



Supplementary Information for

DNA methylation signatures in airway cells from adult children of asthmatic mothers reflect subtypes of severe asthma

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Supplementary Methods

Inclusion and Exclusion Criteria

Subjects with asthma met the following criteria: (1) a physician's diagnosis of asthma; (2) either (a) a fall in baseline FEV₁ ≥20% at ≤25 mg/ml methacholine in subjects whose FEV₁ predicted was ≥70% or (b) a ≥15% increase in baseline FEV₁ after inhalation of a bronchodilator (albuterol) or over time with treatment in subjects whose FEV₁ predicted was <70%; (3) at least two symptoms (cough, wheeze, and dyspnea); (4) fewer than three pack years of cigarette exposure; and (5) no conflicting pulmonary diagnoses. Controls had no current or previous diagnosis of asthma, normal spirometry, and no evidence of bronchial hyperresponsiveness by methacholine challenge tests. For both cases and controls, exclusion criteria included: (1) a smoking history of ≥10 pack years; (2) born premature (≥37 weeks gestation); (3) a history of conflicting pulmonary diagnosis, such as chronic obstructive pulmonary disease, allergic bronchopulmonary aspergillosis, cystic fibrosis, or Churg-Strauss syndrome; or (4) any medical contraindication to bronchoscopy.

Genotyping and QC

SNPs were genotyped using the Illumina Omni2.5-8v1A, Omni1MDuo, or HumanCore+Exome arrays. SNPs on each array were excluded with HWE $P < 0.0001$ within each ethnic group (European American, African American), MAF < 0.05 , SNP call rate < 0.95 , and subject call rates < 0.95 . Ancestry principal component analysis (PCA) was performed in R (*prcomp* function) using the 676 ancestry informative markers (1) that were available in our sample and overlapped with three representative populations from the HapMap release 3 (YRI, Yoruba in Ibadan, Nigeria; CEU, Utah residents with Northern and Western European ancestry; CHB, Han Chinese in Beijing, China).

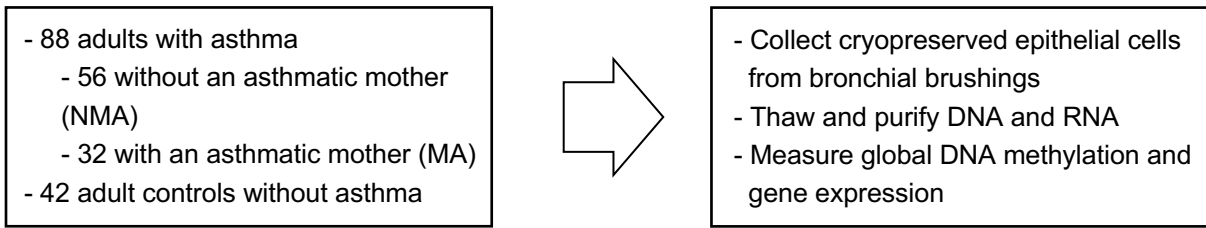
RNA extraction, sequencing, and QC

RNAs were extracted from bronchial epithelial cells and purified using the QIAGEN AllPrep DNA/RNA/miRNA Universal Kit (Hilden, Germany), following manufacturer's instructions. Quality and quantity assessment of RNA were measured at the University of Chicago Functional Genomics Core using an Agilent RNA 6000 Pico assay and the Agilent 2100 Bioanalyzer. cDNA libraries were constructed using the Illumina TruSeq RNA Library Prep Kit v2. RNA sequencing was performed at the University of Chicago Genomics Core on either the Illumina HiSeq 2500 or 4000 platforms.

For the RNA-seq data, potential sample contamination and sample swaps were assessed using VerifyBamID (2). No cross-contamination was detected. Two sample swaps between individuals were identified and corrected. Quality control checks were performed using FastQC (3). RNA sequences were then aligned and annotated to known RNA sequences using Spliced Transcripts Alignment to a Reference using STAR (4). Genes with low count data (< 1 CPM in at least 25% of the sample) and those on the X, Y, and mitochondrial chromosomes were removed. Samples containing $> 8M$ mapped RNA reads were kept, retaining 124 subjects for downstream analyses.

Raw counts were normalized using the trimmed mean of M-values (TMM) method (5). Mean-variance trend was adjusted using variance modeling in voom (6)). Technical sources of variation were identified using PCA for the RNA expression profiles. All potential confounders are described in the Methods section of the main paper.

Sample Composition and 'Omics



Analytical Pipeline

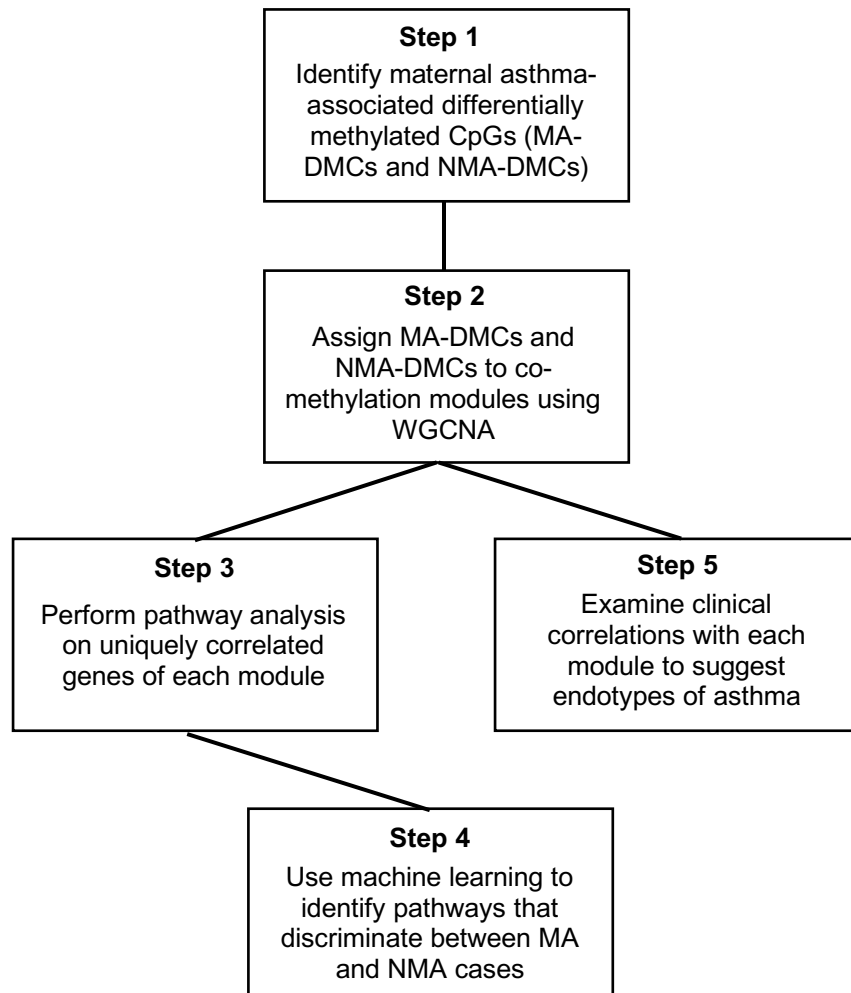


Figure S1. Overview of study design.

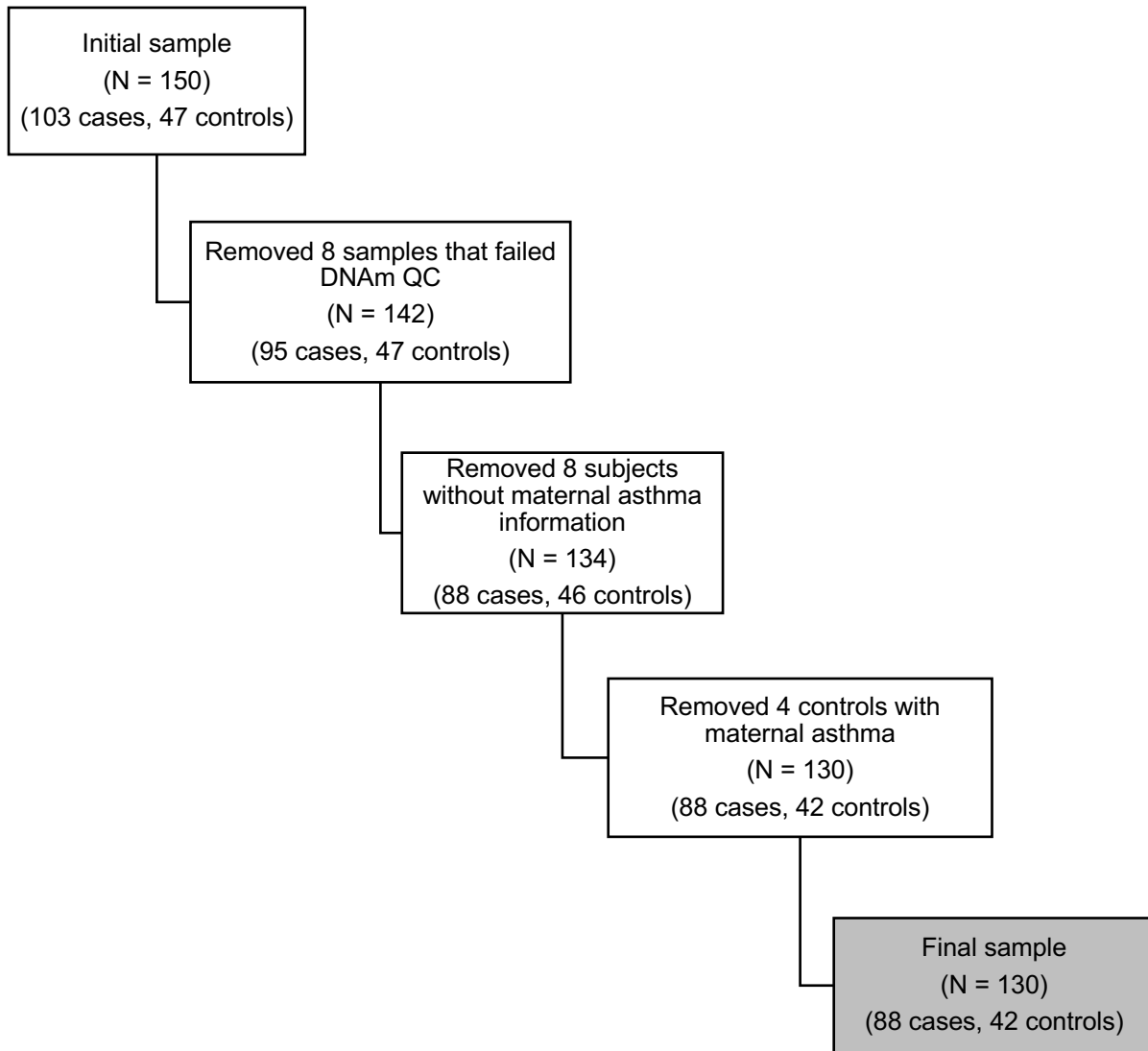


Figure S2. Flow chart of sample selection. Analyses included the 130 subjects shown in the shaded box, as described in **Table 1**.

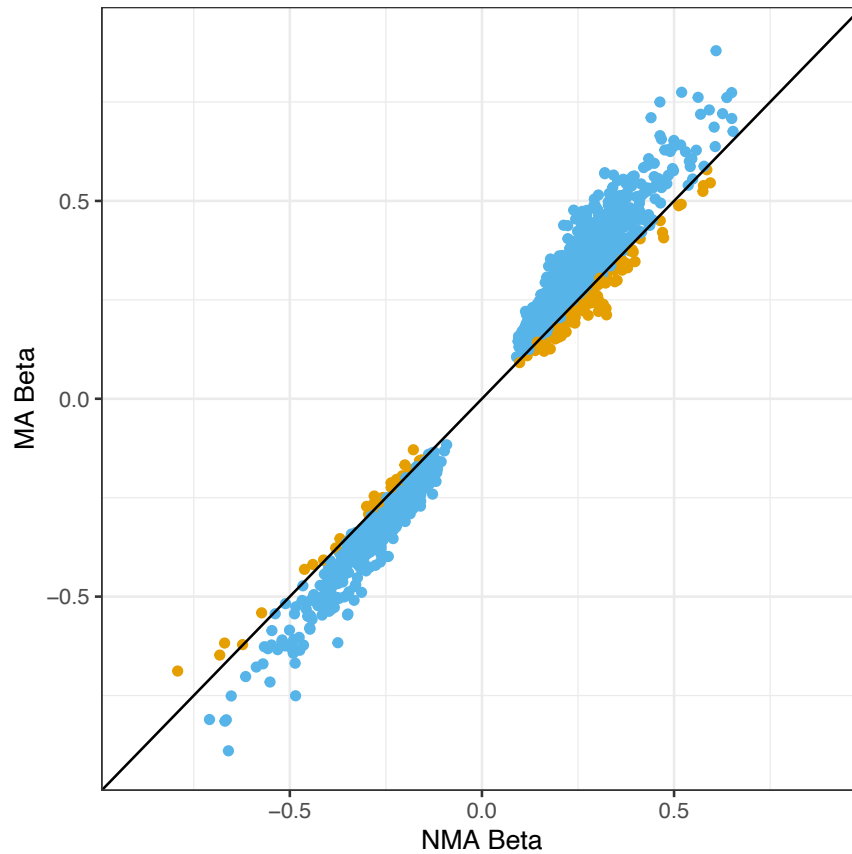


Figure S3. Scatterplot of beta coefficients for the 2,326 CpGs that were differentially methylated in all asthma cases compared to controls (shared DMCs). The beta coefficients are plotted in the NMA cases (x-axis) and MA cases (y-axis). The 2,147 (92.30%) DMCs with larger effects in MA cases compared to NMA cases are shown as blue points; the 179 DMCs (33.15%) with larger effects in NMA cases are shown as orange points. Paired signed-rank test; $P < 2.2 \times 10^{-16}$.

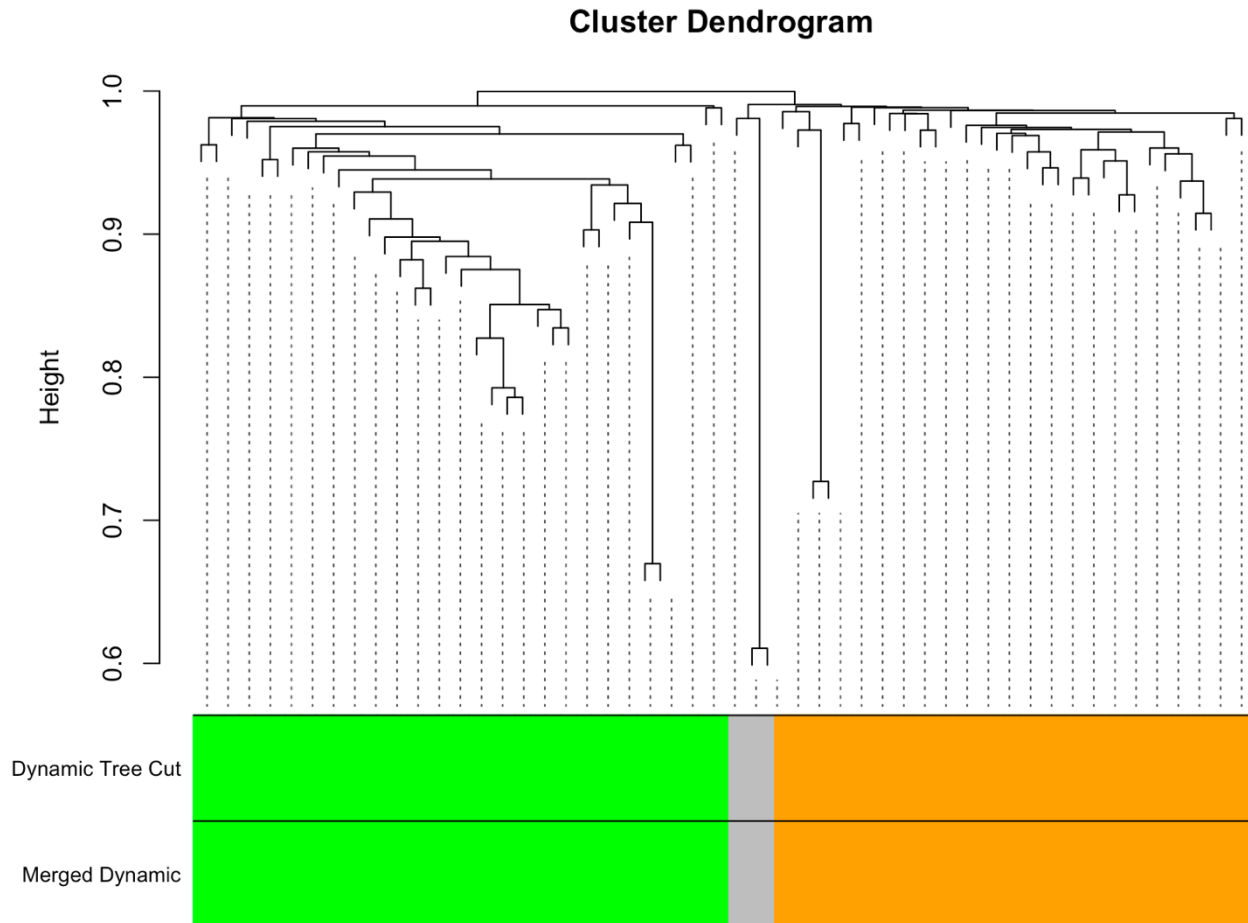


Figure S4. Cluster dendrogram of 69 non-maternal asthma-associated differentially methylated CpGs (NMA-DMCs). Of the 69 NMA-DMCs, 66 (95.65%) formed two co-methylation modules (green and orange). After merging closely related modules using the MergeCloseModules function, as implemented in WGCNA (7), the two co-methylation modules remained distinct (31 and 35 CpGs in each module). The average pairwise Spearman correlation for the CpGs within the orange and green modules was 0.28, 0.35, respectively. There were 3 (4.35%) remaining CpGs assigned to the gray module. The average pairwise Spearman correlation of the three remaining CpGs was 0.50. We only considered modules that contained at least 15 CpGs in our analyses (see **Materials and Methods**).

