E-02	1.14E-01	0.812	0.649	1.017	-	-	-	-
2	GoDMC	JAK2	cg13661497	Asthma	F_T_2	-	-	-0.164	0.096	8.87E-02	8.87E-02	0.849	0.703	1.025	-	-	0.000	0.480
3	GoDMC	ETS1	cg08458745	Asthma	TAGC_2	Wald ratic	1	-0.072	0.048	1.35E-01	3.97E-01	0.930	0.846	1.023	-	-	-	-
3	GoDMC	ETS1	cg08458745	Asthma	Finngen_2	Wald ratic	1	-0.075	0.032	2.10E-02	3.15E-02	0.928	0.871	0.989	-	-	-	-
3	GoDMC	ETS1	cg08458745	Asthma	F_T_2	-	-	-0.074	0.027	5.97E-03	8.96E-03	0.929	0.881	0.979	-	-	0.000	0.967
3	GoDMC	ETS1	cg14718848	Asthma	TAGC_2	IVW	2	0.002	0.056	9.73E-01	9.73E-01	1.002	0.899	1.117	0.029	-	-	-
3	GoDMC	ETS1	cg14718848	Asthma	Finngen_2	IVW	3	0.023	0.020	2.46E-01	2.46E-01	1.023	0.984	1.064	0.273	0.458	-	-
3	GoDMC	ETS1	cg14718848	Asthma	F_T_2	-	-	0.021	0.019	2.70E-01	2.70E-01	1.021	0.984	1.059	-	-	0.000	0.718
3	GoDMC	ETS1	cg23774988	Asthma	TAGC_2	Wald ratic	1	-0.766	0.278	5.84E-03	3.50E-02	0.465	0.270	0.801	-	-	-	-
3	GoDMC	ETS1	cg23774988	Asthma	Finngen_2	Wald ratic	1	-0.362	0.189	5.57E-02	6.68E-02	0.697	0.481	1.009	-	-	-	-
3	GoDMC	ETS1	cg23774988	Asthma	F_T_2	-	-	-0.490	0.156	1.73E-03	6.07E-03	0.613	0.451	0.833	-	-	0.309	0.229
3	GoDMC	ITPKB	cg23717186	Asthma	TAGC_2	Wald ratic	1	0.084	0.071	2.35E-01	3.97E-01	1.088	0.947	1.249	-	-	-	-
3	GoDMC	ITPKB	cg23717186	Asthma	Finngen_2	Wald ratic	1	0.111	0.044	1.20E-02	3.15E-02	1.117	1.025	1.218	-	-	-	-

3	GoDMC	ITPKB	cg23717186	Asthma	F_T_2	-	-	0.103	0.037	5.77E-03	8.96E-03	1.109	1.030	1.193	-	-	0.000	0.750
3	GoDMC	JAK2	cg02405213	Asthma	TAGC_2	IVW	3	-0.013	0.013	3.31E-01	3.97E-01	0.987	0.962	1.013	0.402	0.538	-	-
3	GoDMC	JAK2	cg02405213	Asthma	Finngen_2	IVW	3	-0.026	0.009	2.27E-03	1.36E-02	0.974	0.958	0.991	0.730	0.639	-	-
3	GoDMC	JAK2	cg02405213	Asthma	F_T_2	-	-	-0.022	0.007	2.02E-03	6.07E-03	0.978	0.964	0.992	-	-	0.000	0.391
3	GoDMC	JAK2	cg20394284	Asthma	TAGC_2	IVW	3	0.025	0.026	3.28E-01	3.97E-01	1.026	0.975	1.079	0.569	0.546	-	-
3	GoDMC	JAK2	cg20394284	Asthma	Finngen_2	IVW	2	0.050	0.021	1.76E-02	3.15E-02	1.051	1.009	1.096	0.217	-	-	-
3	GoDMC	JAK2	cg20394284	Asthma	F_T_2	-	-	0.040	0.016	1.39E-02	1.67E-02	1.041	1.008	1.075	-	-	0.000	0.459

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from FSH and outcome from Finngen; TAGC, exposure from FSH and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from FSH→Finngen and FSH→TAGC; Finngen\_2, exposure from GoDMC and outcome from Finngen; TAGC, exposure from GoDMC and outcome from TAGC; F\_T\_2, meta-analysis of results from GoDMC→Finngen and GoDMC→TAGC.

**Table S14 Colocalization analysis between DNA methylation from GoDMC and asthma from UKB**

Source exposure	Gene exposure	ID.exposure	outcome	ID.outcome	p1	p2	p12	PP.H0.abf	PP.H1.abf	PP.H2.abf	PP.H3.abf	PP.H4.abf
GoDMC	ITPKB	cg23717186	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.063	0.000	0.004	0.934
GoDMC	ITPKB	cg16265553	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.161	0.000	0.002	0.837
GoDMC	JAK2	cg02405213	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.078	0.000	0.118	0.804
GoDMC	JAK2	cg20394284	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.102	0.000	0.140	0.758
GoDMC	ETS1	cg23774988	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.277	0.000	0.019	0.704
GoDMC	ETS1	cg08458745	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.374	0.000	0.025	0.601
GoDMC	ETS1	cg14718848	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.373	0.000	0.027	0.600
GoDMC	JAK2	cg13661497	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.335	0.000	0.146	0.520
GoDMC	ETS1	cg14998713	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.504	0.000	0.030	0.466
GoDMC	ITPKB	cg05306109	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.513	0.000	0.023	0.465
GoDMC	ETS1	cg01900413	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.850	0.000	0.053	0.098

p1, a prior probability for a SNP being associated with trait 1 only; p2, a prior probability for a SNP being associated with trait 2 only; p12, a prior probability for a SNP being associated with both traits.

**Table S15 SMR analysis of blood DNA methylation on gene expression**

Source exposure	Gene exposure	ID.exposure	Source outcome	Gene outcome	topSNP	A1	A2	b_SMR	se_SMR	lo_ci	up_ci	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI
GoDMC	ITPKB	cg16265553	eQTLGen	ITPKB	rs835665	A	G	-0.457	0.090	-0.633	-0.281	3.58E-07	5.73E-07	1.87E-02	4
GoDMC	ITPKB	cg23717186	eQTLGen	ITPKB	rs3768410	T	C	-0.509	0.047	-0.601	-0.417	1.81E-27	4.83E-27	1.16E-04	16
GoDMC	JAK2	cg20394284	eQTLGen	JAK2	rs10758669	C	A	0.266	0.014	0.239	0.294	8.41E-82	3.36E-81	5.08E-19	20
GoDMC	JAK2	cg02405213	eQTLGen	JAK2	rs7851556	T	C	-0.185	0.008	-0.200	-0.170	#####	3.70E-125	5.58E-24	20
GoDMC	JAK2	cg13661497	eQTLGen	JAK2	rs10491650	C	T	-2.572	0.339	-3.236	-1.907	3.34E-14	6.67E-14	1.51E-02	8
GoDMC	ETS1	cg23774988	eQTLGen	ETS1	rs4396302	A	G	-0.233	0.057	-0.345	-0.121	4.74E-05	4.74E-05	2.20E-03	20
GoDMC	ETS1	cg14718848	eQTLGen	ETS1	rs4245079	A	C	0.034	0.008	0.019	0.050	1.24E-05	1.66E-05	2.25E-04	20
GoDMC	ETS1	cg08458745	eQTLGen	ETS1	rs4245079	A	C	-0.131	0.030	-0.191	-0.072	1.49E-05	1.70E-05	1.06E-03	20

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs.

**Table S16 TSMR analysis of blood DNA methylation on gene expression**

Source exposure	Gene exposure	ID.exposure	Source outcome	Gene outcome	Method	nsnp	b	se	pval	FDR	lo_ci	up_ci
GoDMC	ITPKB	cg16265553	eQTLGen	ITPKB	Wald ratio	1	-0.457	0.081	1.48E-08	1.48E-08	-0.615	-0.299
GoDMC	JAK2	cg13661497	eQTLGen	JAK2	Wald ratio	1	-2.572	0.110	3.49E-120	#####	-2.788	-2.355

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results.

