

ONLINE SUPPLEMENTARY

CEACAM3 Decreases Asthma Exacerbations and Modulates Respiratory Syncytial Virus

Latent Infection in Children

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SUPPLEMENTARY MATERIALS AND METHODS

Meta-analysis of RSV-related genes

The Gene Expression Omnibus (GEO, <https://www.ncbi.nlm.nih.gov/geo/>) was searched for RSV-related genes using the search terms “RSV” and “blood”, and five gene expression studies were identified. OMics Compendia Commons (OMiCC, <https://omicc.niaid.nih.gov/>) with the RankProd method^{1,2} was performed to detect differentially expressed genes (DEGs) by integrating multiple array platforms.

We conducted the analyses with five gene expression datasets when OMiCC contained data from GEO (OMiCC currently covers up to April 2017). The GSE69606³ includes Affymetrix Human Genome U133 Plus 2.0 Array for 6 severe and 9 moderate subjects in RSV infection acute phase, and 8 severe and 9 moderate subjects in recovery phase. The GSE38900⁴ includes Illumina HumanHT-12 V4.0 for 28 patients with acute RSV infection and 8 healthy controls. The other platform was Illumina HumanWG-6 v3.0 including 107 patients with acute RSV infection and 31 healthy controls. The GSE42026⁵ includes Illumina HumanHT-12 V3.0 for 22 patients with acute RSV infection and 33 healthy controls. The GSE34205⁶ includes Affymetrix Human Genome U133 Plus 2.0 Array for 51 patients with acute RSV infection and 11 healthy controls. The GSE17156⁷ includes Affymetrix Human Genome U133A 2.0 Array 20 subjects in RSV infection acute phase and 8 severe and 20 subjects in recovery phase.

Briefly, we created comparison group pairs (CGPs) where each CGP comprises two conditions of gene-expression profiles (e.g. RSV infection versus healthy controls) in each study. After CGPs were defined, the quantile-normalization and Limma⁸ were used to calculate expression differences between two conditions in each study. Meta-analysis was performed using the RankProd^{1,2} to convert fold-change value into ranks within a CGP. Then, a rank product was calculated for each gene across the CGPs. Lastly, p-value and false-discovery rate (FDR) were calculated based on permuted

expression value. DEGs were considered significant if they had a FDR less than 0.05 to account for multiple testing. Additionally, we visualized gene expression values across studies by using hierarchical clustering with heatmap.2 function of gplots⁹. Normalized gene expression values were calculated with the Combat module from sva package¹⁰ to adjusted for studies with varying gene expression values.

RSV sensitization

We measured RSV-specific IgE to distinguish subjects with or without sensitization to RSV. The presence of IgE anti-RSV Abs was determined by a modification of ELISA using RSV IgG ELISA kit (Arigo, ARG80600). Briefly, samples were directly added (100 µL) to the microwells pre-coated with RSV antigen and incubated at 4°C overnight. HRP-conjugated goat anti-human IgE with (100 µL) (Novus Biologicals, CO, USA), diluted 1:15,000 in 1% BSA buffer was added to each well and incubated for 30 minutes. The following processes were similar to the IgM protocol. Optical density (OD) was measured at 450 nm. An OD reading of 2 standard deviations (SD) above the average control values was defined as positive sensitization to RSV.¹¹ Samples from 46 non-asthmatic controls were detected to calculate the cut-off point, and the mean was 0.22 and SD was 0.18.

eQTL of CEACAM3 mRNA expression

Public available datasets from GTEx

We investigated the target SNPs for association with mRNA levels in lung tissue and whole blood by using eQTL analysis results from GTEx database. The detailed analysis procedure is released on the GTEx website (<https://www.gtexportal.org/home/>). Briefly, genes were selected based on expression thresholds of >0.1 transcripts per million (TPM) in at least 20% of samples and ≥6 reads in at least 20% of samples. Expression values were normalized between samples using trimmed mean of M values

(TMM).¹² For each gene, expression values were normalized across samples using an inverse normal transform. eQTL analysis was performed using FastQTL.¹³

eQTL from the TCCAS cohort

Total RNA extracted from peripheral blood mononuclear cell using the Direct-zol™ RNA MiniPrep (Zymo Research). The quality and integrity of RNA was evaluated by the NanoDrop (Thermo Scientific) and the 2100 Bioanalyzer (Agilent Technologies). RNA samples must have a RIN exceeding 7 for subsequent microarray measurements of mRNA expression profiles. Total RNA samples (1.5 µg) were hybridized to Illumina HT-12 v4.0 Expression BeadChips (Illumina). Microarray images and Initial quality assessment will performed using Illumina's GenomeStudio Gene Expression module. Raw gene expression levels were applied by variance stabilizing transformation (VST)¹⁴ and robust spline normalization (RSN)¹⁵ in the lumi R package. The arrayQualityMetrics package¹⁶ in R was used to assess the overall array quality. All samples were performed in multiple batches at the Yong Lin Biomedical Engineering Center of National Taiwan University.

DNA was extracted from peripheral blood using the QIAamp DNA mini kit (QIAGEN Inc., Catalog No. 51104). Whole genome genotyping was performed using the Affymetrix Axiom™ Genome-Wide CHB 1 Array Plate. Genotype imputation was performed using IMPUTE2,¹⁷ and individuals from phase 3 of the 1000 Genomes Project were used as references. We excluded the imputed SNPs with R² values <0.3. Markers were excluded if minor allele frequencies were less than 0.01, or call rates were less than 95%. We removed one individual from each pair with an IBD (identity by descent) >0.1875, which is halfway between the expected IBD for third- and second-degree relatives.¹⁸ The total genotyping rate in the remaining individuals was 0.99. eQTL analysis was performed using glm model in R to test the trend of genotypes on *CEACAM3* RNA expression.

mRNA analyses in asthmatic subjects in GEO datasets

To determine the relative expression of *CEACAM3* in nasal epithelial samples from asthma we used two freely available gene expression datasets from the Gene Expression Omnibus (GEO) resource (<https://www.ncbi.nlm.nih.gov/geo/>). The GSE19190¹⁹ dataset includes Affymetrix Human Gene 1.0 ST Array data for 6 uncontrolled and 7 controlled asthma subjects. Uncontrolled asthma was defined as if children, aged 6-11 years of age, having one or more of the following features: more than two days/week with trouble breathing, night-time awakening, interference with normal activity, use of short-acting beta agonist >2 days/week, FEV1 ≤80% predicted, FEV1/FVC ≤80% in the last three months, or exacerbations requiring oral systemic corticosteroids during the last year. Children more than 12 years of age were defined with having one or more of the following features: more than two days/week with trouble breathing, night-time awakening, interference with normal activity, use of short-acting beta agonist >2 days/week, FEV1 ≤80% predicted, asthma control test <20 in the last three months, or exacerbations requiring oral systemic corticosteroids during the last year. We also used GSE46171²⁰ dataset, which includes Agilent Whole Human Genome 4X44K, for 10 asthmatics with exacerbations and 24 asthmatics without exacerbations. Asthma exacerbations during acute respiratory illness was defined a priori as either: (1) an increase in asthma symptoms that made the participant increase or start inhaled or oral corticosteroids, or seek medical care in a doctor's office, urgent care clinic or emergency department; or (2) an increase in chest or asthma symptom score by ≥10 points for ≥2 days over average daily scores during baseline week plus at least one of these objective changes: use of ≥4 puffs of albuterol above the average daily use in the baseline week for ≥2 days; decline of ≥10% in FEV1 during ARI (first or second visit) compared to FEV1 at baseline (without acute respiratory illness); or decline of ≥20% in PEF for ≥2 days during the cold week compared with best PEF achieved in the baseline week. Raw gene expression levels were applied by variance stabilizing transformation (VST)¹⁴ and robust spline normalization (RSN)¹⁵ in the lumi R package. The arrayQualityMetrics package¹⁶ in R, a generic set of quality control routines including

array distance examination, principal component plot, and array intensity distribution, was used to assess the overall array quality.

ENCODE analysis of target SNPs

To provide insight into the functional regulatory of SNPs among disease mechanism, we investigated significant SNPs using the HaploReg²¹ and the deep-learning functional prediction resource DeepSEA.²² We used the criteria of $|\text{Log}_2 \text{ fold change}| > 0.585$ (fold change > 1.5) to identify significant alterations in transcription factor activities.