Cluster Dendrogram

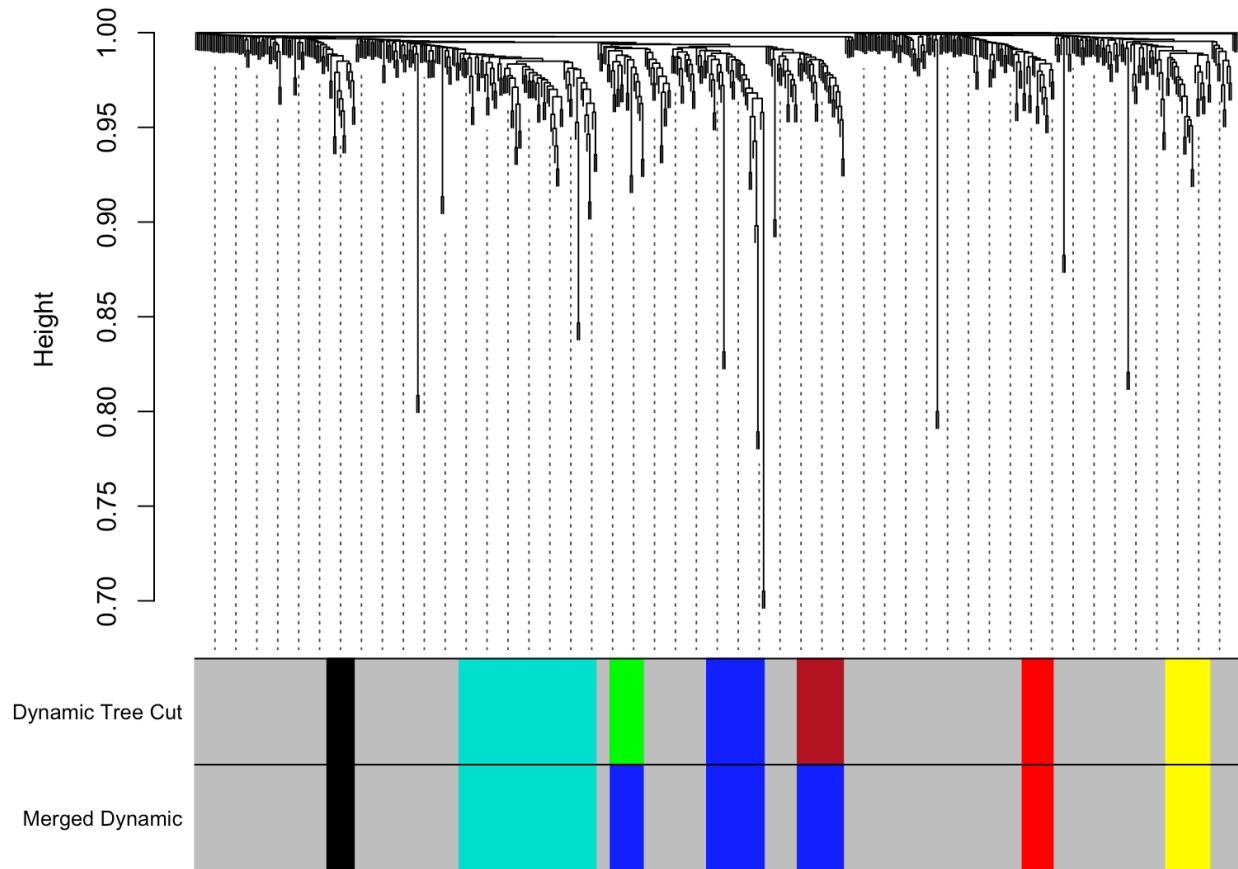


Figure S5. Cluster dendrogram of 554 maternal asthma-associated differentially methylated CpGs (MA-DMCs). Of the 554 MA-DMCs, 203 (36.64%) formed seven co-methylation modules (black, turquoise, green, blue, brown, red, and yellow). After merging closely related modules using the MergeCloseModules function, as implemented in WGCNA (7), five co-methylation modules remained (black, turquoise, blue, red, and yellow; 15 to 74 CpGs in each module). The average pairwise Spearman correlation for the CpGs within the black, turquoise, blue, red, and yellow modules was 0.61, 0.57, 0.52, 0.60, and 0.56, respectively. There were 351 (63.40%) uncorrelated CpGs assigned to the gray module (average pairwise Spearman correlation = 0.04). We only considered the five correlated modules in our analysis (see **Materials and Methods**).

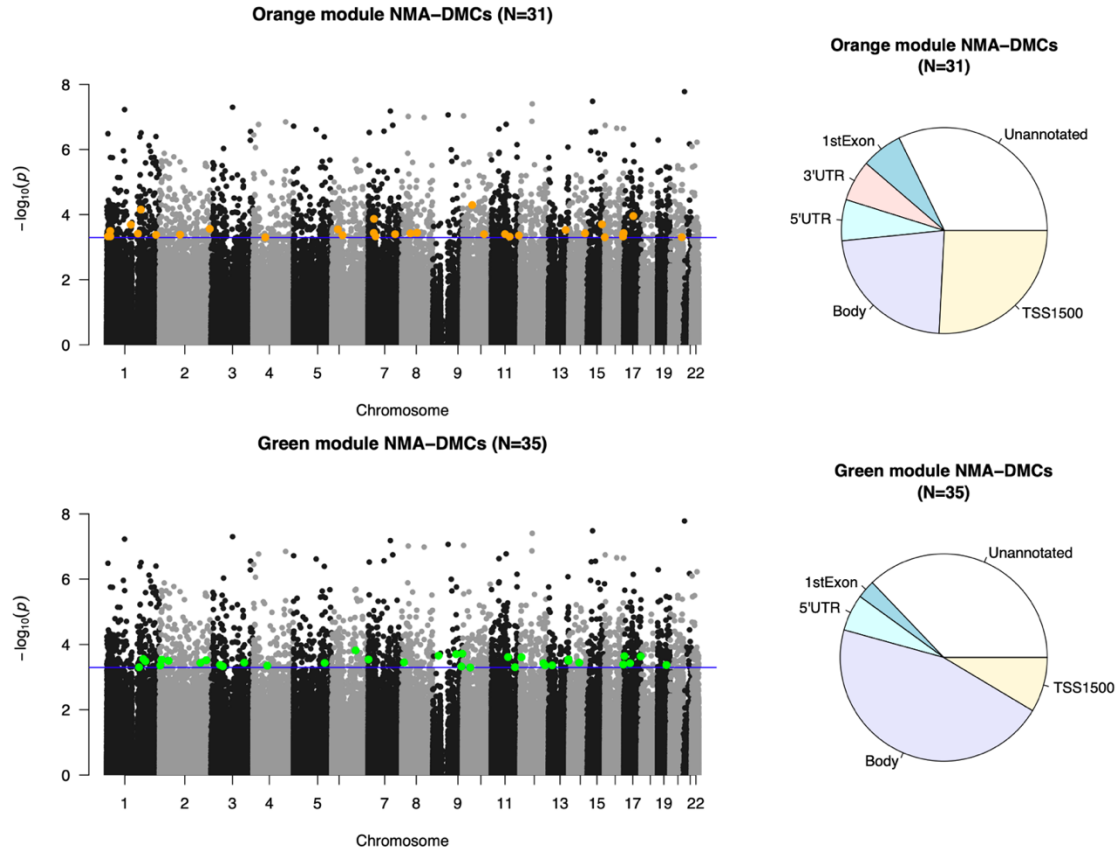


Figure S6. Distribution of NMA-DMCs in each co-methylation module across chromosomes and functional annotations. The y-axes show the $-\log_{10}(p)$ values corresponding to methylation differences between NMA cases and non-asthma controls. Blue horizontal lines show the q value threshold (FDR 0.10). Orange (upper) and green (lower) points are the CpGs assigned to the orange or green modules, respectively. The pie charts on the right show the distribution of the module-specific NMA-DMCs by functional annotations.

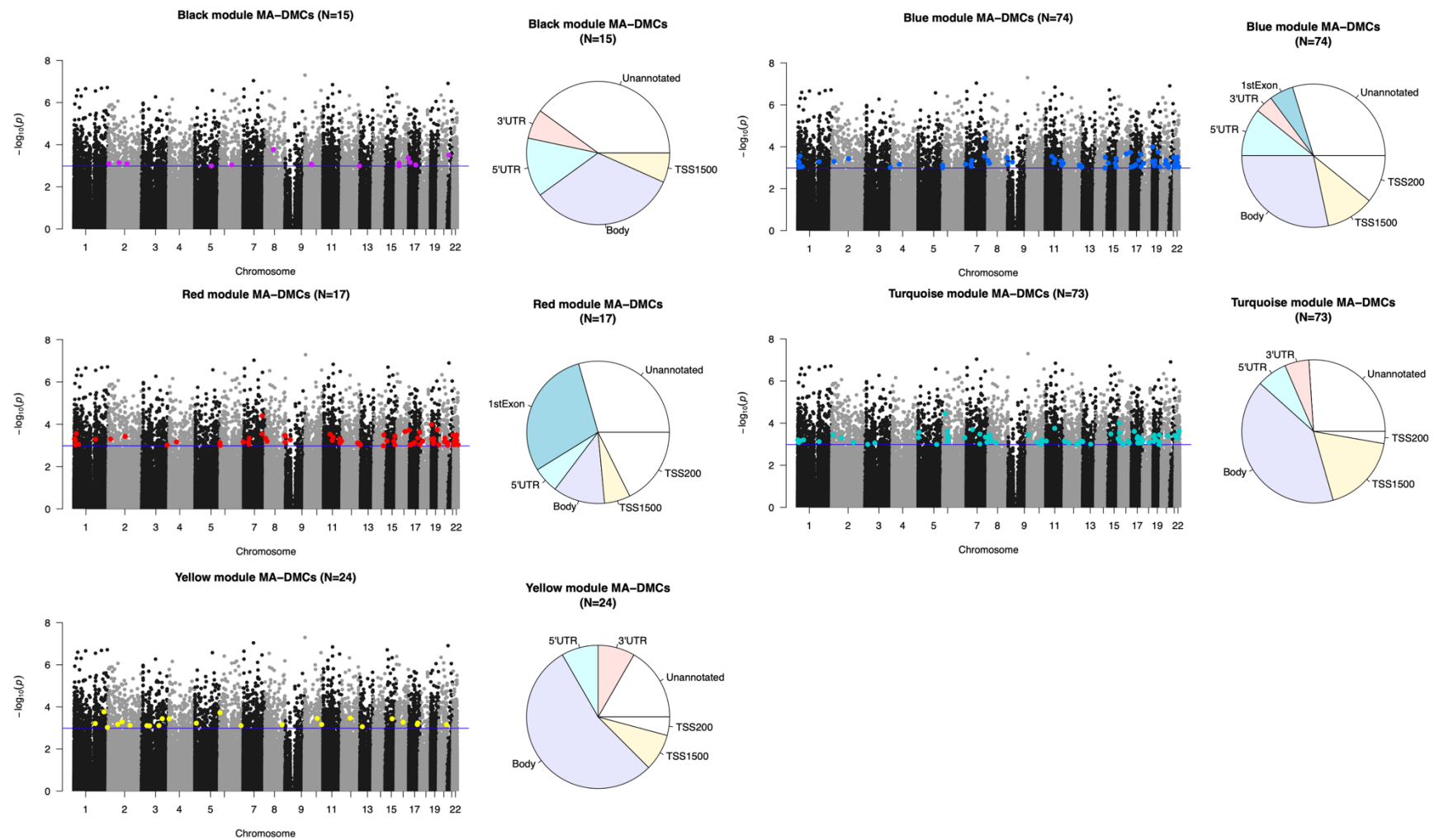


Figure S7. Distribution of MA-DMCs in each co-methylation module across chromosomes and functional annotations. The y-axes show the $-\log_{10}(p\text{-values})$ corresponding to methylation differences between MA cases and non-asthma controls. Blue horizontal lines show the q value threshold (FDR 0.10). Purple (upper left), blue (upper right), red (middle left), turquoise (middle right) and yellow (lower left) points are the CpGs assigned to the black, blue, red, turquoise, and yellow modules, respectively. The pie charts show the distribution of the module-specific MA-DMCs by functional annotations.

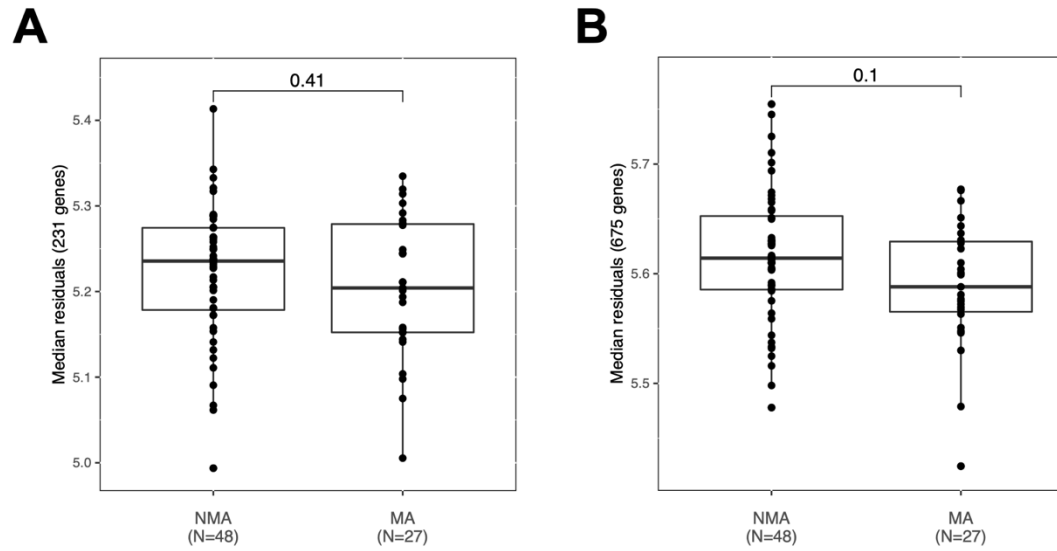


Figure S8. No difference in median and covariate-adjusted gene expression of the 231 genes of the black module and the 675 genes of the yellow module between NMA and MA cases. See list of genes in **Table S4**.

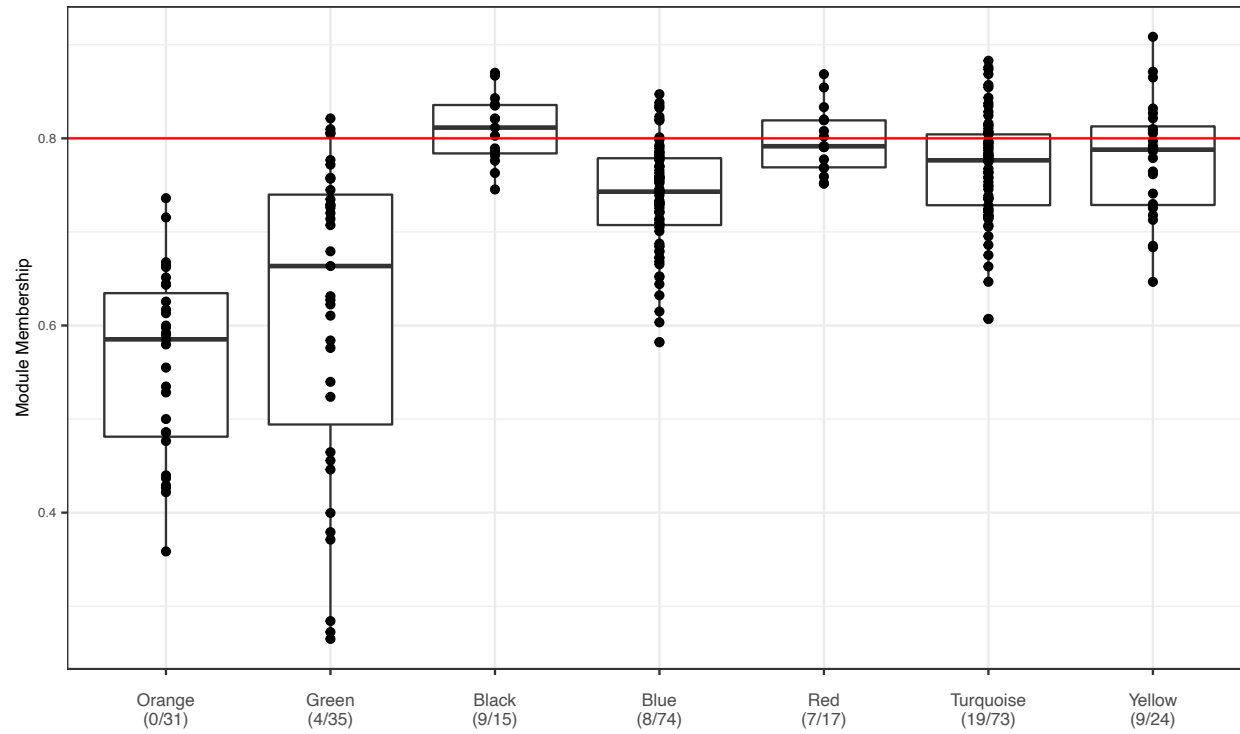


Figure S9. Selection of hub DMCs for each module (module membership > 0.80). The number of hub DMCs of the total DMCs are shown below each module. For each hub DMC, detailed functional information is in **Table S6**.

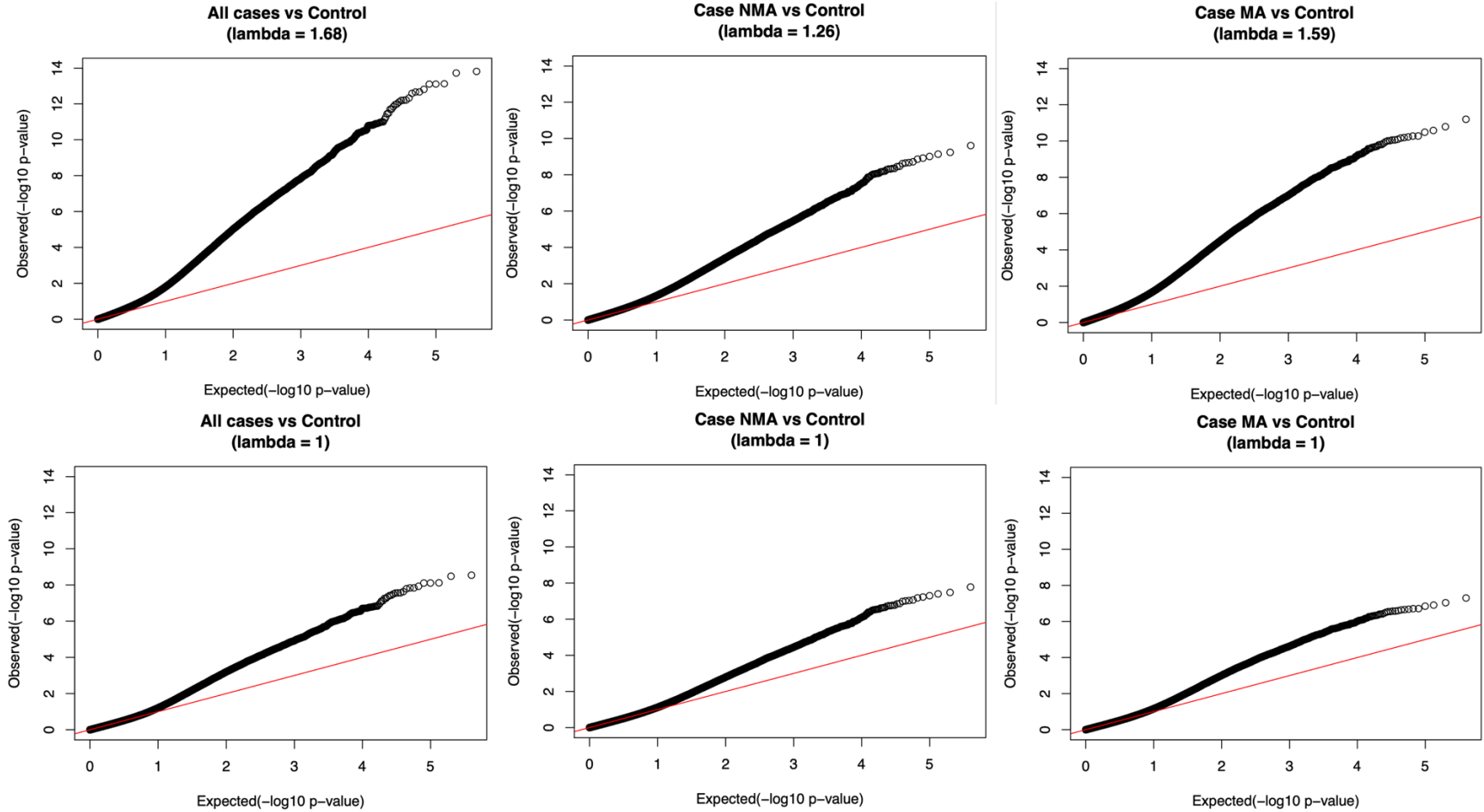
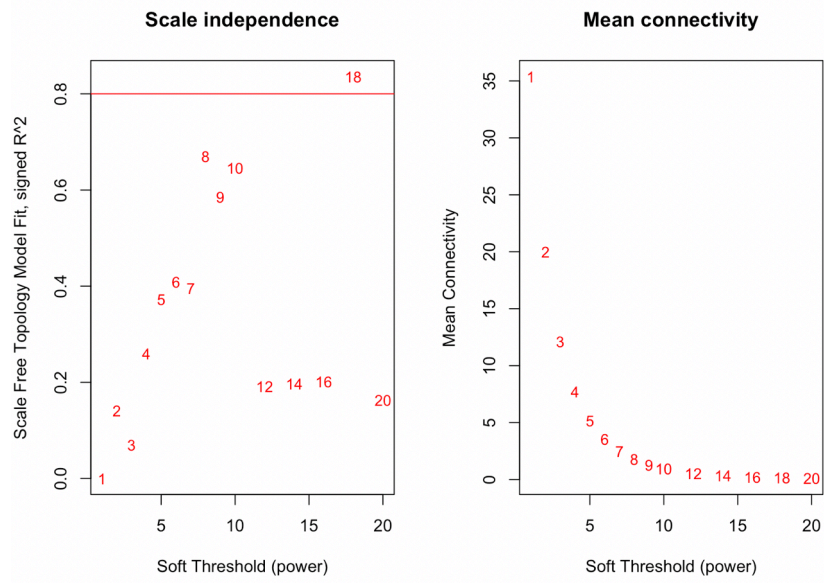


Figure S10. QQ plots before and after controlling for genomic inflation factors (λ) in each of the three DNA methylation analyses.