**Table S17 Colocalization analysis between DNA methylation from GoDMC and gene expression from eQTLGen**

Source exposure	Gene exposure	ID.exposure	Source outcome	Gene outcome	p1	p2	p12	PP.H0.abf	PP.H1.abf	PP.H2.abf	PP.H3.abf	PP.H4.abf
GoDMC	ITPKB	cg16265553	eQTLGen	ITPKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.019	0.981
GoDMC	JAK2	cg13661497	eQTLGen	JAK2	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.261	0.739

p1, a prior probability for a SNP being associated with trait 1 only; p2, a prior probability for a SNP being associated with trait 2 only; p12, a prior probability for a SNP being associated with both traits.



**Table S18 SMR analysis of additional blood DNA methylation on asthma in discovery phase**

Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	topSNP	A1	A2	b_SMR	se_SMR	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI
GoDMC	AFF3	cg04109781	Asthma	UKB	rs13001783	T	A	-0.034	0.008	5.87E-06	5.49E-04	0.017	20
GoDMC	AFF3	cg09521647	Asthma	UKB	rs12992234	A	G	-0.079	0.015	1.48E-07	2.02E-05	0.419	20
GoDMC	AFF3	cg17356467	Asthma	UKB	rs11682173	T	C	-0.278	0.070	6.83E-05	4.68E-03	0.067	11
GoDMC	BACH2	cg09471887	Asthma	UKB	rs61754114	C	G	0.140	0.037	1.26E-04	7.90E-03	0.982	11
GoDMC	BACH2	cg09790829	Asthma	UKB	rs969577	C	T	-0.486	0.057	1.86E-17	6.83E-15	0.328	13
GoDMC	BACH2	cg09818385	Asthma	UKB	rs62408211	T	A	-0.566	0.073	1.16E-14	4.03E-12	0.013	14
GoDMC	BACH2	cg10913050	Asthma	UKB	rs969577	C	T	-0.454	0.053	1.38E-17	5.42E-15	0.272	16
GoDMC	BACH2	cg15380603	Asthma	UKB	rs11757155	T	C	-0.750	0.107	1.93E-12	5.42E-10	0.283	10
GoDMC	BACH2	cg25670076	Asthma	UKB	rs978224	T	G	-0.344	0.071	1.13E-06	1.23E-04	0.030	3
GoDMC	BACH2	cg27644327	Asthma	UKB	rs12212193	G	A	-0.716	0.105	8.65E-12	2.32E-09	0.261	8
GoDMC	BCL6	cg06027254	Asthma	UKB	rs3733018	A	C	-0.163	0.047	5.20E-04	2.60E-02	0.083	17
GoDMC	BCL6	cg17394304	Asthma	UKB	rs1005099	C	A	0.135	0.037	2.57E-04	1.54E-02	0.058	20
GoDMC	BCL6	cg19198148	Asthma	UKB	rs1973791	C	A	0.346	0.096	3.31E-04	1.89E-02	0.050	4
GoDMC	CAMK4	cg23385847	Asthma	UKB	rs10054191	C	T	-0.276	0.061	6.98E-06	6.32E-04	0.015	5
GoDMC	ING5	cg12508715	Asthma	UKB	rs3887696	T	C	0.196	0.044	9.22E-06	7.99E-04	0.010	3
GoDMC	ING5	cg23350296	Asthma	UKB	rs62191353	A	T	0.121	0.023	1.73E-07	2.32E-05	0.085	20
GoDMC	MRV11	cg17542333	Asthma	UKB	rs4909945	T	C	0.287	0.054	1.34E-07	1.88E-05	0.417	14
GoDMC	RAB13	cg23251254	Asthma	UKB	rs6724	C	G	0.241	0.070	6.05E-04	2.97E-02	0.691	20
GoDMC	RAB13	cg24543596	Asthma	UKB	rs11264734	C	T	0.236	0.067	3.92E-04	2.16E-02	0.713	8
GoDMC	RAB13	cg26008365	Asthma	UKB	rs138767862	A	G	0.226	0.065	4.96E-04	2.52E-02	0.623	8
GoDMC	RAB13	cg26336059	Asthma	UKB	rs138767862	A	G	0.179	0.050	4.01E-04	2.19E-02	0.580	20
GoDMC	RBM17	cg02773640	Asthma	UKB	rs41260244	G	A	-0.162	0.046	4.44E-04	2.33E-02	0.011	8
GoDMC	RORC	cg03005293	Asthma	UKB	rs11801866	A	T	-0.187	0.040	2.34E-06	2.38E-04	0.269	13

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs.

Table S19 TSMR analysis of additional blood DNA methylation on asthma in discovery phase

Source exposure	Gene exposure	ID.exposure	outcome	ID.outcome	Method	nsnp	b	se	pval	FDR	or	or_lci95	or_uci95	hetero_pval	ple_pval
GoDMC	AFF3	cg04109781	Asthma	UKB	IVW	3	-0.061	0.025	1.40E-02	1.71E-02	0.941	0.897	0.988	0.014	0.910
GoDMC	AFF3	cg09521647	Asthma	UKB	IVW	3	-0.078	0.015	9.10E-08	4.90E-07	0.925	0.899	0.952	0.881	0.963
GoDMC	AFF3	cg17356467	Asthma	UKB	Wald ratio	1	-0.222	0.083	7.80E-03	1.00E-02	0.801	0.681	0.943	-	-
GoDMC	BACH2	cg09471887	Asthma	UKB	Wald ratio	1	0.140	0.035	7.86E-05	1.89E-04	1.150	1.073	1.233	-	-
GoDMC	BACH2	cg09790829	Asthma	UKB	Wald ratio	1	-0.500	0.049	1.75E-24	4.76E-23	0.607	0.551	0.668	-	-
GoDMC	BACH2	cg09818385	Asthma	UKB	Wald ratio	1	-0.614	0.060	1.20E-24	4.76E-23	0.541	0.481	0.609	-	-
GoDMC	BACH2	cg10913050	Asthma	UKB	Wald ratio	1	-0.472	0.046	2.32E-24	4.76E-23	0.624	0.570	0.683	-	-
GoDMC	BACH2	cg15380603	Asthma	UKB	Wald ratio	1	-0.766	0.078	1.29E-22	2.12E-21	0.465	0.399	0.542	-	-
GoDMC	BACH2	cg25670076	Asthma	UKB	Wald ratio	1	-0.344	0.063	5.00E-08	2.93E-07	0.709	0.627	0.802	-	-
GoDMC	BACH2	cg27644327	Asthma	UKB	Wald ratio	1	-0.716	0.076	7.64E-21	8.95E-20	0.489	0.421	0.568	-	-
GoDMC	BCL6	cg06027254	Asthma	UKB	Wald ratio	1	-0.279	0.069	5.72E-05	1.47E-04	0.757	0.661	0.867	-	-
GoDMC	BCL6	cg17394304	Asthma	UKB	Wald ratio	1	0.135	0.036	2.06E-04	4.38E-04	1.144	1.066	1.228	-	-
GoDMC	BCL6	cg19198148	Asthma	UKB	Wald ratio	1	0.346	0.086	5.33E-05	1.41E-04	1.413	1.195	1.671	-	-
GoDMC	CAMK4	cg23385847	Asthma	UKB	IVW	2	-0.270	0.052	2.26E-07	9.75E-07	0.764	0.690	0.846	0.802	-
GoDMC	ING5	cg12508715	Asthma	UKB	Wald ratio	1	0.248	0.047	1.07E-07	5.18E-07	1.281	1.169	1.404	-	-
GoDMC	ING5	cg23350296	Asthma	UKB	Wald ratio	1	0.147	0.032	3.71E-06	1.38E-05	1.158	1.088	1.233	-	-
GoDMC	MRV11	cg17542333	Asthma	UKB	Wald ratio	1	0.287	0.051	1.84E-08	1.37E-07	1.332	1.206	1.472	-	-
GoDMC	RAB13	cg23251254	Asthma	UKB	Wald ratio	1	0.228	0.070	1.20E-03	1.77E-03	1.256	1.094	1.442	-	-
GoDMC	RAB13	cg24543596	Asthma	UKB	Wald ratio	1	0.236	0.064	2.08E-04	4.38E-04	1.267	1.118	1.435	-	-
GoDMC	RAB13	cg26008365	Asthma	UKB	Wald ratio	1	0.226	0.062	2.74E-04	5.47E-04	1.253	1.110	1.415	-	-
GoDMC	RAB13	cg26336059	Asthma	UKB	Wald ratio	1	0.193	0.058	8.24E-04	1.35E-03	1.213	1.083	1.359	-	-
GoDMC	RBM17	cg02773640	Asthma	UKB	Wald ratio	1	-0.162	0.045	3.20E-04	6.24E-04	0.850	0.778	0.929	-	-
GoDMC	RORC	cg03005293	Asthma	UKB	IVW	2	-0.282	0.051	2.46E-08	1.62E-07	0.754	0.683	0.833	0.694	-

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results.