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SUPPLEMENTARY FIGURE AND TABLES**Table S1. Up-regulated differentially expressed genes in the meta-analysis of RSV infection**

Gene Symbol	Mean	GSE69606 _sR	GSE69606 _moR	GSE38900 _GPL10558	GSE38900 _GPL6884	GSE42026	GSE34205	GSE17156
	log ₂ FC	log ₂ FC	log ₂ FC	log ₂ FC	log ₂ FC	log ₂ FC	log ₂ FC	log ₂ FC
IFI27	4.31	3.55	4.65	4.98	4.45	6.10	5.09	1.34
OLFM4	2.86	5.18	2.74	NA	1.63	NA	3.93	0.81
DEFA4	2.58	4.16	2.05	NA	2.22	3.98	2.25	0.83
CEACAM8	2.52	4.17	2.46	NA	2.07	NA	2.91	1.00
ANXA3	2.39	3.79	3.27	2.57	1.46	NA	2.21	1.03
RSAD2	2.30	2.37	2.50	2.44	1.93	3.13	1.48	2.26
ELANE	2.30	3.64	1.75	1.24	2.04	3.76	3.22	0.45
MPO	2.16	3.38	1.54	NA	1.92	4.23	1.69	0.18
IFI44L	2.11	1.77	2.50	3.24	1.54	2.15	1.75	1.84
HP	2.11	3.21	2.11	NA	2.09	NA	2.61	0.50
FCGR1B	2.09	2.74	2.42	2.61	1.60	2.32	1.54	1.39
IFIT1	1.95	2.85	2.72	2.05	1.05	2.02	0.82	2.12
LTF	1.93	3.28	2.31	0.16	1.00	NA	4.02	0.81
S100A12	1.85	3.04	2.08	1.59	1.48	2.53	1.56	0.64
RNASE2	1.81	3.31	2.49	1.16	1.29	1.81	1.87	0.74
MMP9	1.78	3.34	2.47	2.53	1.53	1.58	1.19	-0.17
IFIT3	1.78	2.40	2.42	2.34	1.07	1.72	1.04	1.46
CEACAM6	1.72	3.51	1.58	0.84	1.95	NA	2.04	0.40
IFI44	1.72	1.70	1.68	2.65	1.33	2.38	0.89	1.38
RETN	1.71	2.81	1.60	1.35	1.13	3.90	1.10	0.08
OASL	1.68	1.61	1.70	3.09	1.67	1.82	0.90	0.95
SIGLEC1	1.65	1.89	2.33	NA	0.90	NA	2.42	0.70

HBD	1.64	3.71	2.37	-0.11	1.30	1.09	2.42	0.70
CD177	1.64	2.57	2.69	NA	0.69	NA	1.70	0.55
ISG15	1.62	1.36	1.60	2.34	1.57	2.22	0.89	1.35
ADM	1.60	2.87	2.83	1.63	0.88	1.05	1.52	0.43
HERC5	1.60	1.89	1.84	2.51	0.93	1.52	1.01	1.48
GYPB	1.59	2.05	0.54	NA	1.65	2.80	1.77	0.73
PGLYRP1	1.56	2.63	1.45	1.47	1.07	1.60	2.66	0.04
S100P	1.55	2.86	2.28	1.46	0.42	1.06	2.40	0.35
LCN2	1.54	2.98	1.85	-0.10	1.06	2.92	1.41	0.63
RNASE3	1.50	2.45	1.32	NA	1.10	NA	1.85	0.79
PLSCR1	1.49	1.72	1.53	1.47	1.24	2.50	1.01	0.95
XK	1.48	2.97	1.77	0.09	1.44	NA	1.28	1.34
AHSP	1.47	3.31	1.38	-0.34	0.90	1.97	2.23	0.84
TNFAIP6	1.44	2.68	2.42	1.16	0.43	0.78	0.97	1.66
HBBP1	1.42	1.86	0.69	0.06	2.50	3.45	1.30	0.10
TCN1	1.42	2.89	1.28	NA	1.21	1.96	0.83	0.35
BST1	1.42	1.96	1.46	2.38	1.10	1.57	1.05	0.39
IFI6	1.36	1.31	1.91	2.09	0.79	1.32	1.00	1.07
CAMP	1.35	1.63	0.88	1.08	1.61	1.31	2.39	0.58
SERPING1	1.33	1.54	1.97	NA	0.61	1.27	1.11	1.51
MX1	1.32	1.52	1.62	1.87	0.78	1.23	1.21	1.04
IFITM3	1.32	0.83	1.27	2.56	1.78	1.83	0.88	0.11
BPI	1.31	1.50	0.68	NA	1.39	2.55	1.22	0.49
FOLR3	1.31	1.33	1.46	2.23	1.09	1.90	1.22	-0.09
OAS3	1.30	1.24	1.15	2.14	1.26	1.36	0.72	1.26
ALAS2	1.26	1.90	1.21	0.02	1.05	1.87	2.14	0.66
OAS1	1.26	1.39	1.43	1.62	1.01	1.84	0.64	0.92
SLC22A4	1.26	2.55	1.82	0.69	0.88	1.37	1.26	0.27
C3AR1	1.26	1.47	1.70	1.57	1.14	1.98	0.59	0.38

SELENBP1	1.26	3.61	1.19	-1.05	0.49	1.13	2.77	0.66
H1F0	1.24	1.67	1.22	0.70	1.07	1.93	1.75	0.31
ACSL1	1.22	2.02	2.02	1.62	0.58	1.05	1.16	0.10
IFIT2	1.21	1.86	1.69	1.85	0.59	0.97	0.38	1.16
MS4A3	1.21	3.02	1.01	0.17	1.03	2.13	0.75	0.38
ASGR2	1.21	1.88	1.61	1.38	0.83	1.54	1.03	0.17
CYP1B1	1.20	2.35	2.05	1.39	0.73	0.93	0.87	0.09
CEACAM1	1.19	1.93	0.75	1.55	0.92	1.85	0.85	0.49
VNN1	1.19	1.72	1.77	NA	1.14	1.78	0.47	0.24
DYSF	1.18	2.04	1.82	1.52	0.79	1.20	0.89	0.01
CLEC5A	1.17	2.55	1.12	NA	0.97	NA	1.10	0.12
EPB42	1.17	3.49	0.96	-1.14	0.31	1.24	2.76	0.58
SLPI	1.17	1.70	0.88	NA	1.78	NA	0.76	0.72
FCGR1A	1.16	0.15	0.36	2.80	1.59	2.38	0.75	0.08
CCR1	1.14	1.70	1.85	1.07	0.85	0.93	1.13	0.44
RAP1GAP	1.13	0.64	0.23	NA	2.19	2.74	0.77	0.21
CTNNAL1	1.13	1.78	1.01	-0.04	0.84	2.45	1.11	0.75
LY6E	1.11	0.99	1.02	1.82	1.01	1.41	0.98	0.52
AZU1	1.11	2.71	0.93	-0.07	1.10	NA	1.78	0.19
HBQ1	1.10	2.17	0.96	-0.57	0.64	1.33	2.75	0.43
IL1RN	1.10	1.26	1.01	1.99	0.78	1.75	0.55	0.35
SIGLEC5	1.10	1.85	1.17	1.78	0.63	1.42	0.84	0.00
AQP9	1.09	2.05	2.26	1.30	0.39	0.39	1.14	0.13
FFAR2	1.09	1.66	2.05	1.25	0.41	0.32	1.68	0.28
CTSG	1.09	1.81	0.73	1.14	1.79	NA	0.92	0.17
HBZ	1.09	1.78	0.67	NA	1.69	NA	1.05	0.25
BPGM	1.08	2.62	0.73	-1.43	1.49	1.49	1.64	1.05
LAP3	1.08	1.04	1.17	1.36	0.94	1.50	0.72	0.85
ALPL	1.08	1.60	1.39	1.80	0.78	1.24	0.64	0.13

CLEC1B	1.08	2.07	1.65	0.10	0.29	2.32	0.86	0.28
SERPINB2	1.08	2.20	1.35	NA	0.60	0.66	1.60	0.06
LIN7A	1.07	1.77	1.18	NA	0.81	1.57	0.81	0.28
CEP55	1.07	1.00	0.88	NA	1.18	1.53	1.71	0.08
CA1	1.06	2.08	0.64	-0.76	1.50	2.62	0.76	0.61
BCL2A1	1.06	1.29	1.69	NA	0.58	NA	1.02	0.72
NFIL3	1.06	1.04	1.85	1.74	0.54	0.98	1.08	0.15
CDC20	1.05	0.63	0.74	1.68	0.99	1.35	1.72	0.22
GYG1	1.04	1.63	1.10	1.09	1.04	1.56	0.66	0.18
TYMS	1.02	0.98	0.99	0.99	1.23	1.54	1.25	0.18
ORM1	1.02	1.87	1.27	1.08	0.35	1.66	1.16	-0.24
XAF1	1.01	1.00	1.06	1.41	0.70	1.22	0.67	1.02
DTL	1.00	1.17	1.09	NA	1.35	NA	1.19	0.22
HK3	1.00	1.73	1.29	1.08	1.07	1.41	0.45	0.01
DDX60	1.00	0.85	0.93	1.22	0.87	1.65	0.51	0.98
APOBEC3A	1.00	1.48	2.12	NA	0.63	NA	0.54	0.24
LMNB1	1.00	1.25	0.82	1.80	1.00	1.16	0.65	0.31
GMPR	1.00	2.35	1.14	-0.74	0.45	1.35	1.83	0.60
TCN2	0.99	0.71	1.09	1.27	1.12	1.92	0.75	0.10
IRF7	0.99	1.30	1.13	1.29	0.80	1.60	0.40	0.40
CXCL10	0.98	2.26	1.23	NA	1.25	NA	-0.34	0.52
CDA	0.98	1.94	1.42	0.98	0.59	0.51	1.52	-0.12
F5	0.98	1.39	1.29	1.96	0.61	0.81	0.72	0.06
SNCA	0.97	1.99	0.87	-0.60	0.80	1.39	1.67	0.70
AIM2	0.96	0.91	0.98	1.72	0.76	1.17	0.28	0.94
KIF20A	0.96	1.10	0.80	1.22	1.21	NA	1.47	-0.01
SCO2	0.96	1.25	1.47	1.26	1.02	0.46	0.89	0.41
IRAK3	0.96	1.19	1.32	1.47	0.66	1.49	0.30	0.33
KRT1	0.96	2.05	0.59	-1.02	0.90	2.22	1.28	0.66