NMA



MA

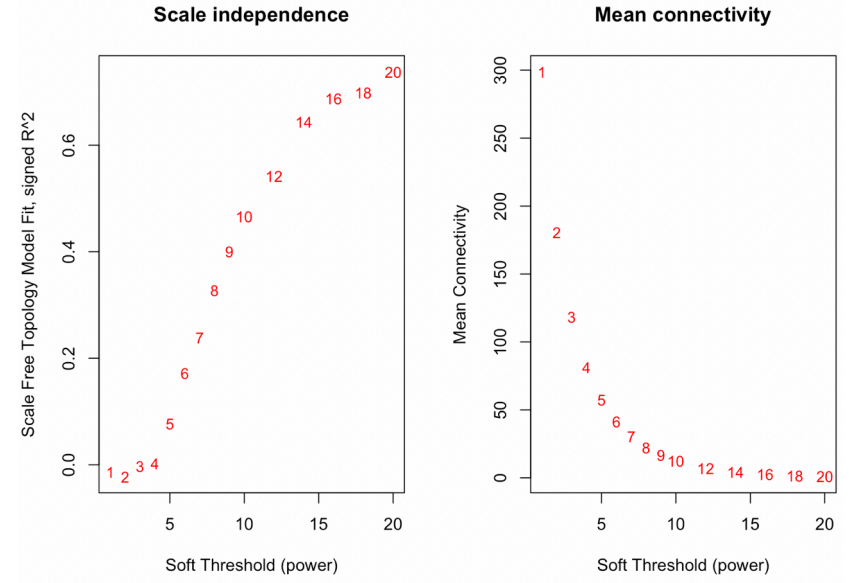


Figure S11. Selection of soft thresholding power for the NMA (left) and MA-focused (right) WGCNA analyses.

Table S1. Characteristics of 130 subjects at the time of bronchoscopy by risk group. Severity was defined by STEP classification (8) of mild, moderate and severe asthma. MA, Maternal Asthma; Af Am, African American; Eur Am, European American; ICS, Inhaled Corticosteroid; OCS, Oral Corticosteroid; FVC, Forced Vital Capacity. Pairwise comparisons were made between controls, asthma cases without an asthmatic mother (Case NMA) and asthma cases with an asthmatic mother (Case MA). Continuous variables were tested with a Wilcoxon rank-sum test and categorical variables were tested using a Fisher's Exact Test. ^A52 Case NMA subjects and 30 Case MA subjects had FeNO measurements. ^B41 controls and 55 Case NMA had BAL eosinophil measurements. ^C41 controls and 55 Case NMA subjects had BAL neutrophil measurements. ^D41 controls had blood eosinophil measurements. Significant p-values after Bonferroni-correcting for 15 tests (variables; $p < 3.33 \times 10^{-3}$) are bolded; ns, not significant ($p > 0.05$).

	Maternal Asthma Risk Groups			Comparisons		
	Control (N = 42)	Case NMA (N = 56)	Case MA (N = 32)	Control vs. Case NMA	Control vs. Case MA	Case NMA vs. Case MA
Covariates						
Age (mean yr ± SD)	37.45 ± 11.75	41.41 ± 12.24	37.56 ± 13.39	ns	ns	ns
Gender (% female)	62	79	66	ns	ns	ns
Ethnicity (%) (Af Am/Eur Am/ Other)	64/29/7	55/45/0	66/34/0	2.0x10⁻³	0.02	ns
% smoker at bronchoscopy	17	4	6	0.04	ns	ns
Clinical Measures						
ICS use (%)	-	75	75	-	-	ns
OCS use (%)	-	45	25	-	-	ns
STEP Category (% mild/% moderate/% severe)	-	22/23/55	28/25/47	-	-	ns
Mean FEV ₁ % Predicted (± SD)	95.36 ± 11.63	75.45 ± 19.73	70.41 ± 18.15	6.6x10⁻⁸	9.7x10⁻⁸	ns
Mean FEV ₁ /FVC (± SD)	0.82 ± 0.05	0.73 ± 0.10	0.83 ± 0.48	9.3x10⁻⁶	2.7x10⁻⁵	ns
Median total serum IgE (IU/mL) (lower, upper quartile)	56.50 (22.00, 169.00)	117.50 (22.00, 305.25)	156.50 (70.25, 626.75)	ns	6.3x10 ⁻³	ns
Median FeNO (ppb) (lower, upper quartile) ^A	14.00 (10.50, 17.75)	23.50 (13.00, 45.75)	27.00 (13.25, 54.75)	2.5x10⁻³	2.9x10⁻³	ns
Median BAL eosinophilia (%) (lower, upper quartile) ^B	0.0 (0.0, 0.4)	2.9 (1.5, 5.6)	3.6 (1.5, 7.1)	7.0x10⁻¹³	5.2x10⁻¹¹	ns
Median BAL neutrophilia (%) (lower, upper quartile) ^C	4.9 (3.0, 5.9)	5.2 (4.2, 6.8)	3.5 (2.2, 6.4)	ns	ns	0.04
Median blood eosinophilia (cells/μl) (lower, upper quartile) ^D	70 (100, 170)	170 (70, 283)	225 (108, 323)	ns	8.4x10⁻⁴	ns
Mean Body Mass Index (± SD)	28.52 ± 5.71	34.64 ± 8.83	33.68 ± 10.48	4.5x10⁻⁴	0.04	ns

Table S2. Genes that were uniquely correlated (FDR < 0.10) with the two NMA-associated and five MA-associated co-methylation module eigenvectors.

Module (# of genes)	Unique genes
Orange (N = 115)	<p><i>GRIK2, WNT16, C10orf143, SERPINE2, TSHZ3, RTEL1, MARCHF4, RPS6KA5, NAB2, RGS1, HDC, RETREG1, SPECC1L, GRASP, SHC2, NOB1, PIP4K2B, ZNF329, GSR, ZNF740, HS3ST1, PMP22, ZMAT4, ERLIN1, TMEM79, SOX30, ST8SIA4, WSB2, RASAL2, E2F7, TCP11L2, BCO2, H3C8, TAB2, NOS2, MCAM, IFRD2, WDR61, POLD3, ARMC10, SMAP1, ING5, KNOP1, MYO3A, DLX4, STK40, MGA, ALG10B, PAQR3, WDR82, ZNF555, DPH2, PTPRJ, CDC16, SERPINF2, NBL1, HDHD5, KRT19, ABCA1, ARL13B, TMEM52, CPEB4, DHX9, PLIN5, OAZ2, KCNE4, GALK1, BCAS1, LAMC1, PRXL2B, NDUFA4L2, ATP8B2, RALGAPA1, ZNF620, AATF, PLD6, POSTN, ZNF846, TTLL6, STOX2, VASN, C1orf74, PLA1A, NFU1, GTF3C4, FAM184A, ZNF613, ZNF766, BAHCC1, SLC2A8, ITGA6, MTHFSD, GTSE1, MTNR1A, NBPF10, FBL, OTUD4, UBXN2A, ZNF155, TJP1, C14orf93, C15orf40, WIPF2, ZDHHC16, GTF2IRD1, DTL, FEN1, JCHAIN, ATP6V0D1, MYCL, ELL3, RAB33B, IQGAP1, ELOVL5, HHLA2</i></p>
Green (N = 110)	<p><i>CAPN13, MYLIP, LRRC17, KRT10, RAPGEFL1, RNASEL, CTSV, NRCAM, SOX21, ADCY2, SF3B3, CANX, TNRC6C, BCAT1, SNX25, CXXC4, PPIF, COL17A1, TMEM243, EML1, C6orf141, NDUFAF6, NAA60, MED29, CHKB, SYT7, DHTKD1, ARHGEF37, SNRNP200, CACNG8, TBCD, TXNIP, ZBTB46, DENND2C, H2BC11, IP6K3, MFSD6, GLG1, THBS1, LSM2, DPF2, ZBTB5, ZNF117, ITFG1, SNX9, AGPAT5, RNF43, PCDHB14, PHF2, TP53BP1, RPL18A, HNRNPAB, TSTD2, CSRP2, MSMB, LAMA4, WDR4, TFCP2, ZNF280B, OCLN, OLFML1, MEX3D, PROM1, SPON2, CPM, LMLN, TMEM141, PPP1R13L, FHL2, TRNP1, TMEM64, NEO1, SEMA4F, LRMDA, DCAF5, THNSL2, TXN, TMEM116, COX7A2, TFAP4, HSPB7, ETFB, NR4A1, AGPS, ARHGAP20, HSF2BP, SLC44A2, SORCS2, TMPPE, SARS2, ARHGEF4, RGCC, SMO, SMO4, SDR39U1, UQCRFS1, APBA1, OSBP, CHCHD10, GRHL2, SLC6A16, EMC1, ZNF345, CEACAM19, CAVIN2, FIGN, BCAR3, C1orf53, ATG4B, DHRS1</i></p>
Black (N = 794)	<p><i>PSMG3, NAA30, FBXL13, SLC4A11, C12orf57, GSS, U2AF1L4, PARD6B, STAP2, SLC35E3, YIPF4, SGSM3, DPY19L4, GPN3, TMEM128, CPEB2, IFITM3, SPIN1, FAM237B, PHIP, THOC6, BCKDHB, AEBP2, LRRC57, N4BP2, CCDC126, WDR17, TFAM, ZYG11B, TGOLN2, SRSF8, CRKL, RIN1, AGAP2, DPH7, HSD17B12, SEC22C, PAXX, ALKBH8, KIAA0825, BORCS7, WWTR1, ZAP70, HACE1, ITGAV, CREBRF, SPAST, METTL15, ZMYND19, ZC3H12A, ZMIZ2, RO60, EXOC6B, PPP1R12C, PLPBP, BMPR1B, AIMP2, GET1, ZBTB41, NRXN3, NBEAL2, MAD2L2, ZNF529, SEPTIN1, PGLS, SLC35F5, C9orf64, NELL2, AKAP10, GYS1, HEXD, HOXC4, CORO1A, TRMT5, SCAMP1, SMAD4, SLC25A28, CXXC1, ANKRD26, SCRIB, PSMD13, FAM189B, SIT1, PI4K2B, SAMD10, TMEM134, MBD3, PLEKHF1, EID1, ADH5, CEP97, FBXL17, OGFR, SDR42E1, ZNF221, WRN, CYP20A1, ZFAND2B, RNF111,</i></p>

RBBP5, PDLIM5, CD3E, CARF, PRPF31, DEGS1, EIF2B4, ZFR, C1orf226, TRIB2, CEP44, MICALL2, ZFAND4, C5orf51, HDAC10, MARCHF6, HYOU1, TMEM214, CYTH2, DPH6, CSNK1G2, TCEA1, ZNF264, PEF1, SLC25A27, SH3BP1, ZNF776, FAM126B, ZNF721, SKP2, SEC24B, ETFBKMT, SBF1, SPTY2D1, LMBRD2, UHRF1BP1L, SPOCK2, MFSD4B, SMIM14, BTN3A3, UBALD1, LNX2, AP2A2, RB1CC1, CST3, AATK, TMEM41B, DCP1A, TMED8, FNIP1, CD3D, ARID4B, TRIM2, CALR, OSBPL11, FAM227B, DAAM1, NFAT5, DDX11, AP1B1, ARFRP1, EIF3B, TRIM33, OTUD7B, WDR11, PIH1D1, UBQLN4, GPR85, RAB21, IMPAD1, PUS10, CARM1, SQOR, DPP8, ABTB2, EVI5, RFX3, NPRL2, CLPP, FBXL3, S100A2, UGDH, CXCR6, RAB34, MPP3, SNRNP48, SMAD2, NAA16, E4F1, BCKDK, CEP112, AUP1, GDPGP1, C1D, CISD3, TUBA4A, DDX56, TMEM51, ZNF383, NMRAL1, NEK7, HGH1, MTMR10, SMAD9, AGGF1, PRR22, B3GNT10, LYRM7, CLCN3, KIFC1, ZNF843, HARS2, FXYD3, ARHGAP5, BTBD6, GCC2, METTL1, PRKCI, MOGS, PSMB10, PCBD2, ZNF579, GPALPP1, FBXL4, GP9, TAF1C, ALG3, CHMP3, PTPN4, CDC40, EXOC8, MIB2, FZR1, BEND7, ZFYVE16, WDR41, MANEA, ZDHHC20, OLFML3, LRRC29, RPRD1B, SIAH1, UTP23, CD8A, SEPTIN9, MYO9B, NR2F6, PELP1, JMY, PTGR2, DENND6A, PSMD4, AP1M1, TMEM184C, ZNF619, CTDSPL2, ATF2, TBCB, ARMH3, TSC2, DIXDC1, OSBPL8, ANKRD36, WDR7, TLCD4, RCOR3, CSTB, TBX21, TTC33, SIRT6, PAFAH1B3, PLEKHA3, BTF3L4, ZNF654, NDOR1, FRA10AC1, JADE1, MICAL3, ZNF708, ROPN1B, ADRM1, ATF7IP, PRRX2, USP8, DTWD2, PCYT2, CTBP1, TSC22D4, SATB1, JAKMIP1, MTAP, XRCC3, SPATA13, ZNF277, RFC3, CEBPZOS, ELF1, ATP2C1, LIMD2, PGGT1B, CLUH, DNAJC30, PCNP, GFI1, CDC42EP1, RHOG, PDLIM1, ZNF566, CERT1, MED13, PRDM5, ARIH1, RBM48, ULK1, NOVA1, ZNF780B, CCDC110, CACNA1A, ARL2, MICU2, AGL, TMEM30A, NUP43, DBR1, CCL5, ORMDL2, ZNF720, SGMS2, NARS2, MINDY1, TIMM50, CHD1, DNAJB4, GIMAP1, TPP2, CNIH3, ABHD13, NRBP1, TMEM106B, ANO5, UQCRC1, CAMTA1, RC3H1, FNDC3A, ZBTB26, MARK2, DNAJC14, EDF1, CCSAP, SAMD13, PIK3CA, EXOSC4, MED17, CD247, RASIP1, KLHL20, C19orf73, GIMAP7, CAT, PLXNB1, KDM7A, EVA1C, ANKAR, TIMM23, MOAP1, PKN2, PSMB3, RPRM, QPCTL, CFBF, FBXO16, HBS1L, CCDC152, SMG1, ANKUB1, TSPAN31, CD2, ZNF829, SDF4, B4GALT7, ODF3B, ALG10, TAF1B, SHQ1, CHCHD5, PDCD1, GTF2I, YIPF5, TMEM68, FBXW9, PGRMC2, KIF2A, EHMT1, CACTIN, ZNF606, SF3A2, RECQL5, NOC2L, PRR14, CAPN7, PDIA4, METTL26, FAM168B, ABI3, MAPK8IP3, ZDHHC17, HNRNPH3, PNKD, MCM8, HBP1, PPM1K, GRSF1, MRPL55, URI1, ROR2, GPR137, STK11, VPS41, MRM1, R3HDM2, VPS28, POLR2E, GCFC2, ICAM3, ARCN1, KCNAB1, PYCARD, DMXL1, VAV3, ACBD5, ANAPC16, CLDN4, PCNX3, SEPTIN8, CC2D1B, ZNF800, OTUB1, SELENOW, DGKZ, TNNC1, SKIL, FAM207A, LENG8, ERO1B, SPATA5, HRAS, ETV4, CARNMT1, MNT, THEM6, SH2D2A, ABCC1, RAPGEF6, CDC73, MAP3K2, NSD2, PDE4C, PYGB, TRIM11, PTPN11, PHF10, MLST8, WIZ, MRPL28, TRH, DRC7, RFESD, GPR171, CSNK2B, STMP1, RPN2, WDPCP, ATE1, IL32, MICOS13, GPSM1, FLOT1, SOX6, CCDC28A, DICER1, DIS3L, KLHDC1, PPP4C, SINHCAF, SHTN1, IDH3B, TRIP11, SH2B1, ABCB8, PUM1, COX11, HSPA4L, DGKH, TOM1L2, G3BP2, BDP1, FAM160B2, KIN, GLMP, UBA7, CRCP, ATXN3, PLEKHF2, SOS2, TASP1, FDXR, PPP2R5D, SRGAP2B, YARS2, BLVRB, SCML4,