Table S20 SMR analysis of additional blood DNA methylation on asthma in replication phase

Group	Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	topSNP	A1	A2	b_SMR	se_SMR	p_SMR	FDR_SMR	p_HEIDI	nsnp_HEIDI	I2	pval_Q
1	FSH	AFF3	cg04109781	Asthma	TAGC	rs13430705	G	A	-0.283	0.315	3.69E-01	4.81E-01	0.926	20	-	-
1	FSH	AFF3	cg04109781	Asthma	Finngen	rs35869550	T	A	-0.780	0.230	6.73E-04	2.46E-03	0.100	20	-	-
1	FSH	AFF3	cg04109781	Asthma	F_T	-	-	-	-0.608	0.185	1.05E-03	5.02E-03	-	-	0.387	0.201
1	FSH	AFF3	cg09521647	Asthma	TAGC	rs13402299	C	T	-0.773	1.017	4.47E-01	5.20E-01	0.821	20	-	-
1	FSH	AFF3	cg09521647	Asthma	Finngen	rs34040706	G	A	-2.439	0.743	1.04E-03	3.42E-03	0.386	20	-	-
1	FSH	AFF3	cg09521647	Asthma	F_T	-	-	-	-1.859	0.600	1.95E-03	8.40E-03	-	-	0.428	0.186
1	FSH	BACH2	cg10913050	Asthma	TAGC	rs2021716	C	T	-13.392	2.499	8.41E-08	1.81E-06	0.184	5	-	-
1	FSH	BACH2	cg10913050	Asthma	Finngen	rs62408211	A	T	-9.728	1.831	1.08E-07	1.17E-06	0.003	9	-	-
1	FSH	BACH2	cg10913050	Asthma	F_T	-	-	-	-11.008	1.477	9.22E-14	1.32E-12	-	-	0.285	0.237
1	FSH	BCL6	cg17394304	Asthma	TAGC	rs1880100	C	T	3.886	2.856	1.74E-01	2.76E-01	0.441	11	-	-
1	FSH	BCL6	cg17394304	Asthma	Finngen	rs3774303	G	C	5.619	1.510	1.98E-04	9.44E-04	0.173	14	-	-
1	FSH	BCL6	cg17394304	Asthma	F_T	-	-	-	5.241	1.335	8.61E-05	4.63E-04	-	-	0.000	0.592
1	FSH	MRVI1	cg17542333	Asthma	TAGC	rs7940646	C	T	18.151	7.913	2.18E-02	5.21E-02	-	-	-	-
1	FSH	MRVI1	cg17542333	Asthma	Finngen	rs4910165	G	C	18.979	5.591	6.87E-04	2.46E-03	-	-	-	-
1	FSH	MRVI1	cg17542333	Asthma	F_T	-	-	-	18.703	4.566	4.20E-05	2.58E-04	-	-	0.000	0.932
1	FSH	RAB13	cg26008365	Asthma	TAGC	rs12048137	T	G	5.262	3.346	1.16E-01	2.07E-01	0.789	3	-	-
1	FSH	RAB13	cg26008365	Asthma	Finngen	rs12048137	T	G	3.917	2.256	8.26E-02	1.97E-01	0.584	4	-	-
1	FSH	RAB13	cg26008365	Asthma	F_T	-	-	-	4.337	1.871	2.04E-02	7.98E-02	-	-	0.000	0.739
1	FSH	RORC	cg03005293	Asthma	TAGC	rs11578418	G	A	-7.710	5.083	1.29E-01	2.14E-01	-	-	-	-
1	FSH	RORC	cg03005293	Asthma	Finngen	rs11204896	C	G	-5.255	3.268	1.08E-01	2.32E-01	-	-	-	-
1	FSH	RORC	cg03005293	Asthma	F_T	-	-	-	-5.973	2.749	2.98E-02	9.85E-02	-	-	0.000	0.685
2	GoDMC	AFF3	cg17356467	Asthma	TAGC_2	rs11682173	T	C	-0.091	0.126	4.70E-01	5.11E-01	0.690	8	-	-
2	GoDMC	AFF3	cg17356467	Asthma	Finngen_2	rs11682173	T	C	-0.231	0.089	9.13E-03	1.52E-02	0.088	11	-	-
2	GoDMC	AFF3	cg17356467	Asthma	F_T_2	-	-	-	-0.185	0.073	1.08E-02	2.26E-02	-	-	0.000	0.363
2	GoDMC	BACH2	cg09745430	Asthma	TAGC_2	rs2021716	T	C	-1.002	0.177	1.43E-08	8.96E-08	0.005	10	-	-
2	GoDMC	BACH2	cg09745430	Asthma	Finngen_2	rs62408211	T	A	-0.714	0.127	1.69E-08	1.41E-07	0.006	13	-	-
2	GoDMC	BACH2	cg09745430	Asthma	F_T_2	-	-	-	-0.812	0.103	3.09E-15	3.86E-14	-	-	0.430	0.185
2	GoDMC	BACH2	cg09818385	Asthma	TAGC_2	rs2021716	T	C	-0.791	0.131	1.45E-09	1.81E-08	0.006	10	-	-
2	GoDMC	BACH2	cg09818385	Asthma	Finngen_2	rs62408211	T	A	-0.580	0.098	2.72E-09	3.41E-08	0.009	14	-	-
2	GoDMC	BACH2	cg09818385	Asthma	F_T_2	-	-	-	-0.656	0.078	5.06E-17	1.26E-15	-	-	0.397	0.198
2	GoDMC	BACH2	cg15380603	Asthma	TAGC_2	rs11757155	T	C	-1.029	0.180	1.06E-08	8.80E-08	0.211	7	-	-
2	GoDMC	BACH2	cg15380603	Asthma	Finngen_2	rs11757155	T	C	-0.683	0.130	1.58E-07	7.88E-07	0.044	9	-	-
2	GoDMC	BACH2	cg15380603	Asthma	F_T_2	-	-	-	-0.833	0.172	1.18E-06	5.89E-06	-	-	0.588	0.119
2	GoDMC	BACH2	cg25670076	Asthma	TAGC_2	rs3752747	T	C	-0.677	0.159	1.96E-05	7.01E-05	-	-	-	-
2	GoDMC	BACH2	cg25670076	Asthma	Finngen_2	rs978224	T	G	-0.382	0.089	1.57E-05	4.36E-05	0.935	3	-	-
2	GoDMC	BACH2	cg25670076	Asthma	F_T_2	-	-	-	-0.500	0.144	5.33E-04	1.33E-03	-	-	0.620	0.105
2	GoDMC	BACH2	cg27644327	Asthma	TAGC_2	rs12212193	G	A	-0.960	0.176	5.28E-08	2.64E-07	0.005	6	-	-
2	GoDMC	BACH2	cg27644327	Asthma	Finngen_2	rs12212193	G	A	-0.619	0.124	5.88E-07	2.10E-06	0.034	7	-	-
2	GoDMC	BACH2	cg27644327	Asthma	F_T_2	-	-	-	-0.766	0.169	5.76E-06	2.06E-05	-	-	0.601	0.114
2	GoDMC	BCL6	cg06027254	Asthma	TAGC_2	rs1005099	C	A	-0.160	0.118	1.75E-01	2.30E-01	0.301	10	-	-
2	GoDMC	BCL6	cg06027254	Asthma	Finngen_2	rs3733018	A	C	-0.290	0.063	4.46E-06	1.39E-05	0.020	17	-	-
2	GoDMC	BCL6	cg06027254	Asthma	F_T_2	-	-	-	-0.261	0.056	2.80E-06	1.17E-05	-	-	0.000	0.330
2	GoDMC	BCL6	cg19198148	Asthma	TAGC_2	rs11717298	G	A	0.320	0.194	9.88E-02	1.45E-01	-	-	-	-
2	GoDMC	BCL6	cg19198148	Asthma	Finngen_2	rs1973791	C	A	0.526	0.134	8.40E-05	2.10E-04	0.218	4	-	-
2	GoDMC	BCL6	cg19198148	Asthma	F_T_2	-	-	-	0.459	0.110	2.99E-05	8.31E-05	-	-	0.000	0.381
2	GoDMC	CAMK4	cg23385847	Asthma	TAGC_2	rs10054191	C	T	-0.385	0.116	8.56E-04	2.38E-03	0.003	3	-	-
2	GoDMC	CAMK4	cg23385847	Asthma	Finngen_2	rs10054191	C	T	-0.386	0.075	2.74E-07	1.14E-06	0.004	5	-	-
2	GoDMC	CAMK4	cg23385847	Asthma	F_T_2	-	-	-	-0.386	0.063	8.95E-10	5.59E-09	-	-	0.000	0.995
2	GoDMC	ING5	cg12508715	Asthma	TAGC_2	rs7420703	C	T	0.571	0.203	4.92E-03	1.02E-02	-	-	-	-
2	GoDMC	ING5	cg12508715	Asthma	Finngen_2	rs7605806	A	G	0.200	0.061	9.50E-04	1.98E-03	0.132	3	-	-
2	GoDMC	ING5	cg12508715	Asthma	F_T_2	-	-	-	0.335	0.178	6.04E-02	7.95E-02	-	-	0.674	0.080
2	GoDMC	ING5	cg23350296	Asthma	TAGC_2	rs10191556	T	C	0.318	0.109	3.42E-03	7.77E-03	-	-	-	-
2	GoDMC	ING5	cg23350296	Asthma	Finngen_2	rs62191353	A	T	0.108	0.031	4.70E-04	1.07E-03	0.013	20	-	-
2	GoDMC	ING5	cg23350296	Asthma	F_T_2	-	-	-	0.187	0.102	6.68E-02	8.35E-02	-	-	0.712	0.062
2	GoDMC	RAB13	cg23251254	Asthma	TAGC_2	rs11264743	T	C	0.117	0.132	3.74E-01	4.25E-01	0.218	15	-	-
2	GoDMC	RAB13	cg23251254	Asthma	Finngen_2	rs6724	C	G	0.159	0.086	6.34E-02	7.55E-02	0.415	20	-	-