CXCL1	0.95	1.74	1.54	NA	0.03	NA	1.48	-0.05
C1QB	0.95	0.84	1.38	NA	1.50	NA	0.65	0.37
NFE2	0.95	2.45	1.39	0.15	0.50	0.64	1.31	0.17
PYGL	0.94	1.72	1.42	0.96	0.62	0.89	0.94	0.03
STOM	0.94	1.88	0.91	-0.04	0.99	1.82	0.68	0.33
TNFSF10	0.94	1.05	1.05	1.33	0.82	0.94	0.38	0.98
DLGAP5	0.93	1.23	1.22	0.61	1.11	NA	1.33	0.10
HMMR	0.93	0.88	0.98	0.91	1.35	NA	1.33	0.11
FPR2	0.93	2.20	1.87	0.84	0.33	0.64	0.51	0.09
PSTPIP2	0.92	1.00	1.07	1.31	0.79	1.34	0.45	0.50
SQRDL	0.92	1.03	0.88	1.96	0.63	1.01	0.67	0.26
KIF11	0.92	1.01	0.79	NA	0.98	1.29	1.26	0.18
LAMP3	0.92	1.16	0.88	0.68	0.76	NA	0.69	1.36
HIST1H1C	0.91	1.20	1.07	0.70	0.88	1.18	1.38	-0.01
TOP2A	0.91	1.05	1.13	NA	1.02	NA	1.21	0.15
CD163	0.91	1.67	1.48	1.27	0.49	0.98	0.46	0.00
DHX58	0.91	0.63	0.64	2.18	0.72	0.99	0.80	0.39
RTP4	0.90	1.08	0.69	1.32	0.86	1.08	0.31	0.99
FECH	0.90	1.81	0.43	-0.42	0.93	1.35	1.18	1.03
IFI35	0.90	0.89	0.86	1.12	0.87	1.34	0.55	0.66
IL1R2	0.89	2.44	2.67	-0.61	-0.13	0.96	0.81	0.12
BMX	0.89	1.67	1.20	0.57	0.40	1.80	0.38	0.23
GPER	0.89	0.35	0.60	1.92	0.67	1.55	1.03	0.11
HPSE	0.89	1.34	1.36	1.00	0.85	0.82	0.57	0.29
MARCO	0.89	0.35	0.94	0.91	1.04	NA	1.74	0.33
TTK	0.89	1.25	0.89	NA	1.15	NA	1.09	0.05
EIF2AK2	0.88	0.77	0.87	1.86	0.50	1.07	0.51	0.62
IFIH1	0.88	0.73	1.02	1.35	0.80	1.35	0.44	0.50
TRIM58	0.88	2.41	1.06	-0.81	0.56	1.48	0.93	0.52

LY96	0.88	1.00	1.26	1.32	0.77	0.62	0.77	0.41
MELK	0.87	0.65	0.83	0.49	1.22	1.26	1.61	0.06
MX2	0.87	1.40	1.27	1.33	0.59	0.69	0.49	0.32
SERPINB1	0.87	1.28	0.94	0.79	0.71	1.24	0.77	0.35
GCA	0.87	1.92	1.48	0.74	0.31	0.72	0.52	0.38
KCNJ15	0.86	1.48	1.37	1.46	0.29	0.39	0.86	0.19
KLF1	0.86	1.65	0.30	NA	0.17	1.46	1.06	0.53
CCNA2	0.86	0.64	0.64	0.86	1.22	1.55	1.05	0.07
NCAPG	0.86	0.88	0.88	NA	1.18	NA	1.29	0.07
MANSC1	0.86	2.09	1.77	0.75	0.42	0.53	0.69	-0.25
CDKN3	0.86	0.88	0.83	NA	1.31	NA	1.11	0.15
ATP8B4	0.85	1.80	0.80	0.58	0.63	1.27	0.75	0.14
NAMPT	0.85	1.08	1.81	0.79	0.14	0.50	1.26	0.38
SLC30A1	0.85	0.96	1.00	0.92	0.87	1.18	0.65	0.37
RAB13	0.85	1.93	1.07	NA	0.46	NA	0.62	0.16
OAS2	0.85	0.97	0.82	1.48	0.63	1.25	0.22	0.57
B4GALT5	0.85	1.42	1.13	1.06	0.64	0.81	0.77	0.09
SLC4A1	0.84	2.00	0.79	-0.77	0.63	1.04	1.54	0.65
TMOD1	0.84	1.54	0.37	-0.79	0.85	1.82	1.28	0.81
CREG1	0.84	1.53	1.08	-0.38	0.91	1.28	0.80	0.64
CASP5	0.84	1.02	0.96	NA	0.96	NA	0.32	0.93
TLR2	0.84	1.30	1.52	NA	0.31	NA	0.95	0.10
SPATS2L	0.84	0.50	0.44	1.08	1.27	1.55	0.49	0.54
LILRA5	0.83	0.91	1.17	1.55	0.53	1.29	0.32	0.05
S100A9	0.83	1.55	1.19	0.95	0.49	0.53	1.01	0.09
IGF2BP3	0.82	0.58	0.52	0.64	0.57	2.85	0.33	0.28
FAS	0.82	0.96	0.80	0.89	0.60	1.08	0.68	0.77
MAFB	0.82	0.98	1.64	0.59	0.60	0.71	1.07	0.16
KCNJ2	0.82	1.84	1.01	1.39	0.53	0.57	-0.15	0.56

RIN2	0.82	0.96	0.94	1.65	0.62	0.84	0.59	0.13
ARG1	0.81	0.23	0.03	1.86	1.83	NA	0.46	0.47
KIF14	0.81	0.93	0.77	0.78	0.94	0.93	1.20	0.14
PFKFB3	0.81	0.94	1.67	0.93	0.46	0.94	0.69	0.05
CKAP4	0.81	1.23	1.17	1.07	0.76	1.16	0.29	-0.01
SAMSN1	0.81	0.87	0.80	1.17	0.78	1.12	0.40	0.52
MCM10	0.81	0.54	0.56	NA	0.81	1.55	1.33	0.07
CA4	0.81	1.09	0.78	1.31	0.94	1.55	0.01	-0.05
DSC2	0.80	1.12	1.07	0.65	0.16	1.14	1.24	0.25
BLVRA	0.80	0.96	1.07	1.16	0.74	0.75	0.51	0.43
TDRD7	0.80	1.11	0.75	1.28	0.53	0.90	0.43	0.62
GPR97	0.80	1.80	1.50	0.96	0.23	0.58	0.77	-0.23
FOXM1	0.80	0.41	0.53	NA	0.51	0.84	2.43	0.08
EPB49	0.80	2.02	0.71	-0.56	0.67	1.31	1.05	0.39
VNN2	0.80	1.22	1.52	0.83	0.25	0.49	1.05	0.22
BAMBI	0.80	1.05	0.82	NA	1.20	NA	0.82	0.08
TLR1	0.79	1.29	1.13	NA	0.48	0.63	0.93	0.29
TLR8	0.79	1.62	1.41	0.99	0.40	0.43	0.44	0.22
MPP1	0.79	1.88	0.88	-0.45	0.70	1.23	0.91	0.36
FAR2	0.79	1.00	0.71	0.78	0.69	1.41	0.84	0.08
CCNB1	0.78	0.78	0.76	NA	0.96	NA	1.23	0.18
FPR1	0.78	1.42	1.48	0.82	0.43	0.34	0.78	0.17
GADD45A	0.78	0.97	0.76	0.26	0.61	1.79	0.62	0.43
SAMD9	0.77	0.78	0.65	0.87	0.60	1.22	0.58	0.71
DOK3	0.77	1.20	0.79	NA	0.79	1.06	0.70	0.10
CHMP5	0.77	0.90	0.84	0.64	0.59	1.32	0.61	0.46
PRC1	0.77	0.84	0.61	NA	0.78	1.17	1.08	0.10
QPCT	0.76	1.86	1.59	0.26	0.33	0.20	1.06	-0.01
TK1	0.75	0.76	0.69	0.24	1.08	1.18	1.17	0.17

CSTA	0.75	1.36	0.89	NA	0.52	0.39	0.58	0.77
VCAN	0.75	1.38	1.03	1.03	0.47	0.52	0.73	0.10
IFIT5	0.75	0.87	0.67	NA	0.67	1.01	0.21	1.06
GBP1	0.75	0.48	0.58	1.00	0.75	0.84	0.39	1.20
FLVCR2	0.74	1.11	0.83	0.62	0.76	1.39	0.18	0.32
CDC42EP3	0.74	1.10	1.08	NA	0.79	NA	0.71	0.01
OTOF	0.74	0.73	0.60	NA	0.12	NA	2.16	0.07
TPX2	0.73	0.79	0.79	0.46	1.11	NA	1.14	0.12
TMCC2	0.73	1.06	0.20	NA	1.28	NA	0.66	0.47
CD14	0.73	1.41	1.19	0.94	0.50	0.26	0.89	-0.07
JAK2	0.73	0.70	0.70	1.16	0.65	1.01	0.40	0.49
GK	0.73	1.10	1.00	1.08	0.35	0.57	0.37	0.65
LGALS1	0.73	1.19	0.92	0.52	0.95	0.66	0.85	0.03
SORT1	0.73	1.10	0.87	0.73	0.66	1.20	0.23	0.28
TLR5	0.72	0.63	0.80	1.30	0.63	1.13	0.21	0.37
TOR1B	0.72	1.09	0.82	0.82	0.63	1.02	0.30	0.39
CD36	0.72	1.22	1.12	0.31	0.53	0.72	0.85	0.28
CCPG1	0.72	1.39	1.02	0.74	0.45	0.87	0.32	0.24
MAPK14	0.72	1.14	0.61	0.56	0.58	1.34	0.43	0.36
NCF4	0.72	1.43	1.25	0.82	0.26	0.41	0.81	0.03
MXD1	0.72	1.37	1.55	0.86	0.10	0.02	0.87	0.24
CD63	0.71	1.10	1.12	0.70	0.60	0.84	0.66	-0.03
MYL4	0.71	1.05	0.58	0.03	0.40	1.02	1.45	0.44
UBE2C	0.71	0.64	0.77	1.62	0.56	1.08	0.32	-0.03
MNDA	0.71	1.58	1.06	0.56	0.37	0.47	0.75	0.16
SLC7A5	0.71	1.07	0.46	0.00	0.90	1.43	0.82	0.27
FCER1G	0.70	1.08	0.96	0.82	0.70	0.91	0.36	0.10
CEACAM3	0.70	0.80	0.70	2.12	0.54	0.23	0.46	0.08
ZBP1	0.70	0.37	0.57	1.42	0.61	0.80	0.54	0.59