	<p>IMP4, SPAG17, CLDN3, YTHDC1, PDE5A, PPP3CA, NAGPA, DPP9, CDK10, GRWD1, AP1G2, ELP4, MCHR1, GRINA, SCAF11, ZBTB25, MRPL10, BRWD1, SORT1, LCORL, RPN1, MOB3A, SCP2, ATP6V1A, WDR92, NHLRC2, TMOD3, TMEM179B, CDC34, FIGNL1, ZBTB18, GIPC2, TMEM54, ECHS1, ZNF664, NFKBIB, DHX36, TRAPPC12, TONSL, RNF11, SLC35A3, CACNG4, COPG1, BAIAP2, TTC21B, CTDNEP1, VCPIP1, FANCC, NCKAP1, MAST3, FZD3, TASOR, LRP8, SLC38A9, AKAP8L, PHOSPHO2, TRMT1, CDKAL1, ZDBF2, PPIP5K2, DENND4C, IKZF2, SELENOH, GCAT, ADAM17, DHX16, ZNF24, CCDC186, PDE6D, ASB4, SMTNL1, MCM5, ITSN2, SLMAP, MED16, MINK1, ZNF286A, CCDC97, ACTN4, COX6B1, TICAM1, DIPK2A, VPS4B, POLDIP2, RCSD1, GFPT1, PITPNM1, PRMT1, RNF138, ADPRM, NEK4, RNF170, CUL3, SF3B5, SMG5, SAMD8, GALK2, ZNF431, CTNNA1, MED7, NT5DC1, KIAA1586, MIER3, STX19, SZRD1, TAOK1, GTF3C5, HSD11B1L, PLIN3, DDHD2, KDF1, SMIM31, SCAND1, DCLRE1B, CDK17, LMNTD2, DNASE1L2, ATP13A2, GARS1, HAUS3, TSNAX, YPEL3, STOML2, PCMTD1, ANKRD52, ADSS2, SLC30A9, PEX16, TIMM13, RAB2A, TCTEX1D4, IFI27L1, KIF5B, CD200R1, CAPZB, RNH1, TMEM102, ARHGDI, SNAPC4, RGS14, AK9, DNAJB14, ZNF580, SNX13, DDX17, ROGDI, FAM216B, AZIN1, KIAA1328, GP2, USF1, AVL9, AGO1, ASXL3, FAM8A1, ATXN2L, H3-3A, ZBTB7B, PM20D2, LRRC45, DIS3, EIF3A, CDK18, PSMC3, DHX29, IPMK, PES1, SLF2, IGSF9B, SHOC2, NCF1, LY6G5C, PIGN, GGA3, HMCES, CCDC12, PRIMPOL, CCDC30, TTC6, ARID3A, ZMPSTE24, PEX1, PSPH, C1orf87, ATP6V1F, PIDD1, CASC3, TBC1D10B, AURKAIP1, AHI1, VPS72, GPLD1, TRAF2, RING1, EML5, SWAP70, ANKMY2, MKLN1, MXRA8, PHAX, TMEM212, MGAT4B, BCLAF1, CCDC69, FAAP100, ZNF880, SSBP4, TTC23L, MRPL37, PCDHB1, NCLN, CRELD1, MST1, PDRG1, SLC22A18, TMEM190, HP1BP3, C8orf82, RAD18, P3H4, PLAAT4, PPP3CB, VWA1, CMTM6, SEPTIN3, TEPP, AGBL3, PPP1R11, MRC2, IMPACT, ST3GAL6, SLC25A17, POLE3, GNS, WDR60, LAMTOR4, PRDX2, CXCR1, CYC1, FNTB, PPIC, BTBD9, CLASRP, ABCC5, TMEM160, UHMK1, NANP, ATG2A, LLGL2, ABHD3, COPS2, PFN2, ITGB7, C1orf35, NDUFS7, KPNA5, TUBGCP4, SNRNP70, FRMPD2, UBE3D, ZNF747, FAM98C, TELO2, PYGL, GRM5, BCDIN3D, GRPEL2, FCHO1, MRPS6, DOLK, PPIB, MRPS17, NFKBIA, CPSF2, TMEM250, MIF4GD, DNAJC24, ZNF260, ZMYM1, MED25, IGFBP7, PIN1, CDKN2AIP, SDCCAG8</p>
Blue (N = 234)	<p>B4GALT1, RAB7B, NOLC1, SLC35F6, HSPA2, MINPP1, MSLNL, SNAI2, ADAMTS17, TYW3, FOXA1, OVGPI1, RIBC2, KITLG, FOXN1, DLK2, RNF212, PDGFC, ITGB1, TINCR, SULT1E1, SMU1, RGMB, DIRAS3, ZFP64, ANKRD29, VIPAS39, PROB1, FAM114A2, RERG, SYTL2, RHEBL1, EIF5, SNF8, ADAMTSL5, RAB20, FAM171B, HYKK, ZFYVE27, HHATL, SUPT16H, SEPTIN2, CDK5RAP2, TET1, ZNF227, PSCA, BMP8A, S100A1, EPHB6, ELAC1, TMPRSS2, CAMLG, AFAP1L2, SULT1C2, TMEM9B, DST, RARB, KRT12, ATAD1, CYP2U1, MMP7, FOXA2, ARF3, AK6, SENP8, CYBRD1, BIK, SV2A, DSEL, EMID1, SELENOS, PNRC2, SNX5, ORC1, XRCC5, LRPPRC, MLIP, KLF5, PERP, RAB3B, TTC32, TMED3, CDK20, BLOC1S5, L3MBTL2, FIBIN, ICA1, KLHL9, BSCL2, ZZEF1, ZNF821, ZNF624, CD164L2, SYNGR1, TCF25, MAST4, STIMATE-MUSTN1, ESF1, HMGB1, FUT4, DERL3, ZNF473, TPST2, OCIAD2, GNPDA1, EPB41L5, PCDHGB4, DACT2, PIGQ, JAK1, ROM1, KCTD17, SEMA3D,</p>

	<p><i>INO80B, CNOT7, ABHD2, FJX1, FERMT2, ASPRV1, TAF5, CNOT11, SHH, VPS26A, ZNF595, FAM83F, STAMBPL1, SPNS1, THUMPD1, FHIT, LARGE1, USP1, INTS10, SPATA5L1, KIRREL1, FPR1, MMP25, PTPRG, C22orf15, TNS1, MED4, SLIT3, APPL2, RPS6KC1, LGALS9B, PPP1R1C, ADARB2, PRUNE1, SDHD, ACER3, TRMU, ABCB6, B3GALT2, FUT10, FANCE, ST20, EXOC2, LGALS9C, MARS2, CWC22, SLC16A8, ZNF420, POLR3D, ZFP2, CCDC200, VWA2, NEU4, MZF1, CDH5, LRRC23, MEGF6, DIO2, QRICH2, NUP54, SUPT5H, GSE1, ABCB4, FAM131A, NPIPB5, PDE7A, ZC3HC1, MEIS1, MYDGF, WDR20, RAB36, ISL1, NDUFB6, ELAVL1, VLDLR, NUP107, ZFP36L2, B3GLCT, FAM153B, ZNF512, ZNF552, CDC23, DRICH1, ZNF146, ZNF436, RILP, STK10, CCL3L1, TESK2, CAPN8, C11orf95, STK3, CR1L, DENND6B, FOXRED2, GJC2, DDX54, ELP3, LONP1, CSE1L, PUS7, MISP3, MAP2K3, LRRC31, TENT2, NOA1, LGALS8, PSMG4, TSPAN5, BRIX1, PTGR1, ITLN1, PCSK5, ZNF571, DIP2A, TGFB11, ABHD16A, ZNF181, CD36, VMAC, ZNF559</i></p>
Red (N = 46)	<p><i>TTC7B, DNHD1, ZNF839, PIAS3, EIF4EBP2, HNRNPUL2, CCNG2, CD83, OGDHL, SMUG1, PATL2, LPP, TDRD9, NPM2, CDHR2, ST6GALNAC5, SAR1A, SNIP1, PLXDC2, TIMP2, TACC2, COLCA2, MKS1, APOC1, LHFPL6, MEX3C, DEPDC5, CLASP1, AGAP9, SLC12A2, LANCL2, RBM27, TMEM130, DNAAF1, POLRMT, FNDC3B, KCNK15, EPC2, ERG28, FN1, DDAH2, ANAPC5, PLEKHA2, WASHC1, CBFA2T3, ELP6</i></p>
Turquoise (N = 85)	<p><i>IFIT2, MILR1, CCR2, HLA-DRB5, FCGR2B, LTB, CSF1R, IL21R, CXCL10, ADGRG5, PLXND1, SYT11, CAPN2, PRKG2, PALD1, SFMBT2, ASB2, CSF1, ATP10A, LAG3, COL3A1, AADAC, NPW, APBA2, BBS5, SALL4, CALCOCO2, C1S, LMNB1, AOA, FNBP1, TLR10, TNFSF14, CARD9, ADSS1, FKBP15, A2M, HLA-DOA, ZNF609, RASSF5, DPYD, FYB1, HLA-DPB1, PTPN7, LRRN1, CNTLN, ADAR, LCP2, GPR18, CGREF1, TTYH2, ST8SIA1, CRTAM, PFDN6, SIRPG, ARHGAP25, TNFRSF11A, PCED1B, PPM1M, TMEM86A, QPRT, CD209, ANG, SLC26A4, CD74, STK33, OPTN, EPB41, DOCK10, IFI44L, AKR1C3, JAK2, CALHM6, RGS7BP, ANKRD39, LAX1, CCR5, HLA-DRA, HLA-DMA, CSF3, IGSF11, CXCL9, SYNPO2, IL4I1, CLEC10A</i></p>
Yellow (N = 391)	<p><i>NAAA, C2orf50, TNC, TNFRSF10B, SERPINB4, NOP53, LSM14B, NEURL1B, AK2, CMTM8, SLC16A11, ATXN1, IFI16, FAR2, IRX3, RPS3, RPL7A, STOM, ANAPC15, DNAJC17, RPL3, ANKRD45, MTFR2, SMIM35, APBB3, GBP6, AKAP6, BIRC5, MYH15, DMAC2L, RPL12, MTRF1, LAMC2, SLC5A8, EMC4, DHDDS, TRMT9B, DSTN, TAF11, EIF3F, AUH, FCGR3B, RPS20, CD55, ISCA2, FAM111B, RNF183, AURKB, EGLN2, GABRP, WDR62, DSP, RNF5, TIGD5, BORA, AKAP9, ST7, CEP85, CTF1, MPHOSPH8, NFIC, TRIM38, LDHA, NABP1, ALDH1A3, LNP1, RUFY4, FAM174A, ACAD8, RPL19, HMGN2, PLEK2, RPL6, RPL29, DPY19L1, SCRIN1, SLC8B1, TTC12, CYP51A1, KHDC1, CPT1B, RPL10A, PMM2, PPIP5K1, UBXN10, GLRB, XAF1, SOGA1, ENO4, ZNF133, CLEC2D, TOB2, ZNF32, TGM3, CEP55, TPK1, FBXO27, NFE2L3, ZNF562, SLC23A1, DTD1, FKBP14, STAT2, LMO1, RPL13A, ARHGAP44, EFCAB11, ADRB1, POC1B, CASS4, ARG2, NBAS, KRTCAP3, CPLANE2, RPLP0, PTGS2, TIMM22, MRFAP1, UTP20, PLPPR3, MUL1, CXCR2, LSMEM1, CD58, HEATR3, MOB3C, ATP6V1FNB, DDX47, PLEKHG4B, ST6GALNAC2, AK8, LRRIQ4, ATP4B, FILIP1, RPL32, DNM1L, MED30, VEPH1,</i></p>

BBS4, GALNT14, NFKBID, KIF20A, RAB4B, PSTPIP2, AURKA, SARAF, FAM118B, SUPT6H, TRAPPC9, JDP2, EPHX2, VEGFB, EEF1B2, RPS14, LPCAT3, SHOC1, RGS16, KLK11, P4HA2, RPS13, EFCAB6, SLC16A14, SETD7, MRPL9, HNRNPA0, PDGFA, HTRA1, TTC39A, PDK2, KHDC4, EGLN3, IVNS1ABP, RPL13, ANLN, RNF19A, SPRYD4, ECSIT, SH3PXD2B, ANKRD66, FARS2, LRRC69, KLF15, ZSCAN18, SP140L, PPA1, DSCAML1, CMC2, SAP30L, CLEC2B, CASP6, MBTPS1, ITPRIPL2, BACE2, FAM135A, FUCA2, PJVK, TAF6, SYTL3, RALBP1, TNFRSF10C, TRIM16, LDLRAD1, TMEM8B, GALNT5, IGF1R, RABIF, FBXO36, USP15, CPNE5, MCU, BUB1B, TOMM7, KDM1B, FYCO1, FBLN7, LNX1, ALPK3, C1RL, ZDHHC4, GNL3, YWHAQ, MCCC2, RND3, CCNI2, GAB2, MAP2K5, ERCC5, DMTN, RACK1, FPR2, ASPM, CKMT1A, SERGEF, ITPRID2, PTPRN2, RELB, FAM222B, DNAH6, FAM98A, ZC2HC1C, GNAZ, VWA5A, PARP14, TGIF1, APCDD1, SPAG7, MRPS18B, TMEM181, PRDM1, RPL30, SLC20A1, COL16A1, GRAMD1A, SHCBP1, C5orf49, COBL, NFKB2, NUPR2, NEK11, FKBP4, RPL37A, PANX2, PROM2, MRPL45, STIP1, C11orf21, WBP2, DMRTA1, KAT5, KBTBD8, ACSL3, BMP8B, GPR39, KCTD14, CDC42EP2, PRR18, AZU1, INPP5F, MAP3K8, ZNF200, MYL12A, AKIP1, SON, PLEKHD1, OAS1, AMPH, PLEKHB2, SAMD9, ZBTB7C, SPATA18, SKA3, WASF1, MGAT5, SEC31B, C1orf21, SOWAHA, TMEM14C, ZFYVE9, LOX, GCNT1, TIMM23B, KCNB1, TIGD3, ECT2, NBPF1, ITGB6, FAM86B1, VPS45, PDK1, TMEM203, MAB21L4, REM2, NUSAP1, SAMD12, PCSK9, CRY2, RPA3, TSTD1, GJB2, LARGE2, RNF10, DAAM2, SLC7A1, KIAA1671, ZNF841, TXNL4B, C6orf223, UNC119B, MPZL1, RHBDL3, TRIM31, MRPS23, LACTB2, RPSA, SDHC, PLEKHS1, CMAS, DYRK3, RBMS2, CDC42SE1, STMND1, COPS5, SRPK1, ADPRHL2, ATP5MC2, SYS1, REXO4, RPS5, C11orf97, GNAS, AK3, CEP152, TMEM117, DHX57, CDC6, HAS3, ARPC3, CFAP57, CSF3R, ITPKB, S100A5, RPS12, TIMM17A, DEPDC1, OXA1L, DDX28, GAPT, JHY, RASSF2, TAF7, PCLAF, NCAPD3, RARS1, PLAAT3, FBXW2, CCNE1, RDH10, RPS11, RAC2, RPLP1, ACAT2, CYP4F3, HACD4, GPSM2, TMEM106C, PITPNC1, ITK, TSC1, MTA2, GPX3, PXMP4

Table S3. Significant pathways for the genes that were correlated with the MA-associated black, turquoise and yellow co-methylation module eigenvectors. The uniquely correlated genes of each module (FDR < 0.10) were included as input for pathway analysis (TopFunn (9)). Eleven, 36, and 33 pathways were significantly enriched for the uniquely correlated genes of the black, turquoise and yellow modules, respectively, at an FDR-adjusted p-value of <0.10. No pathways were enriched for the uniquely correlated genes of the NMA-associated orange or green modules or the MA-associated blue and red modules. The 3, 16, and 18 pathways of the black, turquoise, and yellow modules that discriminated between NMA and MA cases using Random Forests are bolded and listed in **Table S4**.

Black module (794 uniquely correlated genes)

ID	Name	Source	P-value	FDR-adjusted P-value	# of input genes / # of total genes in annotation	Genes from input
1269649	Gene Expression	BioSystems: REACTOME	7.33E-07	1.91E-03	111 / 1844	<i>NR2F6, RPN1, RPN2, MRM1, PIDD1, FANCC, METTL1, CDC40, C1D, ZNF606, TRMT5, DHX16, CARM1, CASC3, TRMT1, SKIL, DIS3, ZNF529, MBD3, TRIM33, SNRNP48, LAMTOR4, PELP1, ZNF747, EIF3A, EIF3B, SNAPC4, SNRNP70, DCP1A, BDP1, SMG1, HBS1L, ARID4B, GARS1, ZNF619, PHAX, JMY, STK11, CRCP, IMP4, EIF2B4, AEBP2, CPSF2, MLST8, TCEA1, GCFC2, TAF1C, TAF1B, NUP43, SMG5, PRDX2, TFAM, DICER1, HARS2, PES1, ZNF566, H3-3A, ZNF431, ZNF721, ZNF664, U2AF1L4, TSC2, TSNAX, GTF3C5, RPRD1B, PIN1, PRMT1, ZNF264, MED17, MED7, EXOSC4, NRBP1, ZNF383, POLR2E, COX6B1, WRN, COX11, WWTR1, ATF2, THOC6, ZNF708, CSNK2B, ZNF221, SF3B5, RNF111, ZNF720, PRPF31, NOC2L, PSMB3, PSMB10, PSMC3, PSMD4, PSMD13, CDKAL1, ZNF776, ALKBH8, CDC73, MED13, ARID3A, AIMP2, MED16, RFC3, NARS2, YARS2, AGO1, MED25, EHMT1, SF3A2, SMAD2, ZNF286A, SMAD4</i>
M9904	T cell receptor signaling pathway	MSigDB C2 BIOCARTA (v7.3)	1.65E-05	1.53E-02	15 / 108	<i>VAV3, NFAT5, SOS2, NFKBIA, NFKBIB, CD3D, CD3E, CD247, CD8A, PDCD1, PIK3CA, HRAS, ZAP70, PPP3CA, PPP3CB</i>
M39843	Cancer immunotherapy by PD-1 blockade	MSigDB C2 BIOCARTA (v7.3)	1.76E-05	1.53E-02	7 / 23	<i>NFAT5, CD3D, CD3E, CD8A, PDCD1, ZAP70, PTPN11</i>
M19784	T Cell Receptor Signaling Pathway	MSigDB C2 BIOCARTA (v7.3)	3.77E-05	2.09E-02	9 / 44	<i>NFKBIA, CD3D, CD3E, CD247, PIK3CA, HRAS, ZAP70, PPP3CA, PPP3CB</i>
83080	T cell receptor signaling pathway	BioSystems: KEGG	4.01E-05	2.09E-02	14 / 103	<i>VAV3, SOS2, NFKBIA, NFKBIB, CD3D, CD3E, CD247, CD8A, PDCD1, PIK3CA, HRAS, ZAP70, PPP3CA, PPP3CB</i>

M13247	T Cytotoxic Cell Surface Molecules	MSigDB C2 BIOCARTA (v7.3)	5.32E-05	2.31E-02	5 / 12	CD2, CD3D, CD3E, CD247, CD8A
M16966	Stathmin and breast cancer resistance to antimicrotubule agents	MSigDB C2 BIOCARTA (v7.3)	7.85E-05	2.92E-02	6 / 20	CD2, CD3D, CD3E, CD247, UHMK1, RB1CC1
1269171	Adaptive Immune System	BioSystems: REACTOME	9.62E-05	3.13E-02	54 / 826	BTBD6, NCF1, FZR1, BTN3A3, AP2A2, AP1B1, HACE1, SEC24B, RNF138, CUL3, FBXW9, SIAH1, SKP2, CD200R1, ASB4, KLHL20, NFKBIA, NFKBIB, AP1M1, MLST8, CALR, CD3D, CD3E, CD247, CD8A, CDC34, TPP2, PDCD1, FBXL13, TSC2, UBA7, PIK3CA, HRAS, ICAM3, MIB2, ZAP70, PPP2R5D, RNF111, PSMB3, PSMB10, PSMC3, PSMD4, PSMD13, ITGAV, ITGB7, FBXL3, FBXL4, PTPN11, TRIM11, MRC2, KIF2A, KIF5B, AGO1, UBE3D
1269192	Class I MHC mediated antigen processing & presentation	BioSystems: REACTOME	1.39E-04	3.92E-02	30 / 376	BTBD6, NCF1, FZR1, HACE1, SEC24B, RNF138, CUL3, FBXW9, SIAH1, SKP2, ASB4, KLHL20, CALR, CDC34, TPP2, FBXL13, UBA7, MIB2, RNF111, PSMB3, PSMB10, PSMC3, PSMD4, PSMD13, ITGAV, FBXL3, FBXL4, TRIM11, MRC2, UBE3D
P00053	T cell activation	PantherDB	1.51E-04	3.92E-02	11 / 76	VAV3, SOS2, NFKBIA, CD3D, CD3E, CD247, PIK3CA, HRAS, ZAP70, PPP3CA, PPP3CB
M19422	IL 17 Signaling Pathway	MSigDB C2 BIOCARTA (v7.3)	1.83E-04	4.34E-02	5 / 15	CD2, CD3D, CD3E, CD247, CD8A
83059	mTOR signaling pathway	BioSystems: KEGG	2.41E-04	4.87E-02	16 / 151	FNIP1, ULK1, SKP2, NPRL2, LAMTOR4, SOS2, ATP6V1A, STK11, MLST8, ATP6V1F, TSC2, PIK3CA, HRAS, SLC38A9, TELO2, FZD3
M39602	Neurodegeneration with brain iron accumulation (NBIA) subtypes pathway	MSigDB C2 BIOCARTA (v7.3)	2.43E-04	4.87E-02	8 / 44	SCP2, ULK1, ATG2A, STK11, MLST8, ATP13A2, TSC2, RB1CC1
Turquoise module (85 uniquely correlated genes)						