2	GoDMC	RAB13	cg23251254	Asthma	F_T_2	-	-	-	0.147	0.072	4.13E-02	5.73E-02	-	-	0.000	0.789
2	GoDMC	RAB13	cg24543596	Asthma	TAGC_2	rs11264743	T	C	0.108	0.122	3.74E-01	4.25E-01	0.224	4	-	-
2	GoDMC	RAB13	cg24543596	Asthma	Finngen_2	rs11264734	C	T	0.153	0.081	6.08E-02	7.55E-02	0.912	6	-	-
2	GoDMC	RAB13	cg24543596	Asthma	F_T_2	-	-	-	0.139	0.068	4.00E-02	5.73E-02	-	-	0.000	0.762
2	GoDMC	RAB13	cg26336059	Asthma	TAGC_2	rs6701341	T	C	0.117	0.099	2.35E-01	2.93E-01	0.269	14	-	-
2	GoDMC	RAB13	cg26336059	Asthma	Finngen_2	rs138767862	A	G	0.119	0.063	5.74E-02	7.55E-02	0.324	20	-	-
2	GoDMC	RAB13	cg26336059	Asthma	F_T_2	-	-	-	0.119	0.053	2.50E-02	4.17E-02	-	-	0.000	0.986
2	GoDMC	RBM17	cg02773640	Asthma	TAGC_2	rs11593569	T	G	-0.282	0.132	3.29E-02	5.49E-02	-	-	-	-
2	GoDMC	RBM17	cg02773640	Asthma	Finngen_2	rs41260244	G	A	-0.112	0.051	2.93E-02	4.58E-02	0.832	8	-	-
2	GoDMC	RBM17	cg02773640	Asthma	F_T_2	-	-	-	-0.134	0.048	5.06E-03	1.15E-02	-	-	0.306	0.230
3	GoDMC	AFB3	cg04109781	Asthma	Finngen_2	rs13001783	T	A	-0.036	0.011	6.66E-04	8.88E-04	0.029	20	-	-
3	GoDMC	AFB3	cg04109781	Asthma	TAGC_2	rs4851244	C	T	-0.014	0.015	3.45E-01	4.27E-01	0.918	20	-	-
3	GoDMC	AFB3	cg04109781	Asthma	F_T_2	-	-	-	-0.028	0.009	9.42E-04	1.51E-03	-	-	0.349	0.215
3	GoDMC	AFB3	cg09521647	Asthma	Finngen_2	rs12992234	A	G	-0.081	0.021	1.18E-04	2.36E-04	0.383	20	-	-
3	GoDMC	AFB3	cg09521647	Asthma	TAGC_2	rs12992234	A	G	-0.012	0.029	6.87E-01	6.87E-01	0.639	20	-	-
3	GoDMC	AFB3	cg09521647	Asthma	F_T_2	-	-	-	-0.049	0.034	1.56E-01	1.56E-01	-	-	0.736	0.052
3	GoDMC	BACH2	cg09790829	Asthma	Finngen_2	rs969577	C	T	-0.459	0.077	3.06E-09	1.22E-08	0.056	12	-	-
3	GoDMC	BACH2	cg09790829	Asthma	TAGC_2	rs943689	T	C	-0.670	0.104	1.02E-10	4.08E-10	0.115	10	-	-
3	GoDMC	BACH2	cg09790829	Asthma	F_T_2	-	-	-	-0.553	0.105	1.30E-07	1.04E-06	-	-	0.623	0.103
3	GoDMC	BACH2	cg10913050	Asthma	Finngen_2	rs969577	C	T	-0.429	0.072	2.85E-09	1.22E-08	0.031	15	-	-
3	GoDMC	BACH2	cg10913050	Asthma	TAGC_2	rs2325292	C	T	-0.636	0.098	7.93E-11	4.08E-10	0.027	10	-	-
3	GoDMC	BACH2	cg10913050	Asthma	F_T_2	-	-	-	-0.522	0.103	3.97E-07	1.59E-06	-	-	0.655	0.089
3	GoDMC	BCL6	cg17394304	Asthma	Finngen_2	rs1005099	C	A	0.222	0.050	9.14E-06	2.44E-05	0.108	20	-	-
3	GoDMC	BCL6	cg17394304	Asthma	TAGC_2	rs1005099	C	A	0.100	0.073	1.74E-01	2.78E-01	0.255	12	-	-
3	GoDMC	BCL6	cg17394304	Asthma	F_T_2	-	-	-	0.183	0.041	9.32E-06	1.86E-05	-	-	0.471	0.169
3	GoDMC	MRV11	cg17542333	Asthma	Finngen_2	rs4909945	T	C	0.249	0.068	2.50E-04	4.00E-04	0.110	14	-	-
3	GoDMC	MRV11	cg17542333	Asthma	TAGC_2	rs4909945	T	C	0.309	0.099	1.83E-03	4.89E-03	0.704	12	-	-
3	GoDMC	MRV11	cg17542333	Asthma	F_T_2	-	-	-	0.269	0.056	1.73E-06	4.61E-06	-	-	0.000	0.619
3	GoDMC	RAB13	cg26008365	Asthma	Finngen_2	rs138767862	A	G	0.151	0.080	5.86E-02	5.86E-02	0.992	8	-	-
3	GoDMC	RAB13	cg26008365	Asthma	TAGC_2	rs11264743	T	C	0.111	0.125	3.74E-01	4.27E-01	0.502	6	-	-
3	GoDMC	RAB13	cg26008365	Asthma	F_T_2	-	-	-	0.139	0.067	3.82E-02	4.36E-02	-	-	0.000	0.789
3	GoDMC	RORC	cg03005293	Asthma	Finngen_2	rs11801866	A	T	-0.095	0.050	5.82E-02	5.86E-02	0.571	11	-	-
3	GoDMC	RORC	cg03005293	Asthma	TAGC_2	rs11578418	A	G	-0.121	0.078	1.22E-01	2.43E-01	0.645	7	-	-
3	GoDMC	RORC	cg03005293	Asthma	F_T_2	-	-	-	-0.102	0.042	1.51E-02	2.02E-02	-	-	0.000	0.776

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from FSH and outcome from Finngen; TAGC, exposure from FSH and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from FSH→Finngen and FSH→TAGC; Finngen\_2, exposure from GoDMC and outcome from Finngen; TAGC, exposure from GoDMC and outcome from TAGC; F\_T\_2, meta-analysis of results from GoDMC→Finngen and GoDMC→TAGC.