TIMP2	0.70	0.88	0.92	1.30	0.31	0.76	0.68	0.04
SELP	0.70	1.36	0.90	NA	0.25	1.30	0.16	0.22
SIGLEC9	0.70	1.20	0.62	0.76	0.41	0.62	1.27	0.01
HERC6	0.70	0.67	0.55	1.08	0.85	1.02	0.30	0.39
WIPI1	0.70	1.24	0.93	0.15	0.59	1.00	0.77	0.20
PADI4	0.69	1.90	1.00	0.18	0.50	0.64	0.90	-0.26
GRN	0.69	1.20	1.12	0.88	0.57	0.66	0.53	-0.11
C5AR1	0.69	1.08	1.54	0.96	0.50	0.21	0.73	-0.18
GNG10	0.69	1.13	0.86	0.68	0.40	0.62	0.73	0.42
SIAH2	0.69	0.93	0.31	-0.02	0.77	1.36	0.79	0.68
CHEK1	0.69	0.52	0.45	NA	0.96	1.46	0.67	0.07
BLVRB	0.69	1.98	0.97	-1.07	0.23	1.01	1.23	0.45
OIP5	0.68	0.80	0.78	0.30	0.90	1.32	0.66	0.03
STEAP4	0.68	1.31	0.96	0.81	0.10	NA	0.75	0.17
S100A11	0.68	0.97	0.95	1.13	0.57	0.44	0.72	-0.02
STX11	0.68	0.98	1.11	0.76	0.42	0.60	0.36	0.52
FAM46C	0.68	1.04	0.14	-0.31	0.85	1.40	1.04	0.60
FCGR3B	0.68	0.77	1.57	1.14	0.18	-0.05	1.05	0.08
PTTG3P	0.68	0.47	0.30	0.48	1.10	1.17	1.19	0.03
SMPDL3A	0.67	1.00	0.59	1.59	0.52	0.83	-0.07	0.23
AURKB	0.67	0.36	0.33	NA	1.29	1.11	0.87	0.06
GINS2	0.67	0.42	0.49	NA	1.11	1.50	0.45	0.04
LMO2	0.67	0.92	0.69	0.68	0.75	1.01	0.37	0.26
CA2	0.67	1.85	0.93	-0.71	0.50	1.58	0.06	0.46
BNIP3L	0.67	1.12	0.28	-0.58	0.74	1.50	0.92	0.66
TXN	0.66	0.58	0.63	0.48	0.83	1.02	0.59	0.51
STAT1	0.66	0.82	0.84	0.92	0.48	0.54	0.33	0.71
CTSL1	0.66	0.43	0.96	0.54	0.57	1.30	0.59	0.23
ADAM9	0.66	1.20	0.84	NA	0.03	0.98	0.52	0.38

MTHFD2	0.65	0.76	0.62	0.74	0.54	1.04	0.31	0.57
PPP1R3D	0.65	1.02	0.57	1.05	0.56	0.44	0.69	0.23
HLX	0.65	1.67	1.43	0.64	0.15	0.29	0.44	-0.06
KIF1B	0.65	1.17	0.80	1.07	0.43	0.67	0.42	0.00
DDX58	0.65	0.54	0.38	1.02	0.49	0.94	0.02	1.16
TRIM22	0.65	0.47	0.38	0.92	0.61	1.10	0.40	0.67
NUSAP1	0.65	0.63	0.64	0.51	0.86	0.98	0.85	0.09
ITGA2B	0.65	1.48	0.74	-0.32	0.19	2.21	0.18	0.06
GGH	0.65	1.14	0.73	0.16	0.99	0.72	0.71	0.09
CD58	0.65	0.87	0.86	0.77	0.73	0.75	0.33	0.22
RAB31	0.64	1.32	1.01	0.60	0.44	0.44	0.60	0.10
MT2A	0.64	0.28	0.77	0.55	1.02	1.02	0.48	0.37
TSPO	0.64	1.45	0.89	0.57	0.52	0.70	0.42	-0.06
ACPP	0.64	1.12	0.68	NA	0.51	0.70	0.68	0.15
LIMK2	0.64	1.11	0.89	0.64	0.18	0.86	0.57	0.21
PTTG1	0.63	0.70	0.59	0.23	1.02	1.01	0.75	0.14
SLC25A37	0.63	1.71	0.77	-0.20	0.11	0.31	1.52	0.21
DHRS9	0.63	1.32	0.98	0.59	0.38	0.60	0.17	0.38
FXYD6	0.63	0.75	0.74	NA	0.75	0.68	0.92	-0.05
GNA15	0.63	1.26	0.94	0.53	0.49	0.67	0.55	-0.04
HIST1H2BD	0.63	0.35	0.57	1.43	0.56	0.93	0.65	-0.08
CLEC4E	0.63	0.63	1.34	NA	0.69	NA	0.29	0.19
BCL6	0.63	0.99	1.06	0.45	0.11	0.99	0.89	-0.09
ELL2	0.63	0.61	0.35	0.48	0.83	0.89	1.00	0.23
TRIP13	0.63	0.71	0.55	0.56	1.09	NA	0.73	0.12
BUB1B	0.62	0.88	0.73	NA	0.42	NA	0.98	0.11
TLR4	0.62	1.06	1.22	0.96	0.24	0.32	0.33	0.22
IGSF6	0.62	1.27	1.17	0.88	0.07	0.23	0.28	0.45
C11orf75	0.62	1.00	1.09	1.10	0.25	0.07	0.38	0.43

CENPM	0.62	0.25	0.46	0.72	0.84	0.70	1.34	0.02
FKBP1B	0.62	1.13	0.93	NA	0.03	NA	0.54	0.46
IFITM2	0.62	0.67	0.89	1.08	0.58	0.42	0.64	0.03
NCF2	0.62	1.25	0.93	0.96	0.33	0.39	0.42	0.03
MMRN1	0.61	1.61	0.99	NA	-0.02	1.17	-0.29	0.22
SLC16A3	0.61	1.24	0.87	0.89	0.57	0.49	0.20	0.02
PGS1	0.61	0.48	0.35	0.94	0.53	0.84	1.07	0.07
SLC2A3	0.61	0.71	0.79	1.04	0.44	0.71	0.65	-0.06
NOD2	0.61	1.17	0.82	1.04	0.53	0.30	0.30	0.11
CDT1	0.61	0.74	0.38	NA	1.14	NA	0.77	0.02
P2RY13	0.61	2.16	1.19	-0.27	0.26	0.50	0.31	0.13
HIST2H2AA3	0.61	0.09	0.45	0.94	0.87	1.07	0.76	0.09
SAT1	0.61	0.45	0.83	0.71	0.57	0.83	0.60	0.28
SMOX	0.61	0.42	0.33	-0.67	0.91	2.15	0.94	0.18
RRAGD	0.61	1.12	0.83	0.49	0.45	0.66	0.57	0.15
SIRPA	0.61	1.09	0.96	0.88	0.50	0.26	0.55	0.03
SOCS3	0.61	0.51	0.61	1.30	0.38	0.91	0.50	0.05
GLRX5	0.61	1.41	0.31	-0.50	0.43	0.79	1.17	0.65
CNIH4	0.61	0.46	0.23	0.90	0.63	1.20	0.32	0.51
BCAT1	0.61	0.88	0.85	NA	0.81	NA	0.51	-0.03
TGFB1I1	0.61	1.56	0.89	NA	0.17	NA	0.40	0.00
HBXIP	0.60	0.40	0.08	2.32	0.22	0.57	0.44	0.20
EPB41L3	0.60	0.88	1.13	0.61	0.59	0.35	0.23	0.42
SKA1	0.60	0.47	0.34	NA	0.54	0.84	1.34	0.07
BIRC5	0.60	0.50	0.50	NA	0.66	NA	1.11	0.23
GPD2	0.60	1.10	0.60	NA	0.29	1.26	0.36	-0.01
LGALS3BP	0.60	0.37	0.49	1.14	0.53	1.06	0.31	0.30
STXBP2	0.60	0.50	0.41	0.70	0.62	1.53	0.47	-0.03
TSPAN2	0.60	1.16	0.71	0.61	0.59	NA	0.52	0.01