ID	Name	Source	P-value	FDR-adjusted P-value	# of input genes / # of total genes in annotation	Genes from input
172846	Staphylococcus aureus infection	BioSystems: KEGG	8.68E-09	3.24E-06	7 / 56	<i>HLA-DMA, FCGR2B, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, C1S</i>
200309	Rheumatoid arthritis	BioSystems: KEGG	1.11E-08	3.24E-06	8 / 90	<i>CSF1, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, LTB, TNFRSF11A</i>
213780	Tuberculosis	BioSystems: KEGG	1.33E-08	3.24E-06	10 / 179	<i>JAK2, HLA-DMA, FCGR2B, HLA-DOA, CARD9, HLA-DPB1, HLA-DRA, HLA-DRB5, CD74, CD209</i>
83078	Hematopoietic cell lineage	BioSystems: KEGG	2.01E-08	3.68E-06	8 / 97	<i>CSF1, CSF1R, CSF3, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
M9809	Cytokine-cytokine receptor interaction	MSigDB C2 BIOCARTA (v7.3)	5.10E-08	7.47E-06	11 / 265	<i>CCR2, CSF1, CSF1R, CSF3, TNFSF14, CXCL10, IL21R, CXCL9, LTB, CCR5, TNFRSF11A</i>
83051	Cytokine-cytokine receptor interaction	BioSystems: KEGG	6.18E-08	7.53E-06	11 / 270	<i>CCR2, CSF1, CSF1R, CSF3, TNFSF14, CXCL10, IL21R, CXCL9, LTB, CCR5, TNFRSF11A</i>
M13950	Asthma	MSigDB C2 BIOCARTA (v7.3)	2.97E-07	3.10E-05	5 / 30	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
83120	Asthma	BioSystems: KEGG	3.52E-07	3.22E-05	5 / 31	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
1269200	MHC class II antigen presentation	BioSystems: REACTOME	6.20E-07	4.90E-05	7 / 103	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, LAG3, CD74</i>
842771	Inflammatory bowel disease (IBD)	BioSystems: KEGG	6.76E-07	4.90E-05	6 / 65	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, IL21R</i>
1269175	Generation of second messenger molecules	BioSystems: REACTOME	7.67E-07	4.90E-05	5 / 36	<i>HLA-DPB1, HLA-DRA, HLA-DRB5, LCP2, FYB1</i>
1469482	Th17 cell differentiation	BioSystems: KEGG	8.04E-07	4.90E-05	7 / 107	<i>JAK2, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, IL21R</i>
M18615	Allograft rejection	MSigDB C2 BIOCARTA (v7.3)	8.84E-07	4.98E-05	5 / 37	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>

83123	Allograft rejection	BioSystems: KEGG	1.01E-06	5.30E-05	5 / 38	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
169642	Toxoplasmosis	BioSystems: KEGG	1.16E-06	5.68E-05	7 / 113	<i>JAK2, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CCR5</i>
M3126	Leishmania infection	MSigDB C2 BIOCARTA (v7.3)	1.25E-06	5.70E-05	6 / 72	<i>JAK2, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
144181	Leishmaniasis	BioSystems: KEGG	1.35E-06	5.77E-05	6 / 73	<i>JAK2, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
M13519	Graft-versus-host disease	MSigDB C2 BIOCARTA (v7.3)	1.50E-06	5.77E-05	5 / 41	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
83124	Graft-versus-host disease	BioSystems: KEGG	1.50E-06	5.77E-05	5 / 41	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
217173	Influenza A	BioSystems: KEGG	1.76E-06	6.07E-05	8 / 173	<i>JAK2, HLA-DMA, HLA-DOA, CXCL10, HLA-DPB1, HLA-DRA, HLA-DRB5, ADAR</i>
83074	Antigen processing and presentation	BioSystems: KEGG	1.86E-06	6.07E-05	6 / 77	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CD74</i>
M12617	Type I diabetes mellitus	MSigDB C2 BIOCARTA (v7.3)	1.91E-06	6.07E-05	5 / 43	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
83095	Type I diabetes mellitus	BioSystems: KEGG	1.91E-06	6.07E-05	5 / 43	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
1269310	Cytokine Signaling in Immune system	BioSystems: REACTOME	2.68E-06	8.17E-05	15 / 763	<i>CCR2, JAK2, CSF1, CSF1R, CSF3, TNFSF14, CXCL10, HLA-DPB1, HLA-DRA, HLA-DRB5, LTB, CCR5, TNFRSF11A, ADAR, IFIT2</i>
377873	Herpes simplex infection	BioSystems: KEGG	2.91E-06	8.52E-05	8 / 185	<i>JAK2, TNFSF14, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CD74</i>
M39693	Ebola Virus Pathway on Host	MSigDB C2 BIOCARTA (v7.3)	3.14E-06	8.84E-05	7 / 131	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CLEC10A, CD209</i>
M615	Intestinal immune network for IgA production	MSigDB C2 BIOCARTA (v7.3)	3.33E-06	9.03E-05	5 / 48	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
1470924	Interleukin-10 signaling	BioSystems: REACTOME	3.70E-06	9.33E-05	5 / 49	<i>CCR2, CSF1, CSF3, CXCL10, CCR5</i>

128760	Intestinal immune network for IgA production	BioSystems: KEGG	3.70E-06	9.33E-05	5 / 49	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
M16004	Antigen processing and presentation	MSigDB C2 BIOCARTA (v7.3)	4.07E-06	9.92E-05	6 / 88	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CD74</i>
M39398	Allograft Rejection	MSigDB C2 BIOCARTA (v7.3)	4.35E-06	1.03E-04	6 / 89	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CXCL9</i>
M4741	Systemic lupus erythematosus	MSigDB C2 BIOCARTA (v7.3)	4.66E-06	1.07E-04	7 / 139	<i>HLA-DMA, FCGR2B, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, C1S</i>
M13103	Autoimmune thyroid disease	MSigDB C2 BIOCARTA (v7.3)	4.98E-06	1.11E-04	5 / 52	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
1458885	Th1 and Th2 cell differentiation	BioSystems: KEGG	5.27E-06	1.14E-04	6 / 92	<i>JAK2, HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
83121	Autoimmune thyroid disease	BioSystems: KEGG	5.48E-06	1.15E-04	5 / 53	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
153910	Phagosome	BioSystems: KEGG	9.15E-06	1.85E-04	7 / 154	<i>HLA-DMA, FCGR2B, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CD209</i>
125138	Viral myocarditis	BioSystems: KEGG	9.35E-06	1.85E-04	5 / 59	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
M6910	Cytokines and Inflammatory Response	MSigDB C2 BIOCARTA (v7.3)	1.09E-05	2.10E-04	4 / 29	<i>CSF1, CSF3, HLA-DRA, HLA-DRB5</i>
M12294	Viral myocarditis	MSigDB C2 BIOCARTA (v7.3)	2.17E-05	4.07E-04	5 / 70	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5</i>
M39363	Type II interferon signaling (IFNG)	MSigDB C2 BIOCARTA (v7.3)	2.94E-05	5.38E-04	4 / 37	<i>JAK2, CXCL10, CXCL9, IFIT2</i>
M1473	B Lymphocyte Cell Surface Molecules	MSigDB C2 BIOCARTA (v7.3)	3.80E-05	6.50E-04	3 / 14	<i>FCGR2B, HLA-DRA, HLA-DRB5</i>

M22023	Antigen Processing and Presentation	MSigDB C2 BIOCARTA (v7.3)	3.80E-05	6.50E-04	3 / 14	<i>HLA-DRA, HLA-DRB5, CD74</i>
193147	Osteoclast differentiation	BioSystems: KEGG	3.82E-05	6.50E-04	6 / 130	<i>CSF1, CSF1R, FCGR2B, TNFRSF11A, LCP2, SIRPG</i>
83122	Systemic lupus erythematosus	BioSystems: KEGG	4.34E-05	7.22E-04	6 / 133	<i>HLA-DMA, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, C1S</i>
M6856	Hematopoietic cell lineage	MSigDB C2 BIOCARTA (v7.3)	6.22E-05	1.01E-03	5 / 87	<i>CSF1, CSF1R, CSF3, HLA-DRA, HLA-DRB5</i>
1269547	Chemokine receptors bind chemokines	BioSystems: REACTOME	8.32E-05	1.31E-03	4 / 48	<i>CCR2, CXCL10, CXCL9, CCR5</i>
1269330	TNF receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway	BioSystems: REACTOME	8.41E-05	1.31E-03	3 / 18	<i>TNFSF14, LTB, TNFRSF11A</i>
1269171	Adaptive Immune System	BioSystems: REACTOME	1.39E-04	2.12E-03	13 / 826	<i>HLA-DMA, FCGR2B, HLA-DOA, HLA-DPB1, HLA-DRA, HLA-DRB5, CRTAM, LAG3, CD74, ASB2, LCP2, FYB1, CD209</i>
1269174	Translocation of ZAP-70 to Immunological synapse	BioSystems: REACTOME	1.57E-04	2.34E-03	3 / 22	<i>HLA-DPB1, HLA-DRA, HLA-DRB5</i>
137998	TCR signaling in naive CD4+ T cells	BioSystems: Pathway Interaction Database	2.00E-04	2.92E-03	4 / 60	<i>RASSF5, HLA-DRA, LCP2, FYB1</i>
Yellow module (391 uniquely correlated genes)						
ID	Name	Source	P-value	FDR-adjusted P-value	# of input genes / # of total genes in annotation	Genes from input

1268690	Eukaryotic Translation Elongation	BioSystems: REACTOME	2.17E-19	3.95E-16	23 / 98	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, EEF1B2, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
M39495	Cytoplasmic Ribosomal Proteins	MSigDB C2 BIOCARTA (v7.3)	5.21E-19	4.74E-16	22 / 90	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268691	Peptide chain elongation	BioSystems: REACTOME	1.13E-18	5.12E-16	22 / 93	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269120	Viral mRNA Translation	BioSystems: REACTOME	1.13E-18	5.12E-16	22 / 93	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268681	Formation of a pool of free 40S subunits	BioSystems: REACTOME	1.83E-18	6.65E-16	23 / 107	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1339156	Selenocysteine synthesis	BioSystems: REACTOME	2.36E-18	7.16E-16	22 / 96	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268692	Eukaryotic Translation Termination	BioSystems: REACTOME	3.01E-18	7.81E-16	22 / 97	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
M189	Ribosome	MSigDB C2 BIOCARTA (v7.3)	5.81E-18	1.23E-15	21 / 88	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269718	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	BioSystems: REACTOME	6.09E-18	1.23E-15	22 / 100	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>

1268686	GTP hydrolysis and joining of the 60S ribosomal subunit	BioSystems: REACTOME	2.28E-17	3.77E-15	23 / 119	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268688	L13a-mediated translational silencing of Ceruloplasmin expression	BioSystems: REACTOME	2.28E-17	3.77E-15	23 / 119	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1339149	Selenoamino acid metabolism	BioSystems: REACTOME	4.95E-17	7.50E-15	23 / 123	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RARS1, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268680	Cap-dependent Translation Initiation	BioSystems: REACTOME	1.04E-16	1.35E-14	23 / 127	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268679	Eukaryotic Translation Initiation	BioSystems: REACTOME	1.04E-16	1.35E-14	23 / 127	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268689	SRP-dependent cotranslational protein targeting to membrane	BioSystems: REACTOME	1.77E-16	2.15E-14	22 / 116	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269716	Nonsense-Mediated Decay (NMD)	BioSystems: REACTOME	4.54E-16	4.86E-14	22 / 121	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269717	Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	BioSystems: REACTOME	4.54E-16	4.86E-14	22 / 121	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>

1268678	Translation	BioSystems: REACTOME	3.92E-15	3.96E-13	24 / 165	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPL10A, RPSA, EEF1B2, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269115	Influenza Viral RNA Transcription and Replication	BioSystems: REACTOME	8.08E-15	7.60E-13	22 / 138	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
83036	Ribosome	BioSystems: KEGG	8.35E-15	7.60E-13	23 / 154	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, MRPL9, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269109	Influenza Life Cycle	BioSystems: REACTOME	3.14E-14	2.71E-12	22 / 147	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1383086	Major pathway of rRNA processing in the nucleolus and cytosol	BioSystems: REACTOME	3.28E-14	2.71E-12	24 / 181	<i>DDX47, RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, UTP20, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1427846	rRNA processing in the nucleus and cytosol	BioSystems: REACTOME	1.39E-13	1.10E-11	24 / 193	<i>DDX47, RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, UTP20, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269108	Influenza Infection	BioSystems: REACTOME	1.45E-13	1.10E-11	22 / 158	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1383085	rRNA processing	BioSystems: REACTOME	4.30E-13	3.13E-11	24 / 203	<i>DDX47, RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, UTP20, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>

1270158	Metabolism of amino acids and derivatives	BioSystems: REACTOME	1.99E-10	1.40E-08	28 / 367	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, ARG2, ACAD8, AUH, MCCC2, RPL10A, CKMT1A, RARS1, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1269056	Infectious disease	BioSystems: REACTOME	7.51E-08	5.06E-06	25 / 393	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, RPL10A, TAF6, TAF7, TAF11, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268682	Formation of the ternary complex, and subsequently, the 43S complex	BioSystems: REACTOME	6.64E-07	4.32E-05	9 / 55	<i>RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPSA</i>
1268685	Ribosomal scanning and start codon recognition	BioSystems: REACTOME	2.17E-06	1.36E-04	9 / 63	<i>RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPSA</i>
1268684	Translation initiation complex formation	BioSystems: REACTOME	2.49E-06	1.51E-04	9 / 64	<i>RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPSA</i>
1268683	Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S	BioSystems: REACTOME	2.84E-06	1.67E-04	9 / 65	<i>RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, EIF3F, RPSA</i>
1268677	Metabolism of proteins	BioSystems: REACTOME	2.61E-05	1.48E-03	53 / 1631	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, ARG2, ACAD8, AUH, MCCC2, RPL10A, CKMT1A, RARS1, RPSA, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>
1268854	Disease	BioSystems: REACTOME	6.14E-05	3.38E-03	33 / 867	<i>RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, PDGFA, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, ZFYVE9, NEURL1B, MCCC2, GAB2, RPL10A, NFKB2, TAF6, TAF7, TAF11, RPSA, AKAP9, RNF5, RPL13A, RPL3, RPL6, RPL7A, RPL12, RPL13, RPL19</i>

1269649	Gene Expression	BioSystems: REACTOME	9.79E-05	5.24E-03	56 / 1844	<i>DDX47, MTA2, RPL30, RPL29, RPL32, RPL37A, RPLP0, RPLP1, RPS3, RPS5, RPS11, RPS12, RPS13, RPS14, RPS20, TSC1, TRMT9B, MED30, KAT5, BIRC5, PPA1, NABP1, FARS2, EIF3F, ZNF133, ZNF562, ZNF200, TNFRSF10C, TNFRSF10B, PRDM1, RPL10A, AURKA, NFIC, SUPT6H, HNRNPA0, UTP20, YWHAQ, TAF6, TAF7, TAF11, RARS1, SAP30L, CASP6, RPSA, CCNE1, TGIF1, EEF1B2, RPL13A, RPA3, RPL3, RPL6, RPL7A, RPL12, RPL13, AURKB, RPL19</i>
M180	Hypoxic and oxygen homeostasis regulation of HIF-1-alpha	MSigDB C2 BIOCARTA (v7.3)	3.56E-04	1.85E-02	4 / 19	<i>RACK1, COPS5, EGLN3, EGLN2</i>
M39529	Photodynamic therapy-induced NF-kB survival signaling	MSigDB C2 BIOCARTA (v7.3)	4.29E-04	2.17E-02	5 / 35	<i>BIRC5, PTGS2, NFKB2, EGLN2, RELB</i>
138033	Signaling by Aurora kinases	BioSystems: Pathway Interaction Database	1.01E-03	4.96E-02	2 / 3	<i>AURKA, AURKB</i>

Table S4. Maternal asthma-discriminatory pathways of the black, turquoise, and yellow modules. For each of the 11, 36, and 33 enriched pathways of the black, turquoise, and yellow modules, respectively, a per-individual median normalized and covariate-adjusted expression level was calculated for all expressed genes (CPM > 1 in at least 25% of subjects) in the pathway (3 to 1,844 per pathway). Random Forests selected pathways that discriminated between asthma cases with (MA; N=27) and without an asthmatic mother (NMA; N=48); 3 (black), 16 (turquoise), and 18 (yellow) discriminatory pathways were identified as having Mean Decrease in Accuracy > 1. There were 231, 535, and 675 unique genes in total for the black, turquoise, and yellow modules, respectively; a median score of the normalized and covariate-adjusted expression for each set of module-specific genes were compared between MA and NMA cases (**Fig. 2** in the main paper; **Fig. S8**).

Black module (231 expressed genes)

ID	Name	Source	Mean Decrease in Accuracy	Median Expression (NMA)	Median Expression (MA)	# of expressed genes / # of total genes	Expressed genes
M9904	T cell receptor signaling pathway	MSigDB C2 BIOCARTA (v7.3)	2.10	5.06	5.00	95 / 108	<i>KRAS, RAF1, PDCD1, AKT3, NRAS, MAP3K8, FOS, PDPK1, PIK3R3, PAK4, MAP3K14, GRB2, CBL, NCK1, RELA, PAK6, LCK, TEC, LCP2, CBL, CBLB, ZAP70, GSK3B, ITK, CHUK, RHOA, MALT1, JUN, RASGRP1, PTPN6, CD3D, CD3E, CD3G, CD247, CD4, MAPK14, PPP3CA, ICOS, MAPK12, PTPRC, PPP3CB, PPP3CC, CD8A, PPP3R1, CD8B, LAT, NFATC1, NFATC2, NFATC3, NFATC4, PIK3CA, PIK3CB, CD28, PIK3CD, PIK3CG, PIK3R1, NFKB1, CHP2, NFKBIA, NFKBIB, NFKBIE, GRAP2, HRAS, PAK1, PAK2, DLG1, AKT1, AKT2, CARD11, BCL10, VAV3, TNF, PRKCQ, PLCG1, MAPK1, MAPK3, IKKB, MAPK11, MAPK9, MAPK13, MAP2K1, MAP3K7, NFAT5, MAP2K2, CDC42, FYN, MAP2K7, PIK3R5, VAV1, VAV2, NCK2, CDK4, CHP1, SOS1, SOS2</i>