Table S21 TSMR analysis of additional blood DNA methylation on asthma in replication phase

Group	Source exposure	Gene exposure	ID.exposure	Outcome	ID.outcome	Method	nsp	b	se	pval	FDR	lo_ci	up_ci	hetero_pval	ple_pval	I2	pval_Q
1	FSH	AFF3	cg04109781	Asthma	TAGC	IVW	2	-0.332	0.504	5.10E-01	5.78E-01	-1.319	0.656	0.283	-	-	-
1	FSH	AFF3	cg04109781	Asthma	Finngen	IVW	4	-0.935	0.461	4.28E-02	1.06E-01	-1.839	-0.030	0.011	0.560	-	-
1	FSH	AFF3	cg04109781	Asthma	F_T	-	-	-0.660	0.340	5.26E-02	1.51E-01	-1.326	0.007	-	-	0.000	0.378
1	FSH	AFF3	cg09521647	Asthma	TAGC	Wald ratio	1	-0.773	1.017	4.47E-01	5.34E-01	-2.766	1.219	-	-	-	-
1	FSH	AFF3	cg09521647	Asthma	Finngen	IVW	2	-2.273	1.086	3.63E-02	9.47E-02	-4.401	-0.145	0.136	-	-	-
1	FSH	AFF3	cg09521647	Asthma	F_T	-	-	-1.474	0.742	4.70E-02	1.51E-01	-2.928	-0.019	-	-	0.017	0.313
1	FSH	BACH2	cg09790829	Asthma	TAGC	Wald ratio	1	-29.659	4.236	2.54E-12	5.46E-11	-37.962	-21.356	-	-	-	-
1	FSH	BACH2	cg09790829	Asthma	Finngen	Wald ratio	1	-20.025	3.187	3.31E-10	7.63E-09	-26.271	-13.778	-	-	-	-
1	FSH	BACH2	cg09790829	Asthma	F_T	-	-	-24.437	4.800	3.56E-07	3.83E-06	-33.846	-15.029	-	-	0.697	0.069
1	FSH	BACH2	cg10913050	Asthma	TAGC	Wald ratio	1	-13.392	1.946	5.95E-12	8.53E-11	-17.207	-9.577	-	-	-	-
1	FSH	BACH2	cg10913050	Asthma	Finngen	Wald ratio	1	-9.728	1.449	1.89E-11	8.89E-10	-12.568	-6.888	-	-	-	-
1	FSH	BACH2	cg10913050	Asthma	F_T	-	-	-11.330	1.817	4.54E-10	6.51E-09	-14.892	-7.768	-	-	0.561	0.131
1	FSH	BCL6	cg17394304	Asthma	TAGC	Wald ratio	1	3.886	2.826	1.69E-01	2.69E-01	-1.652	9.425	-	-	-	-
1	FSH	BCL6	cg17394304	Asthma	Finngen	Wald ratio	1	5.619	1.401	6.05E-05	3.56E-04	2.873	8.365	-	-	-	-
1	FSH	BCL6	cg17394304	Asthma	F_T	-	-	5.277	1.255	2.62E-05	1.41E-04	2.817	7.737	-	-	0.000	0.583
1	FSH	MRV11	cg17542333	Asthma	TAGC	Wald ratio	1	18.151	7.527	1.59E-02	3.80E-02	3.398	32.904	-	-	-	-
1	FSH	MRV11	cg17542333	Asthma	Finngen	Wald ratio	1	18.979	4.975	1.36E-04	6.41E-04	9.228	28.730	-	-	-	-
1	FSH	MRV11	cg17542333	Asthma	F_T	-	-	18.727	4.150	6.42E-06	3.94E-05	10.592	26.862	-	-	0.000	0.927
1	FSH	RAB13	cg26008365	Asthma	TAGC	Wald ratio	1	5.262	3.260	1.07E-01	1.91E-01	-1.128	11.653	-	-	-	-
1	FSH	RAB13	cg26008365	Asthma	Finngen	Wald ratio	1	3.917	2.185	7.31E-02	1.64E-01	-0.366	8.200	-	-	-	-
1	FSH	RAB13	cg26008365	Asthma	F_T	-	-	4.334	1.815	1.70E-02	7.30E-02	0.776	7.892	-	-	0.000	0.732
1	FSH	RORC	cg03005293	Asthma	TAGC	Wald ratio	1	-7.710	4.961	1.20E-01	2.07E-01	-17.434	2.014	-	-	-	-
1	FSH	RORC	cg03005293	Asthma	Finngen	Wald ratio	1	-5.255	3.182	9.86E-02	2.01E-01	-11.491	0.980	-	-	-	-
1	FSH	RORC	cg03005293	Asthma	F_T	-	-	-5.971	2.678	2.58E-02	1.01E-01	-11.220	-0.721	-	-	0.000	0.677
2	GoDMC	AFF3	cg17356467	Asthma	TAGC_2	Wald ratio	1	-0.068	0.179	7.04E-01	7.04E-01	-0.419	0.283	-	-	-	-
2	GoDMC	AFF3	cg17356467	Asthma	Finngen_2	Wald ratio	1	-0.187	0.110	9.01E-02	1.19E-01	-0.402	0.029	-	-	-	-
2	GoDMC	AFF3	cg17356467	Asthma	F_T_2	-	-	-0.154	0.094	1.00E-01	1.28E-01	-0.338	0.030	-	-	0.000	0.573
2	GoDMC	BACH2	cg09745430	Asthma	TAGC_2	Wald ratio	1	-1.002	0.146	5.95E-12	4.96E-11	-1.288	-0.717	-	-	-	-
2	GoDMC	BACH2	cg09745430	Asthma	Finngen_2	Wald ratio	1	-0.714	0.106	1.89E-11	2.37E-10	-0.923	-0.506	-	-	-	-
2	GoDMC	BACH2	cg09745430	Asthma	F_T_2	-	-	-0.841	0.143	3.99E-09	4.99E-08	-1.121	-0.561	-	-	0.608	0.110
2	GoDMC	BACH2	cg09818385	Asthma	TAGC_2	Wald ratio	1	-0.839	0.117	9.00E-13	1.13E-11	-1.069	-0.609	-	-	-	-
2	GoDMC	BACH2	cg09818385	Asthma	Finngen_2	Wald ratio	1	-0.538	0.088	9.97E-10	8.31E-09	-0.710	-0.365	-	-	-	-
2	GoDMC	BACH2	cg09818385	Asthma	F_T_2	-	-	-0.678	0.150	6.17E-06	2.20E-05	-0.972	-0.384	-	-	0.762	0.040
2	GoDMC	BACH2	cg15380603	Asthma	TAGC_2	Wald ratio	1	-1.023	0.152	1.85E-11	1.15E-10	-1.322	-0.725	-	-	-	-
2	GoDMC	BACH2	cg15380603	Asthma	Finngen_2	Wald ratio	1	-0.684	0.114	1.71E-09	1.07E-08	-0.906	-0.461	-	-	-	-
2	GoDMC	BACH2	cg15380603	Asthma	F_T_2	-	-	-0.838	0.169	7.22E-07	6.02E-06	-1.170	-0.507	-	-	0.687	0.074
2	GoDMC	BACH2	cg25670076	Asthma	TAGC_2	Wald ratio	1	-0.677	0.143	2.29E-06	9.54E-06	-0.958	-0.396	-	-	-	-
2	GoDMC	BACH2	cg25670076	Asthma	Finngen_2	Wald ratio	1	-0.382	0.081	2.47E-06	8.82E-06	-0.542	-0.223	-	-	-	-
2	GoDMC	BACH2	cg25670076	Asthma	F_T_2	-	-	-0.506	0.146	5.05E-04	1.40E-03	-0.792	-0.221	-	-	0.688	0.073
2	GoDMC	BACH2	cg27644327	Asthma	TAGC_2	Wald ratio	1	-0.960	0.148	8.42E-11	4.21E-10	-1.249	-0.670	-	-	-	-
2	GoDMC	BACH2	cg27644327	Asthma	Finngen_2	Wald ratio	1	-0.619	0.107	7.89E-09	3.29E-08	-0.829	-0.409	-	-	-	-
2	GoDMC	BACH2	cg27644327	Asthma	F_T_2	-	-	-0.774	0.170	5.17E-06	2.15E-05	-1.107	-0.441	-	-	0.713	0.062
2	GoDMC	BCL6	cg06027254	Asthma	TAGC_2	Wald ratio	1	-0.176	0.121	1.44E-01	1.89E-01	-0.413	0.060	-	-	-	-
2	GoDMC	BCL6	cg06027254	Asthma	Finngen_2	IVW	2	-0.374	0.162	2.10E-02	4.04E-02	-0.691	-0.056	0.063	-	-	-
2	GoDMC	BCL6	cg06027254	Asthma	F_T_2	-	-	-0.247	0.097	1.07E-02	2.44E-02	-0.436	-0.057	-	-	0.000	0.328
2	GoDMC	BCL6	cg19198148	Asthma	TAGC_2	Wald ratio	1	0.320	0.189	9.03E-02	1.41E-01	-0.050	0.689	-	-	-	-
2	GoDMC	BCL6	cg19198148	Asthma	Finngen_2	Wald ratio	1	0.526	0.116	5.36E-06	1.67E-05	0.299	0.752	-	-	-	-
2	GoDMC	BCL6	cg19198148	Asthma	F_T_2	-	-	0.470	0.099	1.89E-06	9.44E-06	0.276	0.663	-	-	0.000	0.351
2	GoDMC	CAMK4	cg23385847	Asthma	TAGC_2	IVW	2	-0.405	0.101	5.71E-05	2.04E-04	-0.603	-0.208	0.682	-	-	-
2	GoDMC	CAMK4	cg23385847	Asthma	Finngen_2	IVW	2	-0.462	0.176	8.64E-03	1.80E-02	-0.807	-0.117	0.006	-	-	-
2	GoDMC	CAMK4	cg23385847	Asthma	F_T_2	-	-	-0.419	0.087	1.61E-06	9.44E-06	-0.590	-0.248	-	-	0.000	0.780
2	GoDMC	ING5	cg12508715	Asthma	TAGC_2	Wald ratio	1	0.571	0.188	2.40E-03	5.15E-03	0.202	0.940	-	-	-	-
2	GoDMC	ING5	cg12508715	Asthma	Finngen_2	Wald ratio	1	0.223	0.064	4.63E-04	1.29E-03	0.098	0.349	-	-	-	-
2	GoDMC	ING5	cg12508715	Asthma	F_T_2	-	-	0.352	0.168	3.58E-02	5.93E-02	0.023	0.681	-	-	0.673	0.080
2	GoDMC	ING5	cg23350296	Asthma	TAGC_2	IVW	2	0.294	0.097	2.47E-03	5.15E-03	0.104	0.485	0.569	-	-	-
2	GoDMC	ING5	cg23350296	Asthma	Finngen_2	Wald ratio	1	0.050	0.042	2.34E-01	2.66E-01	-0.032	0.133	-	-	-	-