IFITM1	0.59	0.44	0.55	0.99	0.66	0.68	0.58	0.25
SPI1	0.59	1.04	0.78	0.83	0.43	0.65	0.59	-0.19
OPLAH	0.59	0.66	0.44	NA	0.58	1.29	0.57	-0.02
RNASE4	0.59	0.98	1.06	0.51	0.56	0.57	0.43	0.01
IFI30	0.59	0.90	0.78	0.60	0.66	0.43	0.64	0.12
MYL9	0.59	1.59	0.84	-0.33	0.45	1.13	0.20	0.23
ASGR1	0.59	0.78	0.86	0.66	0.54	0.57	0.63	0.07
RNF10	0.59	0.94	0.37	-0.26	0.61	1.15	0.91	0.38
NPL	0.59	1.24	1.17	0.03	0.34	0.55	0.70	0.06
POLE2	0.59	0.81	0.69	0.34	0.85	NA	0.71	0.11
HJURP	0.59	0.42	0.39	NA	1.17	NA	0.94	0.01

sR: severe acute phase vs. severe recovery phase

moR: moderate acute phase vs. moderate recovery phase

FC: fold change

Table S2. Down-regulated differentially expressed genes in the meta-analysis of RSV infection

Gene	Mean	GSE69606	GSE69606	GSE38900	GSE38900			
		_sR	_moR	_GPL10558	_GPL6884	GSE42026	GSE34205	GSE17156
Symbol	log ₂ FC							
KLRB1	-1.18	-2.27	-1.15	-1.03	-0.70	-2.21	-1.18	0.26
FCER1A	-1.02	-0.91	-0.39	-1.43	-0.86	-2.73	-1.11	0.31
CLIC3	-0.94	-1.76	-0.64	NA	-0.31	-1.35	-1.17	-0.38
GPR56	-0.93	-1.09	-0.50	-0.98	-0.13	-2.00	-1.47	-0.35
GNLY	-0.83	-2.08	-0.79	-0.31	-0.05	-1.62	-0.70	-0.29
HDC	-0.82	-0.55	0.01	-1.26	-0.51	-2.44	-0.85	-0.15
TGFBR3	-0.82	-1.56	-0.39	-0.62	-0.23	-1.90	-0.66	-0.38
KLRF1	-0.81	-2.09	-0.62	-0.67	-0.14	-1.34	-0.67	-0.11
CD160	-0.78	-2.02	-0.72	NA	-0.32	NA	-0.80	-0.05
KLRD1	-0.78	-1.87	-0.52	-0.66	-0.11	-1.52	-0.79	0.02
PTGDR	-0.74	-0.59	-0.26	-1.00	-0.47	-1.89	-0.89	-0.08
AKR1C3	-0.74	-0.91	-0.50	NA	-0.48	-1.68	-0.99	0.16
NR3C2	-0.73	-0.34	-0.66	NA	-0.52	-1.70	-1.07	-0.10
EMR3	-0.72	-0.17	-0.08	-0.90	-0.78	-2.32	-0.61	-0.18
PRSS23	-0.71	-1.05	-0.59	NA	-0.36	NA	-1.33	-0.24
ABCB1	-0.70	-0.88	-0.45	-0.93	-0.78	-1.21	-0.53	-0.12
IL2RB	-0.69	-1.24	-0.53	-0.95	-0.29	-1.18	-0.35	-0.31
CD1C	-0.68	-0.79	-0.67	-0.75	-0.92	-0.94	-0.54	-0.19
CCR3	-0.67	-0.11	0.01	NA	-0.33	-2.49	-1.12	0.00
LBH	-0.63	-0.72	-0.86	-0.84	-0.43	-0.60	-0.72	-0.23
TPM2	-0.62	-0.21	-0.21	-1.00	-0.43	-1.59	-0.64	-0.28
HLA-DPB1	-0.61	-0.64	-0.54	NA	-0.68	-1.35	-0.39	-0.08
KLF12	-0.61	-0.74	-0.57	-0.66	-0.92	-0.82	-0.50	-0.06

TARP	-0.61	-0.20	-0.26	-1.08	-0.30	-1.61	-0.77	-0.05
GZMH	-0.60	-1.83	-0.55	-0.21	0.46	-2.00	-0.12	0.05
PBXIP1	-0.59	-0.80	-0.53	NA	-0.38	-0.95	-0.52	-0.38
FAIM3	-0.59	-0.81	-0.92	-0.21	-0.68	-0.93	-0.30	-0.30
GOLGA8A	-0.59	-0.58	-0.63	-0.71	-1.20	-0.76	-0.16	-0.06
ID3	-0.59	-0.57	-0.83	-0.84	-0.42	-1.03	-0.12	-0.29

sR: severe acute phase vs. severe recovery phase

moR: moderate acute phase vs. moderate recovery phase

FC: fold change

Table S3. Gene-based main effects of SNPs on asthma exacerbations

Gene	Permutation p	SNPs
Additive genetic model		
BCAT1	0.02	rs11610069 rs11047700 rs4963830 rs1875091 rs12321766
CASP5	0.04	rs9651713
CEACAM3	0.02	rs7251960 rs62117403 rs10425474
CEACAM6	0.01	rs8106277
EPB41L3	0.01	rs4798366 rs76590339 rs77751403 rs1941015 rs145555476
GADD45A	0.04	rs520820
GINS2	0.02	rs35953313
GYPB	0.01	rs72725110 rs55915952
MS4A3	0.01	rs479240 rs12226814 rs2276043 rs11230133 rs72914658
NFE2	0.01	rs73114552
RAB31	0.04	rs7505884 rs56156444 rs1893126 rs674617 rs72955242
TPM2	0.02	rs12351422 rs1078081 rs1078081 rs3763629 rs117076659
WIP1	0.04	rs76185620 rs6501468 rs74252534 rs8067357 rs144763306
Dominant genetic model		
ABCB1	0.003	rs10264856
CEACAM3	0.02	rs1076976 rs7251960 rs10425474
CEACAM6	0.04	rs8106277
EPB41L3	0.01	rs4798366 rs77751403 rs76590339 rs7243561 rs12172862
GINS2	0.03	rs35953313 rs1053328
GYPB	0.01	rs6821092 rs28668163
MS4A3	0.02	rs1286276 rs72914658 rs11230133 rs479240
MTHFD2	0.03	rs62147681 rs6546893
NFE2	0.01	rs73114552
NFIL3	0.04	rs2482358
RAB31	0.03	rs35354526 rs72955242
RNASE3	0.04	rs11156741 rs2771359
ZBP1	0.04	rs35034881

Models adjusted by age, sex, medication use, BMI, PC1-PC2 in TCCAS

Table S4. Genetic main effects of SNPs with asthma exacerbations in TCCAS and CAMP, by additive genetic model

Gene	CHR	SNP	BP	Allele†	Genetic main effect										Interaction with RSV infection in TCCAS	
					TCCAS					CAMP						
					MAF†	OR	L95	U95	P	OR	L95	U95	P	Combined	FDR	
KIF1B	1	rs17034615	10311877	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.59	1.01	2.50	4.52E-02	1.57E-02	3.37E-02	0.64
KIF1B	1	rs72865926	10313703	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.59	1.01	2.50	4.52E-02	1.57E-02	3.37E-02	0.64
KIF1B	1	rs147831053	10316915	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.54	0.86	2.75	1.50E-01	4.32E-02	4.55E-02	0.64
KIF1B	1	rs112448832	10324797	G/T	0.07	1.70	1.00	2.89	4.88E-02	1.51	1.00	2.27	5.09E-02	1.74E-02	3.46E-02	0.64
KIF1B	1	rs112440591	10329735	T/C	0.07	1.70	1.00	2.89	4.88E-02	1.54	0.86	2.75	1.50E-01	4.32E-02	4.55E-02	0.64
KIF1B	1	rs111587396	10337000	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.54	0.86	2.75	1.50E-01	4.32E-02	4.55E-02	0.64
KIF1B	1	rs72865961	10338657	T/C	0.07	1.70	1.00	2.89	4.88E-02	1.54	0.86	2.75	1.50E-01	4.32E-02	4.55E-02	0.64
KIF1B	1	rs72865963	10339129	A/G	0.07	1.71	1.01	2.91	4.58E-02	1.54	0.86	2.75	1.50E-01	4.10E-02	4.48E-02	0.64
GADD45A	1	rs1744586	68147108	A/G	0.36	1.40	1.06	1.85	1.95E-02	1.18	0.91	1.53	2.11E-01	2.68E-02	3.96E-02	0.18
GADD45A	1	rs488778	68147143	T/C	0.36	1.40	1.06	1.85	1.95E-02	1.18	0.91	1.53	2.11E-01	2.68E-02	3.96E-02	0.18
GADD45A	1	rs520820	68148353	T/C	0.44	1.46	1.11	1.93	7.24E-03	1.03	0.82	1.30	8.04E-01	3.58E-02	4.26E-02	0.97
OTOF	2	rs4665865	26738696	C/A	0.24	1.54	1.12	2.11	7.70E-03	1.04	0.73	1.49	8.12E-01	3.80E-02	4.35E-02	0.28
OTOF	2	rs4665866	26738735	A/G	0.24	1.61	1.17	2.21	3.56E-03	1.04	0.69	1.57	8.63E-01	2.09E-02	3.76E-02	0.20
OTOF	2	rs4665867	26739004	C/T	0.24	1.59	1.16	2.19	4.45E-03	1.04	0.73	1.49	8.12E-01	2.39E-02	3.92E-02	0.20
HJURP	2	rs213547	234740758	A/G	0.47	1.33	1.01	1.74	4.18E-02	1.20	0.99	1.46	6.91E-02	1.98E-02	3.76E-02	0.85
HJURP	2	rs658482	234740987	C/G	0.47	1.32	1.01	1.73	4.61E-02	1.19	0.98	1.44	8.02E-02	2.44E-02	3.92E-02	0.86
GYPB	4	rs6821092	144623607	C/A	0.41	1.46	1.10	1.93	9.29E-03	1.07	0.86	1.34	5.54E-01	3.23E-02	4.07E-02	0.43
GYPB	4	rs2019159	144635129	C/A	0.41	1.45	1.10	1.92	9.34E-03	1.06	0.85	1.32	5.99E-01	3.46E-02	4.17E-02	0.47
GYPB	4	rs3931894	144888862	C/G	0.46	1.46	1.10	1.92	8.42E-03	1.71	0.98	2.98	5.85E-02	4.25E-03	2.55E-02	0.90
GYPB	4	rs28419337	144890031	C/T	0.43	1.42	1.07	1.89	1.45E-02	5.59	1.19	26.21	2.91E-02	3.71E-03	2.55E-02	0.63
GYPB	4	rs55915952	144890200	C/T	0.46	1.46	1.10	1.93	8.36E-03	1.75	0.99	3.07	5.37E-02	3.91E-03	2.55E-02	0.90