83059	mTOR signaling pathway	BioSystems: KEGG	2.21	5.30	5.35	131 / 151	<p><i>FNIP2, MAPKAP1, KRAS, RAF1, CAB39, SEH1L, ATP6V1A, ATP6V1B1, DDIT4, ATP6V1B2, ATP6V1C1, AKT3, ATP6V1E1, RNF152, LAMTOR2, NRAS, DEPTOR, FZD3, SLC38A9, SGK1, LAMTOR5, WNT3, PDPK1, RPS6, WNT5A, RPS6KA1, RPS6KA2, WNT7B, ATP6V1E2, RPS6KB1, RPS6KB2, PIK3R3, WNT10B, TBC1D7, WNT2B, INSR, WNT9A, PRR5, DVL1, DVL2, DVL3, GRB2, GRB10, ATP6V1G1, RICTOR, TSC1, ATP6V1F, TSC2, IRS1, WNT4, PTEN, SKP2, CLIP1, AKT1S1, WDR59, GSK3B, SLC3A2, RHEB, RRAGC, CHUK, FZD1, FZD4, RHOA, FZD6, FZD7, WNT5B, FZD8, FZD9, LPIN1, STK11, STRADB, NPRL2, ATP6V1H, IGF1R, LAMTOR4, RRAGD, BRAF, TELO2, PIK3CA, MTOR, PIK3CB, PIK3CD, STRADA, RRAGA, PIK3R1, FZD5, RPTOR, WNT3A, ATP6V1D, EIF4B, WNT16, EIF4E, PRKAA1, EIF4EBP1, PRKAA2, HRAS, NPRL3, MIOS, WNT10A, FLCN, LRP6, LRP5, LAMTOR3, PRKCA, FNIP1, PRKCB, TTI1, SLC7A5, AKT1, CAB39L, AKT2, DEPDC5, SESN2, TNF, ATP6V1C2, ULK1, MAPK1, MAPK3, TNFRSF1A, LAMTOR1, IKBKB, MLST8, MAP2K1, MAP2K2, FZD2, ULK2, WDR24, SEC13, SOS1, EIF4E2, SOS2</i></p>
M39602	Neurodegeneration with brain iron accumulation (NBIA) subtypes pathway	MSigDB C2 BIOCARTA (v7.3)	4.07	5.83	5.85	41 / 44	<p><i>ATG101, PIK3R4, DCAF17, ATG5, SCP2, STK11, CP, MAP1LC3A, PLA2G6, ATG16L1, ATG14, TSC1, FTL, TSC2, GTPBP2, WIPI1, ATG10, PANK2, ULK1, COASY, ATG2A, RB1CC1, DEPTOR, ACACA, MLST8, ATG7, BECN1, ATG3, ATP13A2, PIK3C3, MTOR, AKT1S1, ATG13, FA2H, RPTOR, ATG12, WIPI2, C19orf12, RHEB, PRKAA1, SPTLC1</i></p>
Turquoise module (535 expressed genes)							

ID	Name	Source	Mean Decrease in Accuracy	Median Expression (NMA)	Median Expression (MA)	# of expressed genes / # of total genes	Expressed genes
172846	Staphylococcus aureus infection	BioSystems: KEGG	1.16	5.03	4.67	44 / 56	<i>CFH, SELPLG, CFD, KRT10, FCGR1A, HLA-DMA, FCGR2A, HLA-DMB, FCGR2B, FCGR3A, FCGR3B, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, FPR1, FPR2, HLA-DRB5, ICAM1, FPR3, C1QA, C1QB, C1QC, C1R, C1S, C2, C3, C3AR1, C4A, C4B, C5, C5AR1, PLG, PTAFR, CFI, ITGAL, ITGAM, ITGB2, CFB, MASP2</i>
200309	Rheumatoid arthritis	BioSystems: KEGG	1.87	5.20	5.05	67 / 90	<i>TGFB1, TGFB2, TGFB3, ATP6V1A, ATP6V1B1, JUN, ATP6V1B2, ATP6V1C1, IL15, ATP6V1E1, ATP6V0B, ATP6V1H, IL18, ATP6V0A1, ATP6V0D1, CSF1, ANGPT1, ATP6V0E1, HLA-DMA, HLA-DMB, TNFSF13, HLA-DOA, HLA-DPA1, HLA-DPB1, CD28, HLA-DQA1, CD86, HLA-DQA2, HLA-DQB1, TNFSF13B, FOS, HLA-DRA, HLA-DRB1, ATP6V1D, ATP6V1E2, ACP5, HLA-DRB5, ICAM1, ATP6V0E2, TLR2, ATP6V0A4, TLR4, TCIRG1, CCL2, CCL3, CCL3L1, ATP6V1G1, CCL5, ATP6V1F, LTB, TNF, ATP6V1C2, MMP1, TNFRSF11A, CCL20, IL1B, ITGAL, CXCL6, CXCL5, CXCL1, CTSK, ITGB2, IL23A, CTSL, CXCL12, CXCL8, ATP6V0A2</i>

213780	Tuberculosis	BioSystems: KEGG	1.00	5.28	5.21	142 / 179	<p><i>HSPD1, IL10RA, IL10RB, RAF1, MYD88, IL12A, MRC1, TRADD, AKT3, SPHK2, ATP6V0B, TRAF6, IL18, ATP6V0A1, CEBPB, CEBPG, CALM1, HLA-DMA, HLA-DMB, CALM2, HLA-DOA, CALM3, HLA-DPA1, CALML3, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, CAMK2B, CAMK2D, HLA-DRA, CAMK2G, HLA-DRB1, CAMP, HLA-DRB5, SRC, CYP27B1, BAD, APAF1, RIPK2, FADD, CASP3, ARHGEF12, CLEC7A, BAX, IRAK2, TCIRG1, CASP8, CASP9, CASP10, LAMP1, RELA, BCL2, TLR6, CALML5, CR1, ITGAM, ITGAX, RFX5, CREB1, ITGB2, IL23A, RFXAP, CALML6, CREBBP, CD209, STAT1, BID, NOD2, TGFB1, TGFB2, RHOA, IFNGR1, TGFB3, IFNGR2, JAK1, JAK2, KSR1, MALT1, PLA2R1, CLEC4E, CORO1A, ATP6V1H, MAPK14, ATP6V0D1, PPP3CA, PPP3CB, MAPK12, PPP3CC, PPP3R1, FCER1G, FCGR1A, CD14, FCGR2A, CIITA, FCGR2B, FCGR3A, FCGR3B, PIK3C3, CARD9, SPHK1, MRC2, TIRAP, RFXANK, NFKB1, TLR1, TLR2, ATP6V0A4, TLR4, CYCS, NFYA, NFYB, NFYC, SYK, RAB7A, CD74, C3, LSP1, AKT1, AKT2, BCL10, TNF, CALML4, MAPK1, MAPK3, EEA1, TNFRSF1A, MAPK8, MAPK11, IL1B, MAPK9, MAPK13, CTSD, NOS2, RAB5A, RAB5B, PLK3, CTSS, EP300, HSPA9, RAB5C, ATP6V0A2</i></p>
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83078	Hematopoietic cell lineage	BioSystems: KEGG	3.38	4.37	3.97	70 / 97	<i>IL11RA, EPOR, ANPEP, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB5, CD55, ITGA6, ITGA1, ITGA2, ITGA3, ITGA4, ITGA5, CR1, ITGAM, TFRC, CD1A, CD1C, CD1D, CD1E, CD2, CD3D, CD3E, CD3G, CD4, CD5, CSF1, CD7, CSF1R, CD8A, CD8B, KITLG, CD9, CSF3, CSF3R, FCGR1A, CD14, CD19, MS4A1, CD22, IL1R2, CD33, CD34, CD36, CD37, CD38, CD44, CD24, CD59, TNF, MME, IL1B, IL1R1, KIT, IL4R, IL5RA, IL6R, IL7, IL7R, GP1BA, GP5, GP9</i>
M13950	Asthma	MSigDB C2 BIOCARTA (v7.3)	1.74	6.62	6.27	17 / 30	<i>TNF, FCER1A, MS4A2, FCER1G, EPX, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB5, CD40</i>
1469482	Th17 cell differentiation	BioSystems: KEGG	1.49	5.53	5.48	87 / 107	<i>IL12RB1, HIF1A, RARA, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, FOS, HLA-DRA, HLA-DRB1, HLA-DRB5, TBX21, GATA3, IRF4, RELA, LCK, RUNX1, IL23A, ZAP70, RXRA, RXRB, STAT1, STAT3, STAT5A, STAT5B, STAT6, CHUK, TGFB1, TYK2, IFNGR1, IFNGR2, JAK1, JAK2, JAK3, TGFB1, TGFB2, JUN, CD3D, CD3E, CD3G, CD247, CD4, MAPK14, PPP3CA, PPP3CB, MAPK12, PPP3CC, PPP3R1, LAT, NFATC1, NFATC2, NFATC3, MTOR, NFKB1, IL21R, NFKBIA, NFKBIB, NFKBIE, AHR, RORA, RORC, PRKCQ, PLCG1, MAPK1, MAPK3, IKBKB, MAPK8, MAPK11, IL1B, MAPK9, IL1R1, MAPK13, IL1RAP, IL2RB, IL4R, IL6R, IL6ST, SMAD2, SMAD3, HSP90AA1, SMAD4, IL27RA, HSP90AB1</i>

169642	Toxoplasmosis	BioSystems: KEGG	4.44	5.71	5.63	96 / 113	<i>IL10RA, IL10RB, MYD88, IL12A, AKT3, TRAF6, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, PDPK1, HLA-DRB1, HLA-DRB5, BAD, LAMA1, CASP3, LAMA2, LAMA3, LAMA4, ITGA6, LAMA5, LAMB1, LAMB2, BIRC2, CASP8, BIRC3, CASP9, LAMB3, LAMC1, LAMC2, TAB2, RELA, BCL2, BCL2L1, LY96, ITGB1, LDLR, STAT1, STAT3, PPIF, CHUK, TGFB1, TYK2, TGFB2, IFNGR1, TGFB3, IFNGR2, JAK1, JAK2, MAPK14, MAPK12, PIK3R6, CIITA, PIK3CG, NFKB1, NFKBIA, TLR2, NFKBIB, TLR4, CYCS, CD40, SOCS1, AKT1, AKT2, CCR5, GNAI1, GNAI2, TNF, GNAI3, TAB1, GNAO1, MAPK1, MAPK3, TNFRSF1A, IKBKB, MAPK8, MAPK11, MAPK9, MAPK13, MAP3K7, MAP2K3, HSPA1A, MAP2K6, HSPA1B, HSPA1L, HSPA2, NOS2, PIK3R5, HSPA6, HSPA8, ALOX5</i>
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217173	Influenza A	BioSystems: KEGG	1.86	5.74	5.69	137 / 173	<p>RAF1, MYD88, IL12A, DNAJB1, AKT3, MAP2K4, IL18, TRIM25, RAE1, TMPRSS13, DDX58, HLA-DMA, HLA-DMB, TNFSF10, HLA-DOA, HLA-DPA1, HLA-DPB1, CXCL10, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, TICAM1, NLRX1, HLA-DRB5, ICAM1, PIK3R3, ACTB, SOCS3, NUP98, CASP1, ACTG1, TMPRSS4, CASP9, OAS1, OAS2, OAS3, IRF3, IRF7, RELA, TNFRSF10D, XPO1, TNFRSF10C, TNFRSF10B, HNRNPUL1, TNFRSF10A, FAS, FASLG, ADAR, ATF2, CREBBP, GSK3B, STAT1, STAT2, NLRP3, IFNAR1, IFNAR2, IVNS1ABP, TYK2, IFNGR1, IFNGR2, JAK1, JAK2, IFIH1, IRF9, JUN, CPSF4, RSAD2, MAPK14, RNASEL, MAPK12, MAVS, CIITA, IKBKE, PIK3CA, PABPN1, PIK3CB, EIF2S1, PIK3CD, PIK3R1, FDPS, NXT1, PYCARD, FURIN, NFKB1, TBK1, NFKBIA, NFKBIB, TLR3, TLR4, CYCS, AGFG1, TMPRSS2, PRKCA, PRKCB, CCL2, AKT1, CCL5, AKT2, TNF, EIF2AK4, MAPK1, MAPK3, TNFRSF1A, PLG, EIF2AK1, IKBKB, MAPK8, MAPK11, IL1B, MAPK9, MAPK13, MAP2K1, MAP2K2, MAP2K3, HSPA1A, MAP2K6, HSPA1B, HSPA1L, MAP2K7, HSPA2, EIF2AK2, EIF2AK3, DNAJC3, HSPA6, DDX39B, HSPA8, IL33, EP300, NXF1, MX1, CXCL8, VDAC1, PML, KPNA1, KPNA2</p>
M615	Intestinal immune network for IgA production	MSigDB C2 BIOCARTA (v7.3)	2.18	4.74	4.53	30 / 48	<p>TGFB1, TNFRSF13C, IL15, IL15RA, LTBR, ICOS, ITGA4, CCL28, HLA-DMA, PIGR, TNFSF13, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, CD28, CXCR4, HLA-DQA1, CD86, HLA-DQA2, MADCAM1, HLA-DQB1, ITGB7, TNFSF13B, HLA-DRA, CXCL12, HLA-DRB1, HLA-DRB5, MAP3K14, CD40</p>

1470924	Interleukin-10 signaling	BioSystems: REACTOME	1.82	3.71	3.21	36 / 49	<i>TYK2, IL10RA, IL10RB, JAK1, CCR2, IL12A, LIF, IL18, CSF1, CSF3, IL1R2, CXCL10, CD86, FPR1, ICAM1, CCL2, CCL3, CCL3L1, CCR1, CCL4, CCL5, CCR5, TNF, CCL20, TNFRSF1A, PTAFR, TNFRSF1B, CCL22, IL1B, IL1R1, IL1RN, CXCL1, CXCL2, PTGS2, STAT3, CXCL8</i>
125138	Viral myocarditis	BioSystems: KEGG	3.02	6.23	6.19	47 / 59	<i>ABL1, ABL2, HLA-A, HLA-B, HLA-C, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, SGCB, CD28, HLA-DQA1, CD86, HLA-DQA2, PRF1, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB5, ICAM1, ACTB, HLA-E, EIF4G1, CYCS, CD40, EIF4G2, HLA-F, HLA-G, CD55, CASP3, LAMA2, DAG1, ACTG1, CASP8, CASP9, CCND1, CAV1, EIF4G3, ITGAL, FYN, ITGB2, CXADR, RAC1, RAC2, RAC3, BID</i>
M1473	B Lymphocyte Cell Surface Molecules	MSigDB C2 BIOCARTA (v7.3)	2.02	5.88	5.73	10 / 14	<i>CR1, ITGAL, FCGR2B, ITGB2, HLA-DRA, HLA-DRB1, HLA-DRB5, ICAM1, PTPRC, CD40</i>

193147	Osteoclast differentiation	BioSystems: KEGG	1.09	4.78	4.64	110 / 130	CYLD, AKT3, LILRB3, TRAF2, LILRA2, TRAF6, SPI1, CAMK4, LILRB2, FOS, FOSB, FOSL2, ACP5, PIK3R3, NCF1, MAP3K14, SOCS3, OSCAR, BLNK, LILRA6, GRB2, TAB2, NCF2, NCF4, RELA, RELB, SIRPB1, SIRPA, TNFRSF11A, LCK, PPARG, TEC, LCP2, CREB1, LILRB1, STAT1, STAT2, TNFRSF11B, GAB2, CHUK, IFNAR1, IFNAR2, SIRPG, TGFB1, TYK2, TGFB2, IFNGR1, IFNGR2, JAK1, TGFB1, TGFB2, TYROBP, IRF9, JUN, JUNB, JUND, MAPK14, PPP3CA, CSF1, PPP3CB, MAPK12, CSF1R, PPP3CC, PPP3R1, FCGR1A, NFATC1, FCGR2A, NFATC2, FCGR2B, FCGR3A, FCGR3B, PIK3CA, PIK3CB, PIK3CD, SQSTM1, PIK3R1, NFKB1, NFKB2, NFKBIA, MITF, TREM2, SYK, SOCS1, AKT1, AKT2, TNF, TAB1, PLCG2, MAPK1, MAPK3, TNFRSF1A, IKBKB, MAPK8, MAPK11, IL1B, MAPK9, FHL2, IL1R1, MAPK13, MAP2K1, MAP3K7, FYN, MAP2K6, CTSK, MAP2K7, LILRB5, LILRA5, RAC1, LILRB4, CYBA
1269330	TNF receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway	BioSystems: REACTOME	2.16	4.05	3.99	14 / 18	TNFRSF12A, TNFRSF13C, TNFSF14, TNFSF12, BIRC2, BIRC3, TNFSF13B, LTBR, TRAF2, TRAF3, TNFRSF11A, MAP3K14, CD40
1269174	Translocation of ZAP-70 to Immunological synapse	BioSystems: REACTOME	1.64	5.13	4.57	17 / 22	HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQA2, ZAP70, HLA-DQB1, PTPN22, HLA-DQB2, HLA-DRA, CD3D, HLA-DRB1, CD3E, CD3G, HLA-DRB5, CD247, CD4, LCK

137998	TCR signaling in naive CD4+ T cells	BioSystems: Pathway Interaction Database	3.93	4.77	4.64	56 / 60	<i>STIM1, RASSF5, MALT1, RASGRP1, ORAI1, PAG1, PTPN6, RAP1A, CD3D, CD3E, CD3G, TRAF6, PTPN11, CD247, CD4, PTPRC, CSK, CD28, CD86, MAP3K8, MAP4K1, HLA-DRA, PDPK1, HLA-DRB1, SH3BP2, GRAP2, MAP3K14, DBNL, SHC1, GRB2, PRKCA, PRKCB, PRKCE, SLA2, AKT1, CARD11, NCK1, BCL10, STK39, PRKCQ, PLCG1, LCK, IKBKB, PTEN, LCP2, CBL, FYB1, CDC42, FYN, ZAP70, VAV1, ITK, GAB2, CHUK, RASGRP2, SOS1</i>
Yellow module (675 expressed genes)							
ID	Name	Source	Mean Decrease in Accuracy	Median Expression (NMA)	Median Expression (MA)	# of expressed genes / # of total genes	Expressed genes
1268690	Eukaryotic Translation Elongation	BioSystems: REACTOME	4.27	6.75	6.65	83 / 98	<i>RPL21, RPL22, RPL23A, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, RPS27L, EEF1A1, RPL10A, RPL23, EEF1B2, UBA52, EEF1D, EEF2, FAU, RPL26L1, RPL22L1, RPL35, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i>

M39495	Cytoplasmic Ribosomal Proteins	MSigDB C2 BIOCARTA (v7.3)	4.3	6.78	6.69	79 / 90	<i>RPL10A, RPL21, RPL22, RPL23A, RPL23, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, UBA52, RPL31, RPL36, RPL32, RPL34, FAU, RPL35A, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS6KA1, RPS6KA2, RPS6KB1, RPS6KB2, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, MRPL19, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, RPS27, RPL35, RPS27A, RPS28, RPS29, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i>
1268691	Peptide chain elongation	BioSystems: REACTOME	2.31	6.79	6.69	81 / 93	<i>RPL10A, RPL21, RPL22, RPL23A, RPL23, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, UBA52, RPL31, RPL36, RPL32, EEF2, RPL34, FAU, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPL26L1, RPS6, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPL22L1, RPS26, RPL35, RPS27, RPS27A, RPS28, RPS29, RPL39L, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPS27L, RPL15, EEF1A1, RPL17, RPL18, RPL18A, RPL19</i>

1268681	Formation of a pool of free 40S subunits	BioSystems: REACTOME	1.62	6.7	6.63	92 / 107	RPL21, RPL22, RPL23A, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS7, RPS8, RPS9, RPS11, EIF3E, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, RPS27L, RPL10A, RPL23, UBA52, FAU, RPL26L1, EIF3L, EIF3K, EIF3A, EIF3B, RPL22L1, EIF3C, EIF3D, RPL35, EIF3F, EIF3G, EIF3H, EIF3I, EIF3J, RPL13A, RPL3, RPL4, RPL5, RPL6, EIF3M, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19
1268692	Eukaryotic Translation Termination	BioSystems: REACTOME	2.91	6.68	6.63	84 / 97	RPL21, RPL22, RPL23A, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, TRMT112, RPS5, RPS6, RPS7, RPS8, ETF1, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, APEH, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, GSPT1, RPS27L, RPL10A, RPL23, UBA52, FAU, N6AMT1, RPL26L1, RPL22L1, RPL35, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19

M189	Ribosome	MSigDB C2 BIOCARTA (v7.3)	3.73	6.68	6.59	79 / 88	<i>RPL21, RPL10A, RPL22, RPL23A, RPL23, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, UBA52, RPL31, RPL32, RPL36, RPL34, RPL35A, FAU, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPL26L1, RPS6, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS15, RPS15A, MRPL13, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPL14, RPS24, RPS25, RPL22L1, RPS26, RPL35, RPS27, RPS27A, RPS28, RPS29, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RSL24D1, RPL8, RPL9, RPL11, RPL12, RPS27L, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i>
1269718	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	BioSystems: REACTOME	1.48	6.77	6.68	86 / 100	<i>RPL21, RPL22, RPL23A, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS7, RPS8, ETF1, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, NCBP1, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, UPF1, RPS27, RPS27A, RPS28, RPS29, RPL39L, PABPC1, GSPT1, RPS27L, RPL10A, NCBP2, RPL23, UBA52, FAU, RPL26L1, EIF4G1, RPL22L1, RPL35, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i>