2	GoDMC	ING5	cg23350296	Asthma	F_T_2	-	-	0.157	0.121	1.95E-01	2.33E-01	-0.080	0.393	-	-	0.811	0.021
2	GoDMC	RAB13	cg23251254	Asthma	TAGC_2	Wald ratio	1	0.285	0.191	1.36E-01	1.89E-01	-0.090	0.659	-	-	-	-
2	GoDMC	RAB13	cg23251254	Asthma	Finngen_2	Wald ratio	1	0.133	0.090	1.40E-01	1.75E-01	-0.044	0.311	-	-	-	-
2	GoDMC	RAB13	cg23251254	Asthma	F_T_2	-	-	0.161	0.082	4.86E-02	7.15E-02	0.001	0.321	-	-	0.000	0.474
2	GoDMC	RAB13	cg24543596	Asthma	TAGC_2	Wald ratio	1	0.108	0.121	3.72E-01	4.23E-01	-0.130	0.346	-	-	-	-
2	GoDMC	RAB13	cg24543596	Asthma	Finngen_2	Wald ratio	1	0.153	0.080	5.77E-02	9.01E-02	-0.005	0.311	-	-	-	-
2	GoDMC	RAB13	cg24543596	Asthma	F_T_2	-	-	0.139	0.067	3.80E-02	5.93E-02	0.008	0.271	-	-	0.000	0.761
2	GoDMC	RAB13	cg26336059	Asthma	TAGC_2	Wald ratio	1	0.144	0.115	2.09E-01	2.61E-01	-0.081	0.369	-	-	-	-
2	GoDMC	RAB13	cg26336059	Asthma	Finngen_2	Wald ratio	1	0.132	0.073	6.92E-02	1.02E-01	-0.010	0.275	-	-	-	-
2	GoDMC	RAB13	cg26336059	Asthma	F_T_2	-	-	0.136	0.061	2.73E-02	4.88E-02	0.015	0.256	-	-	0.000	0.930
2	GoDMC	RBM17	cg02773640	Asthma	TAGC_2	Wald ratio	1	-0.282	0.130	3.04E-02	5.43E-02	-0.537	-0.027	-	-	-	-
2	GoDMC	RBM17	cg02773640	Asthma	Finngen_2	Wald ratio	1	-0.112	0.051	2.79E-02	4.98E-02	-0.211	-0.012	-	-	-	-
2	GoDMC	RBM17	cg02773640	Asthma	F_T_2	-	-	-0.134	0.047	4.57E-03	1.14E-02	-0.227	-0.041	-	-	0.325	0.224
3	GoDMC	AFF3	cg04109781	Asthma	Finngen_2	IVW	5	-0.060	0.026	2.10E-02	2.79E-02	-0.111	-0.009	0.119	0.386	-	-
3	GoDMC	AFF3	cg04109781	Asthma	TAGC_2	IVW	3	0.053	0.041	1.96E-01	2.61E-01	-0.027	0.134	0.991	0.922	-	-
3	GoDMC	AFF3	cg04109781	Asthma	F_T_2	-	-	-0.008	0.056	8.90E-01	8.90E-01	-0.118	0.103	-	-	0.815	0.020
3	GoDMC	AFF3	cg09521647	Asthma	Finngen_2	IVW	3	-0.089	0.020	6.65E-06	1.77E-05	-0.128	-0.050	0.591	0.841	-	-
3	GoDMC	AFF3	cg09521647	Asthma	TAGC_2	IVW	3	0.000	0.053	9.98E-01	9.98E-01	-0.104	0.104	0.596	0.767	-	-
3	GoDMC	AFF3	cg09521647	Asthma	F_T_2	-	-	-0.058	0.043	1.73E-01	2.31E-01	-0.142	0.025	-	-	0.599	0.114
3	GoDMC	BACH2	cg09790829	Asthma	Finngen_2	Wald ratio	1	-0.446	0.108	3.85E-05	7.70E-05	-0.658	-0.233	-	-	-	-
3	GoDMC	BACH2	cg09790829	Asthma	TAGC_2	Wald ratio	1	-0.663	0.095	2.58E-12	1.23E-11	-0.848	-0.477	-	-	-	-
3	GoDMC	BACH2	cg09790829	Asthma	F_T_2	-	-	-0.560	0.108	2.31E-07	9.22E-07	-0.773	-0.348	-	-	0.561	0.131
3	GoDMC	BACH2	cg10913050	Asthma	Finngen_2	Wald ratio	1	-0.429	0.067	1.49E-10	1.19E-09	-0.560	-0.298	-	-	-	-
3	GoDMC	BACH2	cg10913050	Asthma	TAGC_2	Wald ratio	1	-0.631	0.090	3.07E-12	1.23E-11	-0.808	-0.454	-	-	-	-
3	GoDMC	BACH2	cg10913050	Asthma	F_T_2	-	-	-0.521	0.101	2.21E-07	9.22E-07	-0.718	-0.324	-	-	0.689	0.073
3	GoDMC	BCL6	cg17394304	Asthma	Finngen_2	Wald ratio	1	0.222	0.049	5.67E-06	1.77E-05	0.126	0.318	-	-	-	-
3	GoDMC	BCL6	cg17394304	Asthma	TAGC_2	Wald ratio	1	0.100	0.073	1.73E-01	2.61E-01	-0.044	0.243	-	-	-	-
3	GoDMC	BCL6	cg17394304	Asthma	F_T_2	-	-	0.184	0.041	5.86E-06	1.17E-05	0.104	0.264	-	-	0.480	0.166
3	GoDMC	MRV11	cg17542333	Asthma	Finngen_2	Wald ratio	1	0.249	0.066	1.60E-04	2.56E-04	0.120	0.379	-	-	-	-
3	GoDMC	MRV11	cg17542333	Asthma	TAGC_2	Wald ratio	1	0.309	0.097	1.45E-03	3.87E-03	0.119	0.500	-	-	-	-
3	GoDMC	MRV11	cg17542333	Asthma	F_T_2	-	-	0.268	0.055	9.02E-07	2.41E-06	0.161	0.375	-	-	0.000	0.611
3	GoDMC	RAB13	cg26008365	Asthma	Finngen_2	Wald ratio	1	0.151	0.079	5.55E-02	6.34E-02	-0.004	0.305	-	-	-	-
3	GoDMC	RAB13	cg26008365	Asthma	TAGC_2	Wald ratio	1	0.111	0.125	3.72E-01	4.25E-01	-0.133	0.356	-	-	-	-
3	GoDMC	RAB13	cg26008365	Asthma	F_T_2	-	-	0.140	0.067	3.61E-02	5.78E-02	0.009	0.270	-	-	0.000	0.788