GYPB	4	rs28607849	144897227	G/A	0.46	1.46	1.10	1.93	8.40E-03	2.70	1.31	5.56	7.11E-03	6.41E-04	1.52E-02	0.90
GYPB	4	rs2175450	144907783	G/T	0.47	1.43	1.08	1.90	1.25E-02	3.96	1.57	10.03	3.67E-03	5.05E-04	1.52E-02	0.93
GYPB	4	rs1984487	144909923	G/C	0.46	1.46	1.10	1.92	8.66E-03	3.03	1.39	6.64	5.46E-03	5.18E-04	1.52E-02	0.91
GYPB	4	rs4317150	144913007	T/C	0.46	1.44	1.08	1.91	1.18E-02	3.58	1.59	8.06	2.12E-03	2.89E-04	1.52E-02	0.89
GYPB	4	rs4273413	144914254	G/A	0.43	1.41	1.05	1.87	2.04E-02	3.44	0.67	17.77	1.40E-01	1.96E-02	3.76E-02	0.64
GYPB	4	rs12503691	144938047	C/T	0.45	1.38	1.03	1.84	2.92E-02	1.78	1.01	3.13	4.72E-02	1.04E-02	2.78E-02	0.84
GYPB	4	rs6844785	144953701	T/C	0.45	1.40	1.05	1.87	2.14E-02	1.43	0.92	2.24	1.16E-01	1.74E-02	3.46E-02	0.84
GYPB	4	rs6854076	144979970	C/T	0.46	1.34	1.01	1.78	4.26E-02	1.48	0.99	2.22	5.69E-02	1.70E-02	3.46E-02	0.86
GYPB	4	rs12508303	144984608	T/A	0.42	1.35	1.01	1.81	4.29E-02	1.83	0.90	3.71	9.55E-02	2.66E-02	3.96E-02	0.31
GYPB	4	rs13132104	144986203	G/A	0.42	1.36	1.02	1.82	3.82E-02	1.78	1.04	3.04	3.64E-02	1.05E-02	2.78E-02	0.37
GYPB	4	rs4560352	144992263	G/A	0.42	1.35	1.01	1.81	4.29E-02	1.54	0.89	2.67	1.21E-01	3.24E-02	4.07E-02	0.31
GYPB	4	rs6817748	144998150	G/A	0.42	1.36	1.01	1.81	4.03E-02	1.54	0.97	2.45	6.68E-02	1.86E-02	3.67E-02	0.31
GYPB	4	rs7657795	145009802	C/A	0.46	1.36	1.03	1.81	3.26E-02	1.39	0.98	1.97	6.56E-02	1.53E-02	3.36E-02	0.87
GYPB	4	rs7679112	145009868	A/G	0.45	1.42	1.07	1.88	1.67E-02	1.33	0.94	1.90	1.12E-01	1.36E-02	3.10E-02	0.68
NR3C2	4	rs76268676	149015244	C/T	0.03	2.86	1.30	6.31	9.31E-03	1.18	0.16	8.53	8.73E-01	4.72E-02	4.84E-02	0.30
NR3C2	4	rs62332046	149219036	T/C	0.12	1.69	1.10	2.60	1.73E-02	1.08	0.87	1.34	4.85E-01	4.85E-02	4.94E-02	0.52
NR3C2	4	rs3911846	149226197	T/C	0.12	1.68	1.09	2.58	1.90E-02	1.09	0.88	1.36	4.17E-01	4.62E-02	4.81E-02	0.53
PTTG1	5	rs2961951	159854278	T/G	0.28	1.41	1.03	1.93	3.26E-02	1.18	0.93	1.50	1.83E-01	3.65E-02	4.27E-02	0.55
CD36	7	rs3211864	80286344	G/A	0.05	2.19	1.18	4.06	1.32E-02	1.14	0.78	1.67	5.07E-01	4.01E-02	4.44E-02	0.99
CD36	7	rs3211879	80288560	A/T	0.05	2.31	1.24	4.32	8.55E-03	1.09	0.75	1.60	6.46E-01	3.42E-02	4.14E-02	0.99
CD36	7	rs3211881	80288854	G/A	0.05	2.28	1.22	4.26	9.61E-03	1.09	0.75	1.60	6.46E-01	3.77E-02	4.35E-02	0.99
PFKFB3	10	rs634506	6228980	G/A	0.45	1.34	1.01	1.77	4.02E-02	1.20	0.97	1.47	9.33E-02	2.47E-02	3.92E-02	0.18
MS4A3	11	rs506846	59829741	A/G	0.31	1.50	1.13	1.98	4.39E-03	1.13	0.92	1.38	2.52E-01	8.64E-03	2.68E-02	0.65
MS4A3	11	rs481950	59830103	A/G	0.29	1.56	1.16	2.09	3.04E-03	1.14	0.93	1.40	1.99E-01	5.09E-03	2.55E-02	0.81
MS4A3	11	rs479240	59830370	T/G	0.35	1.68	1.27	2.24	3.39E-04	1.04	0.85	1.28	6.80E-01	2.16E-03	2.55E-02	0.81
C3AR1	12	rs2377419	8229647	A/G	0.44	1.48	1.10	2.00	9.38E-03	1.01	0.82	1.24	9.12E-01	4.93E-02	4.94E-02	0.08
BCAT1	12	rs16928083	24972244	T/G	0.17	1.53	1.06	2.20	2.25E-02	1.53	0.95	2.47	8.33E-02	1.36E-02	3.10E-02	0.01
BCAT1	12	rs10505952	24974646	A/G	0.17	1.54	1.07	2.22	2.14E-02	1.63	1.00	2.67	5.18E-02	8.64E-03	2.68E-02	0.01
BCAT1	12	rs80310895	24976248	A/T	0.17	1.50	1.04	2.18	3.02E-02	1.63	1.00	2.67	5.18E-02	1.17E-02	2.96E-02	0.01