1268686	GTP hydrolysis and joining of the 60S ribosomal subunit	BioSystems: REACTOME	2.78	6.63	6.60	102 / 119	<p><i>RPL21, RPL22, RPL23A, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, EIF4H, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS7, RPS8, RPS9, RPS11, EIF3E, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, RPL14, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, RPS27L, RPL10A, RPL23, UBA52, FAU, EIF2S1, RPL26L1, EIF4A1, EIF4A2, EIF4B, EIF4E, EIF3L, EIF4G1, EIF2S2, EIF5, EIF5B, EIF3K, EIF3A, EIF3B, RPL22L1, EIF3C, EIF3D, RPL35, EIF3F, EIF3G, EIF3H, EIF3I, EIF3J, RPL13A, RPL3, RPL4, RPL5, RPL6, EIF3M, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i></p>
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1339149	Selenoamino acid metabolism	BioSystems: REACTOME	1.18	6.57	6.50	106 / 123	<p><i>RPL21, RPL22, RPL23A, EEFSEC, RPL24, RPL26, EPRS1, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, AIMP2, RARS1, RPLP0, RPLP1, RPLP2, AIMP1, RPS2, RPS3, MARS1, RPS3A, MAT1A, IARS1, RPS5, EEF1E1, RPS6, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS14, LARS1, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, DARS1, RPS20, RPSA, RPS21, RPS23, SCLY, RPS24, RPL14, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, GNMT, RPL39L, PAPSS2, PAPSS1, HNMT, GSR, RPS27L, TXNRD1, RPL10A, RPL23, UBA52, PSTK, SEPSECS, FAU, KARS1, SARS1, RPL26L1, INMT, AHCY, SECISBP2, CTH, RPL22L1, RPL35, RPL13A, QARS1, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i></p>
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1269716	Nonsense-Mediated Decay (NMD)	BioSystems: REACTOME	1.99	6.56	6.52	105 / 121	<i>RPL21, RPL22, RPL23A, RPL24, SMG1, RPL26, CASC3, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL36, RPL32, MAGOH, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, RPLP1, RPLP2, RPS2, RPS3, RPS3A, EIF4A3, RPS5, RPS6, RPS7, RPS8, ETF1, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, MAGOHB, RPS16, RPS17, PNRC2, NCBP1, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, SMG5, RPL14, UPF3A, RPS25, RPS26, UPF1, RPS27, RPS27A, RPS28, RPS29, RPL39L, PABPC1, GSPT1, RPS27L, RPL10A, NCBP2, RPL23, PPP2CA, SMG8, PPP2R1A, UBA52, PPP2R2A, FAU, SMG7, UPF2, RNPS1, RPL26L1, EIF4G1, SMG9, RBM8A, RPL22L1, RPL35, RPL13A, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, DCP1A, RPL17, RPL18, SMG6, RPL18A, RPL19</i>
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1269115	Influenza Viral RNA Transcription and Replication	BioSystems: REACTOME	4.63	6.32	6.28	125 / 138	<p><i>RPL21, RPL22, IPO5, RPL23A, TPR, SEH1L, RPL24, RPL26, NUP50, RPL27, RPL30, RPL27A, RPL28, RPL29, RANBP2, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, NUP85, RPLP1, RAE1, NUP107, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, POLR2A, POLR2B, POLR2C, POLR2D, RPS7, RPS8, POLR2E, RPS9, POLR2G, POLR2H, RPS11, POLR2I, RPS12, NUP88, POLR2J, RPS13, NUP98, RPS14, POLR2K, RPS15, POLR2L, RPS15A, NUP43, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, NUP62, RPS24, NUP214, RPL14, RPS25, RPS26, RPS27, RPS27A, NUP42, RPS28, NUP58, RPS29, RPL39L, POM121C, GRSF1, NUP35, RPS27L, NUP54, NUP205, RPL10A, RPL23, UBA52, GTF2F1, GTF2F2, FAU, AAAS, NDC1, POM121, NUP155, NUP37, RPL26L1, NUP210, NUP133, RPL22L1, NUP188, NUP93, RPL35, RPL13A, RPL3, DNAJC3, RPL4, RPL5, NUP160, RPL6, RPL7, RPL7A, RPL8, NUP153, RPL9, RPL11, RPL12, HSP90AA1, RPL13, RPL15, RPL17, RPL18, RPL18A, RPL19</i></p>
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1269109	Influenza Life Cycle	BioSystems: REACTOME	4.59	6.42	6.37	134 / 147	<p><i>RPL21, RPL22, IPO5, RPL23A, TPR, SEH1L, RPL24, RPL26, NUP50, RPL27, RPL30, RAN, RPL27A, RPL28, RPL29, RANBP2, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, NUP85, RPLP1, RAE1, NUP107, RPLP2, CALR, RPS2, RPS3, RPS3A, RPS5, RPS6, CANX, POLR2A, POLR2B, POLR2C, POLR2D, RPS7, RPS8, POLR2E, RPS9, POLR2G, POLR2H, RPS11, POLR2I, RPS12, NUP88, POLR2J, RPS13, NUP98, RPS14, POLR2K, RPS15, POLR2L, RPS15A, NUP43, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, NUP62, RPS24, NUP214, RPL14, RPS25, RPS26, RPS27, RPS27A, NUP42, RPS28, NUP58, XPO1, RPS29, RPL39L, POM121C, GRSF1, NUP35, RPS27L, NUP54, NUP205, RPL10A, RPL23, UBA52, GTF2F1, GTF2F2, FAU, AAAS, NDC1, POM121, NUP155, NUP37, RPL26L1, NUP210, CLTA, CLTC, NUP133, RPL22L1, NUP188, NUP93, RPL35, RPL13A, HSPA1A, RPL3, DNAJC3, RPL4, RPL5, NUP160, RPL6, RPL7, RPL7A, RPL8, NUP153, RPL9, RPL11, RPL12, HSP90AA1, RPL13, RPL15, RPL17, KPNA1, RPL18, KPNB1, RPL18A, RPL19</i></p>
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1269108	Influenza Infection	BioSystems: REACTOME	5.35	6.30	6.27	144 / 158	<p> <i>KPNA4, RPL21, KPNA5, RPL22, IPO5, RPL23A, TPR, SEH1L, RPL24, RPL26, NUP50, RPL27, RPL30, RAN, RPL27A, RPL28, RPL29, RANBP2, RPL31, RPL36, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, RPLP0, NUP85, RPLP1, RAE1, NUP107, RPLP2, CALR, RPS2, RPS3, RPS3A, RPS5, RPS6, CANX, POLR2A, POLR2B, POLR2C, POLR2D, RPS7, RPS8, POLR2E, RPS9, POLR2G, POLR2H, RPS11, POLR2I, RPS12, NUP88, POLR2J, RPS13, NUP98, RPS14, POLR2K, RPS15, POLR2L, RPS15A, NUP43, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, NUP62, RPS24, NUP214, RPL14, RPS25, RPS26, RPS27, RPS27A, NUP42, RPS28, NUP58, XPO1, RPS29, RPL39L, POM121C, GRSF1, NUP35, RPS27L, NUP54, NUP205, RPL10A, TGFB1, RPL23, KPNA7, UBA52, GTF2F1, CPSF4, GTF2F2, FAU, AAAS, NDC1, POM121, NUP155, ISG15, PABPN1, NUP37, RPL26L1, NUP210, CLTA, CLTC, NUP133, RPL22L1, NUP188, NUP93, RPL35, RPL13A, HSPA1A, EIF2AK2, RPL3, DNAJC3, RPL4, RPL5, NUP160, RPL6, RPL7, RPL7A, RPL8, NUP153, RPL9, RPL11, RPL12, HSP90AA1, RPL13, RPL15, RPL17, KPNA1, RPL18, KPNA1, RPL18A, KPNA3, RPL19</i> </p>
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1383085	rRNA processing	BioSystems: REACTOME	3.03	5.52	5.49	180 / 203	<p>RPL21, RPL22, DDX47, RPL23A, UTP6, RPL24, RPL26, RPL27, RPL30, RPL27A, RPL28, RPL29, RPL31, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPP21, RPL38, RPL41, RPLP0, RPLP1, RPLP2, FBL, RPS2, RPS3, RPS3A, RPP40, RPS5, RPS6, MRM1, SENP3, RPS7, RPS8, RPS9, NOL6, WDR46, RPS11, RPS12, BMS1, RPS13, RPS14, RPS15, RPS15A, PNO1, RPS16, RPS17, WDR18, RIOK3, EXOSC8, RPS18, RPS19, RPS20, RPS21, EXOSC5, RPS23, RPS24, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, TEX10, ELAC2, WDR43, RPL10A, RPP25, RPL23, WDR3, UBA52, TRMT10C, FAU, DIMT1, WDR75, GAR1, UTP15, RRP36, IMP4, EXOSC6, PWP2, BYSL, EMG1, C1D, SNU13, NOC4L, UTP20, RRP7A, BOP1, NOP10, RPL22L1, UTP3, TSR3, NOP2, EXOSC4, MRM2, NSUN4, RPL36, EXOSC9, EXOSC10, XRN2, RIOK1, DCAF13, DDX49, WDR36, NOP56, DHX37, DDX52, TRMT112, NOB1, RPP30, RPP38, EXOSC3, EXOSC1, NOL11, THUMPD1, RPSA, RPL14, HEATR1, NOL9, ERI1, RPP14, KRR1, NHP2, MTERF4, EXOSC2, TBL3, RPS27L, BUD23, FCF1, MRM3, NOP58, UTP18, NOP14, UTP25, TFB1M, PELP1, TSR1, CSNK1D, UTP11, CSNK1E, RRP9, RPL26L1, UTP4, PES1, NAT10, RCL1, PDCD11, WDR12, ISG20L2, LTV1, MPHOSPH10, MPHOSPH6, RPL35, PRORP, MTREX, RPL13A, RIOK2, EXOSC7, IMP3, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, UTP14C, RPL18, RPL18A, RPL19</p>
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1270158	Metabolism of amino acids and derivatives	BioSystems: REACTOME	8.68	5.93	5.88	288 / 367	<p>RPL21, RPL22, RPL23A, TPO, RPL24, HGD, RPL26, EPRS1, RPL27, RPL30, RPL27A, RPL28, PHYKPL, RPL29, RPL31, RPL32, RPL34, RPL35A, RPL36AL, RPL37, RPL37A, RPL38, RPL41, GLS2, RPLP0, RPLP1, GAMT, ACADSB, IDO1, AUH, RPLP2, ACAT1, AIMP1, PDHB, RPS2, RPS3, MARS1, RPS3A, MAT1A, RPS5, PSMA1, RPS6, PSMA2, PSMA3, PSMA4, PSMA5, PSMA6, BCKDK, PSMA7, RPS7, PSMB1, PSMB2, RPS8, RPS9, PSMB3, PSMB4, PSMB5, RPS11, PSMB6, RPS12, PSMB7, RPS13, NMRAL1, RPS14, PSMB8, RPS15, PSMB9, RPS15A, SRM, PSMB10, PSMC1, GATM, PIPOX, PSMC2, PSMC3, PSMC4, PSMC5, RPS16, BCAT1, PSMC6, RPS17, PSMD1, BCAT2, PSMD2, PSMD3, PSMD4, RPS18, GCDH, RPS19, DARS1, PSMD5, RPS20, PSMD7, BCKDHA, SERINC2, BCKDHB, PSMD8, PSMD9, RPS21, RPS23, RPS24, PSMD11, PSMD12, RPS25, PSMD13, MCCC2, UROC1, RPS26, PSME1, RPS27, RPS27A, PSME2, RPS28, MCCC1, PSPH, RPS29, DBT, TST, GNMT, RPL39L, NDUFAB1, DCT, HNMT, SQOR, DDC, ENOPH1, PHGDH, NAGS, CKB, TXNRD1, IVD, RPL10A, AFMID, PAOX, RPL23, PSMD6, CKMT1B, FAH, CKMT2, UBA52, DUOX1, FAU, KARS1, SARS1, PSME4, HIBCH, GRHPR, SUOX, GCLC, GCLM, HPD, SERINC1, CSAD, GLS, GLUD1, AHCY, GLUL, NQO1, DIO1, DIO2, PYCR1, ALDH18A1, DLAT, SECISBP2, DLD, SERINC3, LIPT2, DLST, RPL22L1, ALDH9A1, PYCR2, SMOX, QARS1, CARNS1, GPT2, QDPR, DHTKD1, IL4I1, BBOX1, ALDH6A1, KYNU, PYCR3, TAT, GOT1, GOT2,</p>
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						<i>CKMT1A, EEFSEC, LIAS, PSAT1, RPL36, NAALAD2, PSMF1, MRI1, ASRGL1, AIMP2, RARS1, HYKK, FOLH1, AZIN2, SEM1, ASPG, IARS1, EEF1E1, GPT, IYD, LARS1, SHMT1, DUOX2, OAT, DDO, RPSA, OAZ1, OAZ2, OCA2, SCLY, RPL14, ODC1, PPM1K, PAPSS2, PAPSS1, OGDH, HIBADH, PDHX, KYAT1, KMO, GSR, SLC3A2, RPS27L, AZIN1, ARG2, APIP, GSTZ1, SLC6A12, LIPT1, PSTK, SEPSECS, CRYM, ACAD8, MTAP, ADO, GCAT, AASS, RPL26L1, INMT, ETHE1, ASL, SLC25A15, ASNS, SLC25A10, ASS1, CNDP2, MTR, AGMAT, MTRR, HAAO, KYAT3, SLC7A5, ALDH4A1, CTH, PSME3, CARNMT1, RPL35, ADI1, SERINC5, AADAT, RPL13A, PCBD1, PSMD14, OAZ3, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, ALDH7A1, RPL9, RPL11, RPL12, RPL13, RPL15, HDC, RPL17, RPL18, RPL18A, TPH1, RPL19</i>
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1269056	Infectious disease	BioSystems: REACTOME	3.17	6.06	6.05	349 / 393	<p>RPL21, CBLL1, CDK9, RPL22, RPL23A, TPR, SEH1L, RPL24, RPL26, RPL27, RPL30, EPS15, RPL27A, RPL28, STAM2, RPL29, RPL31, RPL32, ERCC2, RPL34, RPL35A, RPL36AL, ERCC3, RPL37, RPL37A, RPL38, RPL41, RPLP0, NUP85, RPLP1, HLA-A, RPLP2, RPS2, RPS3, RPS3A, RPS5, RPS6, RPS7, RPS8, RPS9, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, APOBEC3G, RPS17, RPS18, RPS19, RCC1, RPS20, RPS21, TSG101, RPS23, NUP62, RPS24, RPS25, HMGA1, RPS26, RPS27, RPS27A, RPS28, RPS29, RPL39L, NUP54, TXNRD1, RPL23, MET, KPNA7, UBA52, UBB, UBC, AP2M1, FAU, AP1S1, AP2S1, AP2A1, AP2A2, AP1B1, AP2B1, AP1G1, NUP37, NMT2, CLTA, FEN1, CLTC, GTF2H5, ANTXR1, CCR5, RPL22L1, HSPA1A, MNAT1, HSP90AA1, HSP90AB1, CHMP4C, MAP2K4, RPL36, PSMF1, VPS37A, RAE1, SLC25A4, AP1S3, NELFCD, NELFA, VPS4B, POLR2A, CHMP5, POLR2B, SH3GL1, POLR2C, POLR2D, SH3GL3, POLR2E, POLR2G, POLR2H, POLR2I, POLR2J, NELFB, POLR2K, POLR2L, VTA1, XPO1, XRCC4, XRCC5, SKP1, POM121C, PPIA, ARF1, NUP35, CHMP2B, NCBP2, PACS1, ATP6V1H, CHMP4A, NDC1, NUP155, ISG15, NUP133, CHMP3, NUP93, CTNNB1, CTNND1, MAP2K1, MAP2K2, FYN, MAP2K3, MAP2K6, MAP2K7, EIF2AK2, DNAJC3, XRCC6, NUP50, RNMT, RNGTT, VPS4A, PSMA1, PSMA2, PSMA3, PSMA4, PSMA5, B2M, PSMA6, PSMA7, PSMB1, PSMB2, SRC, PSMB3, PSMB4, PSMB5, PSMB6, PSMB7, PSMB8, PSMB9, PSMB10, PSMC1, PSMC2, PSMC3, PSMC4, PSMC5,</p>
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							<p> <i>PSMC6, PSMD1, PSMD2, PSMD3, PSMD4, NCBP1, PSMD5, PSMD7, PSMD8, PSMD9, PSMD11, PSMD12, PSMD13, PSME1, PSME2, NUP58, SSRP1, CHMP2A, CCNK, BANF1, ELMO1, NUP205, RPL10A, PSMD6, CHMP7, CPSF4, STX1A, POM121, ANTXR2, PSME4, SV2B, SUPT4H1, CXCR4, SV2A, SUPT5H, NUP210, VAMP1, VAMP2, SYT1, AP1M1, TAF2, TAF4, TAF4B, TAF5, TAF6, TAF7, TAF9, TAF10, TAF11, TAF12, NMT1, TAF13, NUP160, BTRC, VPS37D, NUP153, RAC1, RBX1, KPNA1, TBP, KPNA1, KPNA2, KPNA3, KPNA4, NELFE, KPNA5, DOCK2, IPO5, NPM1, TCEA1, VPS37C, ELOC, ELOB, ELOA, RAN, RANBP1, RANBP2, RANGAP1, CHMP6, NEDD4L, PDCD6IP, CALM1, NUP107, CALM2, CALM3, SEM1, CALR, HBEGF, CANX, NUP88, NUP98, GRB2, AP1M2, NUP43, RPSA, NUP214, RPL14, SYT2, NUP42, STAM, LCK, CBL, CHMP4B, VPS37B, GRSF1, RPS27L, TGFB1, CUL5, CCNH, CCNT1, CCNT2, LIG1, GTF2A1, LIG4, GTF2A2, GTF2B, GTF2E1, GTF2E2, EEF2, GTF2F1, GTF2F2, GTF2H1, TAF3, GTF2H2, AAAS, CD247, GTF2H3, CD4, CD8B, CD9, PSIP1, GUCY2C, PABPN1, CD28, RPL26L1, FURIN, HGS, SUPT16H, CTDP1, PAK2, PSME3, NUP188, RPL35, VPS28, LTF, RPL13A, PSMD14, CDH1, PDZD3, RPL3, RPL4, RPL5, HCK, RPL6, RPL7, ELL, RPL7A, RPL8, RPL9, RPL11, RPL12, RPL13, RPL15, RPL17, RPL18, CDK7, RPL18A, RPL19</i> </p>
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1268685	Ribosomal scanning and start codon recognition	BioSystems: REACTOME	1.47	6.48	6.46	53 / 63	<i>FAU, EIF4H, RPS2, RPS3, EIF2S1, RPS3A, RPS5, RPS6, EIF4A1, EIF4A2, EIF4B, EIF4E, RPS7, RPS8, EIF3L, RPS9, EIF4G1, RPS11, EIF3E, RPS12, EIF2S2, RPS13, EIF5, RPS14, RPS15, RPS15A, EIF3K, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, EIF3A, EIF3B, RPS25, RPS26, EIF3C, EIF3D, RPS27, RPS27A, EIF3F, RPS28, EIF3G, EIF3H, RPS29, EIF3I, EIF3J, EIF3M, RPS27L</i>
1268683	Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S	BioSystems: REACTOME	2.01	6.44	6.40	54 / 65	<i>FAU, EIF4H, RPS2, RPS3, EIF2S1, RPS3A, RPS5, RPS6, EIF4A1, EIF4A2, EIF4B, EIF4E, RPS7, RPS8, EIF3L, EIF4EBP1, RPS9, EIF4G1, RPS11, EIF3E, RPS12, EIF2S2, RPS13, RPS14, RPS15, RPS15A, EIF3K, RPS16, RPS17, RPS18, RPS19, RPS20, RPSA, RPS21, RPS23, RPS24, EIF3A, EIF3B, RPS25, RPS26, EIF3C, EIF3D, RPS27, RPS27A, EIF3F, RPS28, EIF3G, EIF3H, RPS29, EIF3I, EIF3J, PABPC1, EIF3M, RPS27L</i>

Table S5. Differentially expressed (DE) genes in the maternal asthma-discriminatory pathways of the turquoise module (see **Figure 2** of the main paper) for bronchial (discovery) and nasal (replication) epithelial cells. Of 535 genes that were annotated in the 16 pathways and expressed in bronchial epithelial cells, one gene was DE between asthma cases with (N = 27) and without (N = 48) an asthmatic mother (FDR < 0.10). Of 531 genes that were annotated in the 16 pathways and expressed in nasal epithelial cells, 27 genes were DE between asthma cases with (N = 82) and without (N = 46) an asthmatic mother at (FDR < 0.10). These genes were among 13 of the 16 maternal asthma-discriminatory pathways.