nsnp, the number of SNPs; CI, confidence intervals; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis; Finngen, exposure from FSH and outcome from Finngen; TAGC, exposure from FSH and outcome from Trans-National Asthma Genetic Consortium (TAGC); F\_T, meta-analysis of results from FSH→Finngen and FSH→TAGC; Finngen\_2, exposure from GoDMC and outcome from Finngen; TAGC\_2, exposure from GoDMC and outcome from TAGC; F\_T\_2, meta-analysis of results from GoDMC→Finngen and GoDMC→TAGC.

Table S22 Colocalization analysis between additional DNA methylation from GoDMC and asthma from UKB

Source exposure	Gene exposure	ID.exposure	outcome	ID.outcome	p1	p2	p12	PP.H0.abf	PP.H1.abf	PP.H2.abf	PP.H3.abf	PP.H4.abf
GoDMC	AFF3	cg04109781	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.004	0.000	0.465	0.531
GoDMC	AFF3	cg09521647	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.036	0.963
GoDMC	AFF3	cg17356467	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.018	0.000	0.374	0.608
GoDMC	BACH2	cg09745430	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.260	0.740
GoDMC	BACH2	cg09790829	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.028	0.972
GoDMC	BACH2	cg09818385	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.044	0.956
GoDMC	BACH2	cg10913050	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.070	0.930
GoDMC	BACH2	cg15380603	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.044	0.956
GoDMC	BACH2	cg25670076	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.278	0.722
GoDMC	BACH2	cg27644327	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.310	0.690
GoDMC	BCL6	cg06027254	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.305	0.000	0.070	0.625
GoDMC	BCL6	cg17394304	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.213	0.000	0.093	0.694
GoDMC	BCL6	cg19198148	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.091	0.000	0.001	0.908
GoDMC	CAMK4	cg23385847	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.002	0.000	0.018	0.981
GoDMC	ING5	cg12508715	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.001	0.000	0.062	0.937
GoDMC	ING5	cg23350296	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.029	0.971
GoDMC	MRV11	cg17542333	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.000	0.000	0.016	0.984
GoDMC	RAB13	cg23251254	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.245	0.000	0.076	0.678
GoDMC	RAB13	cg24543596	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.232	0.000	0.067	0.701
GoDMC	RAB13	cg26008365	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.241	0.000	0.055	0.705
GoDMC	RAB13	cg26336059	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.252	0.000	0.073	0.675
GoDMC	RBM17	cg02773640	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.138	0.000	0.061	0.801
GoDMC	RORC	cg03005293	Asthma	UKB	1.00E-04	1.00E-04	1.00E-05	0.000	0.001	0.000	0.009	0.990

p1, a prior probability for a SNP being associated with trait 1 only; p2, a prior probability for a SNP being associated with trait 2 only; p12, a prior probability for a SNP being associated with both traits.

Table S23 Mediation analysis using SMR: DNA methylation on asthma through gene expression in discovery phase

Expo Gene	Expo ID	Media Gene	Outcome	Outco ID	XY b	XY se	XY FDR	XZ b	XZ se	XZ FDR	YZ b	YZ se	YZ FDR	Media effect pro	lo Media pro	up Media pro	Media p	Media FDR
ITPKB	cg16265553	ITPKB	Asthma	UKB	-0.457	0.090	5.73E-07	0.251	0.069	3.87E-03	-0.194	0.057	2.25E-02	0.353	0.108	0.598	4.76E-03	4.76E-03
JAK2	cg13661497	JAK2	Asthma	UKB	-2.572	0.339	6.67E-14	-0.323	0.102	7.62E-03	0.122	0.033	9.57E-03	0.967	0.392	1.543	9.86E-04	1.97E-03

Expo, DNA methylation; Media, gene expression; Outcome, asthma; XY, the effect of DNA methylation on gene expression; XZ, the effect of DNA methylation on asthma; YZ, the effect of gene expression on asthma.



Table S24 Mediation analysis using TSMR: DNA methylation on asthma through gene expression in discovery phase

Expo Gene	Expo ID	Media Gene	Outcome	Outc o ID	XY b	XY se	XY FDR	XZ b	XZ se	XZ FDR	YZ b	YZ se	YZ FDR	Media effect pro	lo Media pro	up Media pro	Media p	Media FDR
ITPKB	cg16265553	ITPKB	Asthma	UKB	-0.457	0.081	1.48E-08	0.251	0.066	1.15E-03	-0.194	0.056	8.37E-04	0.353	0.120	0.586	3.00E-03	3.00E-03
JAK2	cg13661497	JAK2	Asthma	UKB	-2.572	0.110	6.98E-120	-0.323	0.094	2.39E-03	0.131	0.029	2.28E-05	1.041	0.580	1.503	9.81E-06	1.96E-05

Expo, DNA methylation; Media, gene expression; Outcome, asthma; XY, the effect of DNA methylation on gene expression; XZ, the effect of DNA methylation on asthma; YZ, the effect of gene expression on asthma.

**Table S25 Mediation analysis using SMR: DNA methylation on asthma through gene expression in replication phase**

Expo Gene	Expo ID	Media Gene	Outcome	Outco ID	XY b	XY se	XY FDR	XZ b	XZ se	XZ FDR	YZ b	YZ se	YZ FDR	Media effect pro	lo Media pro	up Media pro	Media p	Media FDR
ITPKB	cg16265553	ITPKB	Asthma	F_T_2	-0.457	0.090	5.73E-07	0.204	0.074	1.52E-02	-0.184	0.078	4.30E-02	0.412	0.033	0.791	3.33E-02	3.33E-02
JAK2	cg13661497	JAK2	Asthma	F_T_2	-2.572	0.339	6.67E-14	-0.162	0.098	9.75E-02	0.119	0.036	1.63E-03	1.879	0.655	3.102	2.62E-03	5.24E-03

Expo, DNA methylation; Media, gene expression; Outcome, asthma; XY, the effect of DNA methylation on gene expression; XZ, the effect of DNA methylation on asthma; YZ, the effect of gene expression on asthma.