BCAT1	12	rs112686716	24978239	A/G	0.17	1.49	1.02	2.18	3.80E-02	1.40	0.87	2.27	1.68E-01	3.86E-02	4.35E-02	0.01
BCAT1	12	rs7968607	24990454	A/G	0.16	1.55	1.06	2.26	2.25E-02	1.29	0.98	1.69	6.76E-02	1.14E-02	2.95E-02	0.02
BCAT1	12	rs6487427	24992081	C/T	0.16	1.58	1.09	2.28	1.51E-02	1.28	0.95	1.70	1.02E-01	1.15E-02	2.95E-02	0.01
BCAT1	12	rs61914868	25004093	A/G	0.18	1.55	1.08	2.22	1.68E-02	1.22	0.88	1.70	2.27E-01	2.50E-02	3.92E-02	0.08
BCAT1	12	rs12422599	25009028	T/C	0.19	1.59	1.11	2.27	1.08E-02	1.22	0.88	1.70	2.27E-01	1.72E-02	3.46E-02	0.08
BCAT1	12	rs61914869	25021065	G/A	0.13	1.75	1.15	2.66	9.07E-03	1.05	0.73	1.52	7.83E-01	4.22E-02	4.55E-02	0.64
BCAT1	12	rs58322095	25030384	C/G	0.13	1.74	1.15	2.65	9.48E-03	1.05	0.73	1.52	7.83E-01	4.38E-02	4.60E-02	0.64
BCAT1	12	rs9668094	25079296	G/C	0.26	1.62	1.17	2.24	3.58E-03	1.11	0.90	1.37	3.23E-01	8.96E-03	2.68E-02	0.42
BCAT1	12	rs10771144	25092474	A/G	0.30	1.38	1.02	1.88	4.00E-02	1.26	1.02	1.56	3.22E-02	9.86E-03	2.76E-02	0.22
NFE2	12	rs73114552	54710793	T/C	0.18	1.74	1.21	2.50	2.65E-03	1.24	0.89	1.71	2.05E-01	4.61E-03	2.55E-02	0.20
NFE2	12	rs12231389	54712700	G/T	0.19	1.62	1.14	2.30	7.63E-03	1.21	0.87	1.68	2.54E-01	1.41E-02	3.15E-02	0.38
NFE2	12	rs12231393	54712773	C/T	0.22	1.67	1.19	2.34	3.35E-03	1.17	0.85	1.61	3.34E-01	8.72E-03	2.68E-02	0.45
NFE2	12	rs4758957	54715745	C/T	0.22	1.57	1.12	2.19	8.83E-03	1.24	0.90	1.71	1.84E-01	1.21E-02	3.02E-02	0.48
NFE2	12	rs11170866	54716092	T/G	0.22	1.57	1.12	2.19	8.83E-03	1.23	0.89	1.70	2.05E-01	1.33E-02	3.10E-02	0.48
NFE2	12	rs12578224	54717282	G/A	0.19	1.50	1.06	2.12	2.14E-02	1.22	0.88	1.70	2.25E-01	3.05E-02	4.05E-02	0.53
NFE2	12	rs11170869	54717698	G/A	0.19	1.50	1.06	2.12	2.14E-02	1.24	0.90	1.71	1.95E-01	2.70E-02	3.96E-02	0.53
NFE2	12	rs11170871	54720141	A/G	0.19	1.50	1.06	2.12	2.14E-02	1.21	0.87	1.69	2.49E-01	3.32E-02	4.08E-02	0.53
NFE2	12	rs76292014	54721912	A/T	0.19	1.50	1.06	2.12	2.14E-02	1.22	0.88	1.69	2.28E-01	3.08E-02	4.05E-02	0.53
NFE2	12	rs10876552	54722983	T/G	0.19	1.49	1.06	2.10	2.37E-02	1.22	0.88	1.69	2.28E-01	3.35E-02	4.08E-02	0.52
RNASE3	14	rs11156741	21356925	C/G	0.17	1.73	1.19	2.51	3.85E-03	1.04	0.80	1.35	7.87E-01	2.06E-02	3.76E-02	0.22
ATP8B4	15	rs12443320	50234263	A/G	0.27	1.55	1.14	2.12	5.40E-03	1.04	0.68	1.58	8.66E-01	2.97E-02	4.01E-02	0.21
ATP8B4	15	rs4143620	50268059	A/G	0.27	1.53	1.13	2.08	6.21E-03	1.07	0.70	1.64	7.45E-01	2.95E-02	4.00E-02	0.20
WIP1	17	rs10153240	66433456	G/C	0.36	1.50	1.11	2.03	8.09E-03	1.06	0.87	1.30	5.49E-01	2.85E-02	3.98E-02	0.87
EPB41L3	18	rs186904821	5390043	A/G	0.01	4.91	1.44	16.73	1.09E-02	1.95	0.46	8.32	3.66E-01	2.61E-02	3.94E-02	0.24
EPB41L3	18	rs9964022	5454355	T/A	0.02	4.99	1.64	15.16	4.59E-03	1.55	0.73	3.27	2.55E-01	9.06E-03	2.68E-02	0.33
EPB41L3	18	rs77751403	5480030	C/T	0.05	2.90	1.49	5.63	1.67E-03	1.35	0.81	2.24	2.45E-01	3.60E-03	2.55E-02	0.57
EPB41L3	18	rs74980340	5480661	G/C	0.05	2.87	1.48	5.57	1.90E-03	1.24	0.74	2.06	4.10E-01	6.35E-03	2.55E-02	0.56
RAB31	18	rs11081496	9726631	T/C	0.50	1.60	1.19	2.15	1.70E-03	1.19	0.95	1.49	1.40E-01	2.21E-03	2.55E-02	0.63
RAB31	18	rs1893128	9727321	C/T	0.42	1.37	1.03	1.83	2.97E-02	1.20	0.97	1.48	9.70E-02	1.97E-02	3.76E-02	0.49

RAB31	18	rs1893129	9727732	G/A	0.42	1.37	1.03	1.83	2.97E-02	1.16	0.92	1.44	2.04E-01	3.70E-02	4.30E-02	0.49
RAB31	18	rs7232534	9727992	G/A	0.42	1.37	1.03	1.83	2.97E-02	1.17	0.94	1.46	1.71E-01	3.19E-02	4.07E-02	0.49
RAB31	18	rs11877030	9728228	T/C	0.42	1.37	1.03	1.83	2.97E-02	1.21	0.98	1.49	8.34E-02	1.73E-02	3.46E-02	0.49
RAB31	18	rs9963622	9728453	T/C	0.42	1.37	1.03	1.83	2.97E-02	1.22	0.98	1.50	6.89E-02	1.47E-02	3.26E-02	0.49
RAB31	18	rs2864781	9728876	C/A	0.42	1.36	1.02	1.81	3.67E-02	1.16	0.93	1.45	1.96E-01	4.28E-02	4.55E-02	0.47
RAB31	18	rs8089464	9732209	G/T	0.45	1.45	1.08	1.95	1.36E-02	1.10	0.89	1.36	3.74E-01	3.20E-02	4.07E-02	0.10
RAB31	18	rs6506684	9732373	A/G	0.45	1.45	1.08	1.95	1.36E-02	1.10	0.89	1.36	3.74E-01	3.20E-02	4.07E-02	0.10
CEACAM6	19	rs1971787	42267632	T/C	0.37	1.53	1.13	2.07	5.59E-03	1.16	0.94	1.43	1.73E-01	7.68E-03	2.64E-02	0.73
CEACAM6	19	rs8105477	42267670	G/C	0.37	1.53	1.13	2.07	5.59E-03	1.11	0.90	1.37	3.33E-01	1.35E-02	3.10E-02	0.73
CEACAM6	19	rs8106277	42267724	T/C	0.37	1.54	1.14	2.08	4.95E-03	1.19	0.96	1.47	1.05E-01	4.46E-03	2.55E-02	0.74
CEACAM6	19	rs10418434	42267864	T/C	0.37	1.53	1.13	2.07	5.59E-03	1.16	0.94	1.43	1.61E-01	7.21E-03	2.60E-02	0.73
CEACAM6	19	rs10408842	42270588	T/C	0.37	1.52	1.13	2.06	6.14E-03	1.24	1.01	1.54	4.43E-02	2.51E-03	2.55E-02	0.72
CEACAM6	19	rs10413359	42271006	C/T	0.37	1.51	1.12	2.04	6.93E-03	1.16	0.94	1.43	1.61E-01	8.70E-03	2.68E-02	0.71
CEACAM6	19	rs8104232	42272611	G/A	0.37	1.51	1.12	2.04	7.43E-03	1.12	0.90	1.38	3.11E-01	1.64E-02	3.45E-02	0.71
CEACAM6	19	rs2116943	42273489	C/T	0.37	1.52	1.13	2.06	6.14E-03	1.21	0.98	1.50	7.12E-02	3.82E-03	2.55E-02	0.72
CEACAM6	19	rs7258008	42274159	C/A	0.36	1.50	1.11	2.03	7.99E-03	1.25	1.01	1.55	3.96E-02	2.87E-03	2.55E-02	0.71
CEACAM6	19	rs10403840	42274895	G/T	0.37	1.52	1.13	2.06	5.98E-03	1.18	0.96	1.46	1.17E-01	5.77E-03	2.55E-02	0.73
CEACAM6	19	rs2701	42275099	A/G	0.37	1.49	1.10	2.01	9.52E-03	1.24	1.00	1.53	4.91E-02	4.05E-03	2.55E-02	0.67
CEACAM6	19	rs12460461	42277077	C/T	0.37	1.51	1.12	2.04	6.93E-03	1.16	0.94	1.42	1.79E-01	9.55E-03	2.71E-02	0.71
CEACAM6	19	rs6508997	42278288	A/T	0.37	1.52	1.12	2.05	6.67E-03	1.12	0.91	1.39	2.82E-01	1.37E-02	3.10E-02	0.72
CEACAM3	19	rs7251960	42306043	T/C	0.40	1.71	1.28	2.30	3.53E-04	1.19	0.96	1.47	1.19E-01	4.65E-04	1.52E-02	0.05
CEACAM3	19	rs7251336	42306326	A/G	0.41	1.69	1.26	2.27	4.19E-04	1.19	0.96	1.47	1.17E-01	5.34E-04	1.52E-02	0.06
CEACAM3	19	rs7251783	42306436	G/A	0.41	1.65	1.23	2.21	7.60E-04	1.19	0.96	1.47	1.17E-01	9.16E-04	1.77E-02	0.05
CEACAM3	19	rs7251799	42306477	G/A	0.41	1.65	1.23	2.21	7.60E-04	1.19	0.96	1.47	1.17E-01	9.16E-04	1.77E-02	0.05
CEACAM3	19	rs10418100	42306894	C/A	0.41	1.68	1.25	2.25	5.49E-04	1.20	0.97	1.49	9.87E-02	5.86E-04	1.52E-02	0.07
CEACAM3	19	rs10419827	42306984	T/C	0.41	1.68	1.25	2.25	5.49E-04	1.20	0.97	1.49	9.87E-02	5.86E-04	1.52E-02	0.07
CEACAM3	19	rs34819714	42307316	C/G	0.41	1.68	1.25	2.25	5.49E-04	1.20	0.97	1.49	9.10E-02	5.45E-04	1.52E-02	0.07
CEACAM3	19	rs10426020	42308031	G/A	0.39	1.57	1.17	2.10	2.41E-03	1.14	0.92	1.42	2.21E-01	4.55E-03	2.55E-02	0.07
CEACAM3	19	rs10426049	42308080	G/C	0.39	1.57	1.17	2.10	2.52E-03	1.15	0.93	1.43	1.94E-01	4.22E-03	2.55E-02	0.07