Bronchial epithelial cells (one DE gene)					
Gene	Name	Pathway(s)	logFC	P-value	FDR-adjusted P-value
<i>ICOS</i>	Inducible T Cell Costimulator	Intestinal immune network for IgA production	-0.97	1.61E-04	0.062
Nasal epithelial cells (27 DE genes)					
Gene	Name	Pathway(s)	logFC	P-value	FDR-adjusted P-value
<i>IL2RB</i>	Interleukin 2 Receptor Subunit Beta	Th17 cell differentiation	-0.54	1.05E-06	5.58E-04
<i>CCL5</i>	C-C Motif Chemokine Ligand 5	Rheumatoid arthritis, Influenza A, Interleukin-10 signaling	-0.37	3.13E-06	8.32E-04
<i>CD3E</i>	CD3e Molecule	Translocation of ZAP-70 to immunological synapse, TCR signaling in naïve CD4+ T cells	-0.35	4.52E-05	8.00E-03
<i>CD3D</i>	CD3d Molecule	Hematopoietic cell lineage, Th17 cell differentiation, Translocation of ZAP-70 to immunological synapse, TCR signaling in naïve CD4+ T cells	-0.32	7.59E-05	0.010
<i>CD8A</i>	CD8a Molecule	Hematopoietic cell lineage	-0.43	1.29E-04	0.012
<i>TCIRG1</i>	T Cell Immune Regulator 1, ATPase H+ Transporting V0 Subunit A3	Rheumatoid arthritis	0.11	1.36E-04	0.012
<i>C1QA</i>	Complement C1q A Chain	Staphylococcus aureus infection	-0.30	4.04E-04	0.031
<i>C1QC</i>	Complement C1q C Chain	Staphylococcus aureus infection	-0.43	6.10E-04	0.040
<i>CD2</i>	CD2 Molecule	Hematopoietic cell lineage	-0.28	7.28E-04	0.041
<i>FYN</i>	FYN Proto-Oncogene, Src Family Tyrosine Kinase	Viral myocarditis, Osteoclast differentiation, TCR signaling in naïve CD4+ T cells	-0.29	7.85E-04	0.041
<i>C4B</i>	Complement C4B (Chido Blood Group)	Staphylococcus aureus infection	-0.65	8.78E-04	0.041
<i>STAT1</i>	Signal Transducer And Activator Of Transcription 1	Tuberculosis, Th17 cell differentiation, Toxoplasmosis, Influenza A, Osteoclast differentiation	-0.16	9.32E-04	0.041
<i>PLK3</i>	Polo Like Kinase 3	Tuberculosis	0.28	1.09E-03	0.044

<i>MAP4K1</i>	Mitogen-Activated Protein Kinase Kinase Kinase 1	TCR signaling in naïve CD4+ T cells	-0.38	1.38E-03	0.052
<i>PRF1</i>	Perforin 1	Viral myocarditis	-0.54	1.63E-03	0.058
<i>HIF1A</i>	Hypoxia Inducible Factor 1 Subunit Alpha	Th17 cell differentiation	0.14	1.75E-03	0.058
<i>PML</i>	PML Nuclear Body Scaffold	Influenza A	-0.12	1.96E-03	0.060
<i>RASSF5</i>	Ras Association Domain Family Member 5	TCR signaling in naïve CD4+ T cells	0.15	2.02E-03	0.060
<i>IL7</i>	Interleukin 7	Hematopoietic cell lineage	-0.24	2.24E-03	0.063
<i>LAMB2</i>	Laminin Subunit Beta 2	Toxoplasmosis	0.18	2.54E-03	0.066
<i>FPR1</i>	Formyl Peptide Receptor 1	Staphylococcus aureus infection, Interleukin-10 signaling	0.38	2.63E-03	0.066
<i>CD9</i>	CD9 Molecule	Hematopoietic cell lineage	0.05	3.08E-03	0.071
<i>EP300</i>	E1A Binding Protein P300	Tuberculosis, Influenza A	0.10	3.09E-03	0.071
<i>IL4R</i>	Interleukin 4 Receptor	Hematopoietic cell lineage, Th17 cell differentiation	0.14	3.58E-03	0.079
<i>PIK3R5</i>	Phosphoinositide-3-Kinase Regulatory Subunit 5	Toxoplasmosis	0.36	4.19E-03	0.087
<i>SIRPB1</i>	Signal Regulatory Protein Beta 1	Osteoclast differentiation	0.56	4.39E-03	0.087
<i>HSPA2</i>	Heat Shock Protein Family A (Hsp70) Member 2	Toxoplasmosis, Influenza A	0.27	4.44E-03	0.087

Table S6. Detailed functional information for each hub DMC.

IlmnID	Module	CHR	BP (Build 37)	UCSC_RefGene_Name	UCSC_RefGene_Accession	UCSC_RefGene_Group
cg05277504	Green	17	79961614	<i>ASPSCR1</i>	NM_024083	Body
cg21531873	Green	12	110778616	<i>ATP2A2</i>	NM_001681	Body
cg20436206	Green	5	146910671			
cg07317846	Green	2	42648344			
cg09459548	Black	5	119942454	<i>PRR16</i>	NM_016644	Body
cg25921502	Black	10	50363896	<i>C10orf128</i>	NM_001010863	3'UTR
cg07270021	Black	8	60627336			
cg11964006	Black	10	53852689	<i>PRKG1</i>	NM_001098512	Body
cg03296565	Black	17	51191056			
cg16284238	Black	6	87196595			
cg09175338	Black	17	10372273	<i>MYH4</i>	NM_017533	5'UTR
cg20699079	Black	2	137199850			
cg18437033	Black	12	130188284	<i>TMEM132D</i>	NM_133448	Body
cg03179496	Blue	15	29212340	<i>APBA2</i>	NM_005503	TSS1500
cg00030588	Blue	16	87100811			
cg15787712	Blue	19	13948243	<i>MIR24-2</i>	NR_029497	TSS1500
cg14236389	Blue	20	58631038	<i>C20orf197</i>	NM_173644	1stExon
cg04661929	Blue	17	75320035	<i>SEPT9</i>	NM_001113492	5'UTR
cg24292665	Blue	11	69065779			
cg11850468	Blue	5	180231185	<i>MGAT1</i>	NM_001114620	TSS1500
cg05007163	Blue	22	39266069	<i>CBX6</i>	NM_014292	Body
cg14993283	Red	6	100906182	<i>SIM1</i>	NM_005068	Body
cg17098147	Red	10	22634142	<i>SPAG6</i>	NM_172242	TSS1500
cg07416383	Red	7	155302899	<i>CNPY1</i>	NM_001103176	5'UTR
cg22717227	Red	10	50887568	<i>C10orf53</i>	NM_182554	TSS200
cg16066272	Red	14	52535949	<i>NID2</i>	NM_007361	TSS200
cg05323725	Red	17	35294713	<i>LHX1</i>	NM_005568	1stExon
cg00073837	Red	2	223177008			
cg04030584	Turquoise	16	67871218	<i>CENPT</i>	NM_025082	5'UTR
cg22689324	Turquoise	1	1562397	<i>MIB2</i>	NM_001170687	Body
cg10410146	Turquoise	7	44112411	<i>POLM</i>	NM_013284	3'UTR
cg01259126	Turquoise	22	29705157	<i>GAS2L1</i>	NM_152237	Body
cg09440150	Turquoise	5	6159585			
cg05991685	Turquoise	16	2818793	<i>SRRM2</i>	NM_016333	Body
cg04662250	Turquoise	17	21157499	<i>C17orf103</i>	NM_152914	TSS1500
cg01005308	Turquoise	20	48768686	<i>TMEM189</i>	NM_001162505	Body
cg12492380	Turquoise	7	98872169	<i>MYH16</i>	NR_002147	Body

cg06082897	Turquoise	1	7767716	<i>CAMTA1</i>	NM_015215	Body
cg19874640	Turquoise	5	134527449			
cg04841389	Turquoise	6	32015083	<i>TNXB</i>	NM_019105	Body
cg13120756	Turquoise	17	42386950	<i>RUNDC3A</i>	NM_001144826	Body
cg14444710	Turquoise	16	2587080	<i>PDPK1</i>	NM_031268	TSS1500
cg04662836	Turquoise	15	95334933			
cg01191154	Turquoise	22	37593672			
cg04329382	Turquoise	22	46480891	<i>LOC400931</i>	NR_027033	TSS1500
cg08758352	Turquoise	17	46205147			
cg24221742	Turquoise	17	74868220	<i>MGAT5B</i>	NM_198955	TSS1500
cg09690040	Yellow	3	126569599	<i>CHCHD6</i>	NM_032343	Body
cg05877397	Yellow	16	49672444	<i>ZNF423</i>	NM_015069	Body
cg19807237	Yellow	1	218470982	<i>RRP15</i>	NM_016052	Body
cg19077494	Yellow	2	158723291	<i>ACVR1</i>	NM_001105	5'UTR
cg00251716	Yellow	1	243479948	<i>SDCCAG8</i>	NM_006642	Body
cg22060153	Yellow	2	101889653	<i>SNORD89</i>	NR_003070	TSS200
cg07016095	Yellow	15	71519190	<i>THSD4</i>	NM_024817	Body
cg25061701	Yellow	17	62608856	<i>SMURF2</i>	NM_022739	Body
cg25697442	Yellow	6	1708713	<i>GMDS</i>	NM_001500	Body

Table S7. Associations between co-methylation modules and clinical measures after correcting for hub DMCs. **(A)** For each module, the number of correlated genes and hub DMCs are shown. No genes were associated with any of the modules after correcting for all of the module's respective hub DMCs (FDR-corrected $P > 0.999$). **(B)** Correlation coefficients and p-values are shown between clinical measures and module eigenvectors. Significant p-values after Bonferroni-correcting for nine tests (clinical phenotypes; $p < 5.56 \times 10^{-3}$) are shown in bold. The numbers of subjects with measurements for each variable are shown. Asthma severity is determined by STEP classification (1). ns, not significant ($p > 0.05$).

Variables	WGCNA co-methylation modules (number of DMCs)						
	NMA-associated		MA-associated				
	Orange (31)	Green (35)	Black (15)	Blue (74)	Red (17)	Turquoise (73)	Yellow (24)
A. Correlated Genes and hub DMCs							
Number of correlated genes		0	0	0	0	0	0
Number of hub DMCs	0	4	9	8	7	19	9
B. Clinical Measures							
Asthma Severity (N = 142)		-4.21 4.6×10^{-5}	-2.34 0.021	-3.07 2.5×10^{-3}	ns	-3.04 2.8×10^{-3}	3.07 2.6×10^{-3}
FEV ₁ % Predicted (N = 142)		ns	ns	ns	ns	ns	ns
FEV ₁ /FVC (N = 142)		ns	ns	0.20 0.018	ns	ns	ns
Total Serum IgE (N = 141)		ns	0.21 0.013	ns	ns	ns	-0.18 0.037
FeNO (N = 135)		ns	ns	ns	ns	ns	ns
BAL Eosinophilia (N = 140)		ns	ns	ns	ns	ns	ns
BAL Neutrophilia (N = 140)		ns	ns	ns	ns	ns	ns
Blood Eosinophilia (N = 141)		ns	ns	ns	ns	ns	ns
Body Mass Index (N = 142)		ns	ns	ns	ns	ns	ns

Table S8. Covariate selection. Principal Components Analysis (PCA) of the 398,186 CpGs that passed quality control was performed using the R function, *prcomp*, to identify potential technical or biological confounders. The DNA methylation PC1-PC10 and the % variance explained by each PC are shown in the first column, followed by four potential technical (platform, batch, chip, recruitment source), seven biological (age, sex, self-reported race/ethnicity, current smoking, and ancestry PCs 1-3) covariates. The p-values for tests of association between each PC and each variable are shown. Associations were tested in a step-wise fashion, regressing out the effects of covariates in succession until there were no significant correlations with any of the top 10 DNA methylation PCs. P-values for the associations are shown for the (A) raw data, (B) after removing “chip effect” using ComBat (24), and (C) after further regressing out the effects of sex, age, current smoking status, and the first three ancestry PCs. The latter six variables, along with cigarette smoking at time of bronchoscopy, were included as covariates in all analyses. Although the smoking variable was not associated with any of the 10 DNA methylation PCs, we included it as a covariate because smoking is known to have strong effects on global DNA methylation levels. Significant p-values after correcting for 11 tests (potential confounders) using a Bonferroni correction ($p < 4.55 \times 10^{-3}$) are shown in bold font. The effects of asthma and maternal asthma on each of the 10 DNA methylation PCs are also shown.

A. Raw													
k	Technical Variables				Biological Variables							Asthma	Maternal Asthma
	Platform	Batch	Chip	Recruitment Source	Age	Sex	Self-reported Race/Ethnicity	Current Smoking	Ancestry PC1	Ancestry PC2	Ancestry PC3		
PC1 (19%)	5.11E-109	3.95E-107	2.81E-111	1.46E-04	0.356	0.504	0.722	0.117	0.058	0.573	0.223	0.019	0.966
PC2 (12%)	0.817	0.010	4.67E-07	1.60E-03	0.287	0.182	2.72E-03	0.385	0.027	0.668	0.730	0.315	0.870
PC3 (9%)	0.621	2.20E-18	1.73E-25	2.35E-17	0.647	0.936	0.034	0.186	0.006	0.176	0.134	0.432	0.367
PC4 (5%)	0.171	5.43E-04	4.37E-07	0.011	3.35E-03	0.182	0.608	0.120	0.588	0.544	0.133	0.168	0.230
PC5 (4%)	0.669	0.093	0.577	5.26E-05	2.15E-17	0.409	0.022	0.501	0.696	0.069	0.327	7.98E-07	0.303
PC6 (2%)	0.415	1.75E-03	6.23E-14	4.80E-04	0.542	0.249	5.40E-04	0.694	2.46E-04	0.029	0.365	0.045	0.014
PC7 (2%)	0.747	0.288	0.082	7.46E-06	0.065	0.889	4.19E-14	0.564	3.78E-20	1.24E-06	0.198	0.855	0.874
PC8 (2%)	0.454	0.609	4.92E-08	0.195	0.088	0.941	0.571	0.735	0.911	0.984	0.663	0.096	0.309
PC9 (1%)	0.757	0.741	0.308	0.113	9.05E-05	0.080	2.18E-07	0.417	3.95E-09	0.002	0.478	9.67E-05	0.021
PC10 (1%)	0.935	2.98E-03	3.78E-11	0.005	0.810	0.071	0.560	0.104	0.589	0.933	0.557	0.089	0.764
B. After ComBat													
k	Technical Variables				Biological Variables							Asthma	Maternal Asthma
	Platform	Batch	Chip	Recruitment Source	Age	Sex	Self-reported Race/Ethnicity	Current Smoking	Ancestry PC1	Ancestry PC2	Ancestry PC3		
PC1 (14%)	0.791	0.937	1.000	0.208	0.328	0.322	0.036	0.604	0.479	0.131	0.294	0.052	0.401
PC2 (7%)	0.507	0.859	0.999	0.549	0.020	0.107	0.130	0.395	0.641	0.662	0.891	0.020	0.089
PC3 (6%)	0.969	0.777	1.000	8.93E-04	1.70E-18	0.485	0.112	0.114	0.435	0.241	0.093	8.09E-05	0.716
PC4 (3%)	0.858	0.329	0.999	8.85E-05	0.658	0.155	6.27E-16	0.584	7.93E-24	2.60E-08	0.505	0.404	0.425
PC5 (2%)	0.812	0.920	1.000	0.288	2.73E-03	0.273	0.720	0.571	0.622	0.777	0.103	2.64E-05	1.08E-03
PC6 (2%)	0.688	0.976	1.000	0.737	0.003	0.076	2.46E-07	0.871	2.19E-08	1.03E-03	0.734	0.040	0.461
PC7 (2%)	0.690	0.889	1.000	0.015	0.005	9.27E-06	0.013	0.408	0.023	0.017	0.021	0.779	0.333
PC8 (1%)	0.893	0.873	1.000	0.555	0.990	0.292	0.080	0.698	0.138	0.461	0.602	0.207	0.405
PC9 (1%)	0.929	0.969	1.000	0.215	0.203	0.046	0.061	0.241	0.232	0.694	0.612	0.099	0.511
PC10 (1%)	0.252	0.690	1.000	0.422	0.038	0.823	0.256	0.791	0.078	0.083	0.264	0.154	0.636
C. After ComBat, ancestry PCs 1-3, age, sex, and current smoking status													

k	Technical Variables				Biological Variables							Asthma	Maternal Asthma
	Platform	Batch	Chip	Recruitment Source	Age	Sex	Self-reported Race/Ethnicity	Current Smoking	Ancestry PC1	Ancestry PC2	Ancestry PC3		
PC1 (15%)	0.569	0.849	1.000	0.148	0.887	1.000	0.729	0.570	0.944	0.996	0.878	0.095	0.660
PC2 (8%)	0.404	0.749	0.998	0.903	0.834	1.000	0.406	0.832	0.917	0.994	0.822	0.172	0.156
PC3 (4%)	0.932	0.998	1.000	0.099	0.854	1.000	0.614	0.206	0.927	0.995	0.843	1.51E-08	0.010
PC4 (3%)	0.982	0.817	1.000	0.112	0.994	1.000	0.984	0.567	0.997	1.000	0.994	0.061	0.094
PC5 (2%)	0.438	0.520	0.999	0.601	0.908	1.000	0.846	0.730	0.954	0.997	0.901	0.103	0.643
PC6 (2%)	0.466	0.897	1.000	0.817	0.971	1.000	0.653	0.345	0.986	0.999	0.969	0.440	0.422
PC7 (2%)	0.270	0.426	0.999	0.465	0.838	1.000	0.987	0.072	0.919	0.994	0.826	0.793	0.808
PC8 (1%)	0.696	0.955	1.000	0.701	0.912	1.000	0.706	0.325	0.956	0.997	0.906	0.623	0.882
PC9 (1%)	0.486	0.747	1.000	0.010	0.909	1.000	0.610	0.133	0.955	0.997	0.902	0.023	0.996
PC10 (1%)	0.629	0.875	1.000	0.865	0.946	1.000	0.894	0.962	0.973	0.998	0.942	0.066	0.748

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