Table S26 Mediation analysis using TSMR: DNA methylation on asthma through gene expression in replication phase

Expo Gene	Expo ID	Media Gene	Outcome	Outco ID	XY b	XY se	XY FDR	XZ b	XZ se	XZ FDR	YZ b	YZ se	YZ FDR	Media effect pro	lo Media pro	up Media pro	Media p	Media FDR
ITPKB	cg16265553	ITPKB	Asthma	F_T_2	-0.457	0.081	1.48E-08	0.205	0.073	2.05E-02	-0.184	0.075	3.21E-02	0.410	0.053	0.768	0.025	2.45E-02
JAK2	cg13661497	JAK2	Asthma	F_T_2	-2.572	0.110	6.98E-120	-0.164	0.096	8.87E-02	0.109	0.032	7.57E-04	1.712	0.705	2.718	0.001	1.72E-03

Expo, DNA methylation; Media, gene expression; Outcome, asthma; XY, the effect of DNA methylation on gene expression; XZ, the effect of DNA methylation on asthma; YZ, the effect of gene expression on asthma.

Table S27 SMR analysis of lung gene expression on asthma

Source exposure	Gene exposure	outcome	ID.outcome	topSNP	A1	A2	b_SM	se_SM	p_SM	FDR_SM	p_HEIDI	nsnp_HEIDI	I2	pval_Q
Gtex	RBM6	Asthma	Finngen	rs4688755	A	G	-0.072	0.022	8.19E-04	2.46E-03	0.051	20	-	-
Gtex	RBM6	Asthma	TAGC	rs2245365	A	C	-0.042	0.031	1.66E-01	4.53E-01	0.578	20	-	-
Gtex	RBM6	Asthma	UKB	rs4688755	A	G	-0.059	0.016	3.25E-04	9.74E-04	0.200	20	-	-
Gtex	RBM6	Asthma	SUM	-	-	-	-0.060	0.012	4.68E-07	1.40E-06	-	-	0.000	0.724
Gtex	HOXB-AS1	Asthma	Finngen	rs6504340	G	A	0.023	0.030	4.40E-01	4.40E-01	0.173	20	-	-
Gtex	HOXB-AS1	Asthma	TAGC	rs6504340	G	A	0.045	0.044	3.02E-01	4.53E-01	0.842	20	-	-
Gtex	HOXB-AS1	Asthma	UKB	rs6504340	G	A	0.054	0.024	2.09E-02	2.09E-02	0.252	20	-	-
Gtex	HOXB-AS1	Asthma	SUM	-	-	-	0.043	0.017	1.20E-02	1.20E-02	-	-	0.000	0.711
Gtex	CEP95	Asthma	Finngen	rs17650301	C	A	-0.186	0.083	2.45E-02	3.68E-02	-	-	-	-
Gtex	CEP95	Asthma	TAGC	rs17650301	C	A	-0.054	0.118	6.46E-01	6.46E-01	-	-	-	-
Gtex	CEP95	Asthma	UKB	rs17650301	C	A	-0.237	0.077	2.15E-03	3.22E-03	-	-	-	-
Gtex	CEP95	Asthma	SUM	-	-	-	-0.184	0.051	3.10E-04	4.64E-04	-	-	0.000	0.432

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis.

Table S28 TSMR analysis of lung gene expression on asthma

Source exposure	Gene exposure	Outcome	ID.outcome	Method	nsp	b	se	pval	FDR	or	or_lci95	or_uci95	I2	pval_Q
Gtex	RBM6	Asthma	Finngen	Wald ratio	1	-0.072	0.021	6.83E-04	2.05E-03	0.931	0.893	0.970	-	-
Gtex	RBM6	Asthma	TAGC	Wald ratio	1	-0.040	0.031	1.97E-01	4.60E-01	0.961	0.904	1.021	-	-
Gtex	RBM6	Asthma	UKB	Wald ratio	1	-0.059	0.016	2.55E-04	3.83E-04	0.943	0.914	0.973	-	-
Gtex	RBM6	Asthma	SUM	-	-	-0.060	0.012	3.73E-07	1.12E-06	0.942	0.920	0.964	0.000	0.692
Gtex	HOXB-AS1	Asthma	Finngen	Wald ratio	1	0.023	0.030	4.38E-01	4.38E-01	1.023	0.965	1.085	-	-
Gtex	HOXB-AS1	Asthma	TAGC	Wald ratio	1	0.044	0.043	3.07E-01	4.60E-01	1.045	0.960	1.138	-	-
Gtex	HOXB-AS1	Asthma	UKB	Wald ratio	1	0.054	0.023	1.63E-02	1.63E-02	1.056	1.010	1.104	-	-
Gtex	HOXB-AS1	Asthma	SUM	-	-	0.043	0.017	9.58E-03	9.58E-03	1.044	1.011	1.079	0.000	0.704
Gtex	CEP95	Asthma	Finngen	Wald ratio	1	-0.186	0.072	9.59E-03	1.44E-02	0.830	0.721	0.956	-	-
Gtex	CEP95	Asthma	TAGC	Wald ratio	1	-0.054	0.117	6.44E-01	6.44E-01	0.947	0.753	1.192	-	-
Gtex	CEP95	Asthma	UKB	Wald ratio	1	-0.237	0.057	3.03E-05	9.08E-05	0.789	0.706	0.882	-	-
Gtex	CEP95	Asthma	SUM	-	-	-0.197	0.042	2.29E-06	3.44E-06	0.821	0.757	0.891	0.000	0.369

nsp, the number of SNPs; CI, confidence intervals; I2, I2 statistic assessing the heterogeneity of meta-analysis; pval\_Q, p-value of Cochran's Q test of meta-analysis.

**Table S29 Phenoscanner: Identifying Instrumental Variables Related to Outcomes and Confounding Factors**

Source	Gene.exposure	ID.exposure	SNP	A1	A2	trait	ancestry	b	se	p
Blood	ETS1	ENSG00000134954	rs55836957	A	C	Eosinophil count	European	-0.027	0.004	8.91E-10
Blood	ETS1	ENSG00000134954	rs55836957	A	C	Eosinophil percentage of granulocytes	European	-0.024	0.004	2.25E-08
Blood	ETS1	ENSG00000134954	rs55836957	A	C	Eosinophil percentage of white cells	European	-0.025	0.004	8.84E-09
Blood	ETS1	ENSG00000134954	rs55836957	A	C	Allergic disease	European	-0.049	0.007	1.94E-12
Blood	JAK2	cg02405213	rs11789744	A	G	Eosinophil count	European	0.031	0.004	5.56E-15
Blood	JAK2	cg02405213	rs11789744	A	G	Eosinophil percentage of granulocytes	European	0.024	0.004	2.07E-09
Blood	JAK2	cg02405213	rs11789744	A	G	Eosinophil percentage of white cells	European	0.028	0.004	1.64E-12
Blood	JAK2	cg02405213	rs11789744	A	G	Neutrophil percentage of granulocytes	European	-0.023	0.004	1.23E-08
Blood	JAK2	cg02405213	rs11789744	A	G	Platelet count	European	-0.025	0.004	6.10E-10
Blood	JAK2	cg02405213	rs11789744	A	G	Sum eosinophil basophil counts	European	0.031	0.004	1.09E-14

**Table S30 TSMR/SMR analysis of blood gene expression on asthma after removing SNP related to outcomes or confounding factors**

Gene.exposure	ID.exposure	Outcome	ID.outcome	Method	b	se	pval	or	or_lci95	or_uci95	hetero_pval	ple_pval	p_HEIDI	nsnp_HEIDI
cg02405213	JAK2	Asthma	UKB	TSMR/IVW	-0.024	0.011	2.76E-02	0.976	0.955	0.997	0.074	0.951	-	-
ENSG00000134954	ETS1	Asthma	UKB	TSMR/IVW	0.464	0.080	5.73E-09	1.590	1.360	1.859	0.723	-	-	-
ENSG00000134954	ETS1	Asthma	UKB	SMR	0.486	0.117	3.12E-05	1.626	1.293	2.044	-	-	2.74E-02	10

HEIDI: heterogeneity in dependent instruments; nsnp, the number of SNPs; hetero\_pval, p-value of Cochran Q test assessing heterogeneity of MR analysis; ple\_pval, p-value of MR-Egger regression examining horizontal pleiotropy effect of MR results.