CEACAM3	19	rs10426243	42308145	G/T	0.39	1.54	1.15	2.06	3.53E-03	1.20	0.97	1.49	9.55E-02	3.03E-03	2.55E-02	0.06
CEACAM3	19	rs10401370	42308164	T/G	0.39	1.51	1.13	2.02	4.92E-03	1.21	0.98	1.50	8.27E-02	3.58E-03	2.55E-02	0.19
CEACAM3	19	rs10401528	42308183	T/G	0.38	1.54	1.15	2.05	3.60E-03	1.21	0.98	1.50	8.27E-02	2.72E-03	2.55E-02	0.19
CEACAM3	19	rs8113283	42308287	A/G	0.38	1.54	1.15	2.05	3.60E-03	1.21	0.98	1.50	8.27E-02	2.72E-03	2.55E-02	0.19
CEACAM3	19	rs8113720	42308440	G/C	0.39	1.55	1.16	2.07	3.15E-03	1.21	0.98	1.50	8.27E-02	2.41E-03	2.55E-02	0.20
CEACAM3	19	rs8113538	42308500	A/C	0.38	1.54	1.15	2.05	3.60E-03	1.21	0.98	1.50	8.27E-02	2.72E-03	2.55E-02	0.19
CEACAM3	19	rs8113813	42308535	G/T	0.38	1.54	1.15	2.05	3.60E-03	1.21	0.98	1.50	8.27E-02	2.72E-03	2.55E-02	0.19
CEACAM3	19	rs8113641	42308552	C/T	0.38	1.54	1.15	2.05	3.60E-03	1.21	0.98	1.50	8.27E-02	2.72E-03	2.55E-02	0.19
CEACAM3	19	rs8113741	42308603	C/T	0.39	1.53	1.14	2.04	4.23E-03	1.22	0.98	1.50	7.46E-02	2.86E-03	2.55E-02	0.19
CEACAM3	19	rs10408367	42309686	A/G	0.38	1.54	1.15	2.05	3.67E-03	1.20	0.97	1.49	9.87E-02	3.23E-03	2.55E-02	0.19
CEACAM3	19	rs10416824	42310388	T/C	0.38	1.53	1.14	2.06	5.01E-03	1.16	0.94	1.43	1.72E-01	6.95E-03	2.55E-02	0.23
CEACAM3	19	rs1811564	42310919	A/G	0.38	1.52	1.13	2.04	5.92E-03	1.20	0.96	1.48	1.04E-01	5.16E-03	2.55E-02	0.22
CEACAM3	19	rs2199829	42313557	T/C	0.38	1.51	1.12	2.03	6.34E-03	1.19	0.96	1.47	1.17E-01	6.07E-03	2.55E-02	0.22
CEACAM3	19	rs3795022	42313803	T/C	0.38	1.51	1.12	2.03	6.34E-03	1.20	0.97	1.49	9.87E-02	5.24E-03	2.55E-02	0.22
CEACAM3	19	rs734107	42313921	G/T	0.39	1.51	1.12	2.03	7.08E-03	1.16	0.94	1.43	1.72E-01	9.39E-03	2.70E-02	0.25
CEACAM3	19	rs899662	42315281	G/T	0.38	1.51	1.12	2.03	6.34E-03	1.19	0.96	1.48	1.14E-01	5.94E-03	2.55E-02	0.22
CEACAM3	19	rs2008808	42315300	G/T	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.93	1.42	1.97E-01	7.45E-03	2.60E-02	0.23
CEACAM3	19	rs2008798	42315406	A/G	0.38	1.54	1.14	2.07	4.73E-03	1.16	0.94	1.43	1.76E-01	6.74E-03	2.55E-02	0.23
CEACAM3	19	rs10419111	42315813	C/T	0.37	1.53	1.13	2.06	5.65E-03	1.14	0.93	1.41	2.10E-01	9.17E-03	2.68E-02	0.21
CEACAM3	19	rs8110199	42316236	G/A	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.93	1.42	1.96E-01	7.40E-03	2.60E-02	0.23
CEACAM3	19	rs2199830	42317003	G/A	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.94	1.42	1.81E-01	6.89E-03	2.55E-02	0.23
CEACAM3	19	rs8099934	42317279	C/T	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.94	1.42	1.81E-01	6.89E-03	2.55E-02	0.23
CEACAM3	19	rs8100182	42317451	C/T	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.94	1.42	1.81E-01	6.89E-03	2.55E-02	0.23
CEACAM3	19	rs10401928	42317651	A/C	0.38	1.51	1.13	2.03	6.20E-03	1.19	0.96	1.48	1.07E-01	5.52E-03	2.55E-02	0.22
CEACAM3	19	rs10407619	42317872	A/G	0.38	1.54	1.14	2.07	4.73E-03	1.15	0.94	1.42	1.81E-01	6.89E-03	2.55E-02	0.23
CEACAM3	19	rs10410918	42318486	T/C	0.38	1.51	1.12	2.03	6.34E-03	1.19	0.96	1.48	1.07E-01	5.63E-03	2.55E-02	0.22
CEACAM3	19	rs6508998	42319560	T/C	0.38	1.51	1.12	2.03	6.34E-03	1.18	0.95	1.46	1.31E-01	6.74E-03	2.55E-02	0.22
CEACAM3	19	rs4480913	42320394	G/A	0.38	1.51	1.13	2.03	6.20E-03	1.19	0.96	1.48	1.07E-01	5.52E-03	2.55E-02	0.22
CEACAM3	19	rs28821622	42321344	T/C	0.39	1.52	1.14	2.04	4.75E-03	1.19	0.96	1.47	1.17E-01	4.72E-03	2.55E-02	0.23

CEACAM3	19	rs6508999	42322547	G/A	0.40	1.51	1.13	2.04	6.22E-03	1.15	0.93	1.42	1.91E-01	9.20E-03	2.68E-02	0.34
CEACAM3	19	rs6509000	42322577	G/C	0.40	1.49	1.11	2.00	8.78E-03	1.18	0.95	1.47	1.28E-01	8.76E-03	2.68E-02	0.31
CEACAM3	19	rs28824227	42323491	G/A	0.40	1.51	1.13	2.04	6.22E-03	1.15	0.93	1.42	1.91E-01	9.20E-03	2.68E-02	0.34
CEACAM3	19	rs10407206	42323636	A/G	0.40	1.49	1.11	2.00	8.12E-03	1.20	0.97	1.48	9.97E-02	6.57E-03	2.55E-02	0.33
CEACAM3	19	rs10407797	42323681	G/T	0.40	1.51	1.13	2.04	6.22E-03	1.14	0.93	1.41	2.14E-01	1.02E-02	2.78E-02	0.34
CEACAM3	19	rs8106505	42324088	A/G	0.40	1.47	1.09	1.97	1.17E-02	1.19	0.96	1.47	1.20E-01	1.06E-02	2.78E-02	0.29
CEACAM3	19	rs10414823	42324599	C/T	0.40	1.49	1.10	2.00	9.03E-03	1.15	0.93	1.42	1.91E-01	1.27E-02	3.08E-02	0.29
CEACAM3	19	rs12979253	42325196	A/G	0.40	1.49	1.10	2.00	9.07E-03	1.21	0.97	1.49	8.65E-02	6.39E-03	2.55E-02	0.30
RIN2	20	rs6046342	19800248	A/C	0.01	6.34	1.16	34.72	3.31E-02	1.45	0.84	2.50	1.80E-01	3.65E-02	4.27E-02	0.43

Models adjusted by age, sex, medication use, BMI, PC1-PC2 in TCCAS

Models adjusted by age, sex, race, treatment groups, BMI, PC1-PC10 in CAMP

CHR: chromosome; BP: base pair; OR: odds ratio; L95: lower 95% confidence interval of OR; U95: upper 95% confidence interval of OR

†Effect allele/referent allele; MAF: minor allele frequency on TCCAS cohort.

Table S5. Genetic main effects of SNPs with asthma exacerbations in TCCAS and CAMP, by dominant genetic model

Gene	CHR	SNP	BP	Allele†	Genetic main effect										Interaction with RSV infection in TCCAS		
					TCCAS					CAMP					Combined p value	FDR	FDR
					MAF†	OR	L95	U95	P	OR	L95	U95	P				
KIF1B	1	rs17034615	10311877	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.73	1.08	2.78	2.32E-02	8.79E-03	3.83E-02	0.35	
KIF1B	1	rs72865926	10313703	A/G	0.07	1.70	1.00	2.89	4.88E-02	1.73	1.08	2.78	2.32E-02	8.79E-03	3.83E-02	0.35	
KIF1B	1	rs112448832	10324797	G/T	0.07	1.70	1.00	2.89	4.88E-02	1.61	1.03	2.51	3.66E-02	1.31E-02	4.77E-02	0.35	
SPATS2L	2	rs985256	2.01E+08	A/C	0.15	1.54	1.01	2.36	4.43E-02	1.37	1.01	1.85	4.01E-02	1.30E-02	4.77E-02	1.00	
MS4A3	11	rs1286276	59817661	A/G	0.22	2.06	1.37	3.09	4.88E-04	1.20	0.89	1.61	2.39E-01	1.17E-03	7.04E-03	0.75	
MS4A3	11	rs1286278	59818347	C/T	0.22	2.06	1.37	3.10	5.36E-04	1.13	0.84	1.52	4.22E-01	2.13E-03	1.15E-02	0.76	
MS4A3	11	rs12226814	59818483	A/C	0.22	2.06	1.37	3.10	5.36E-04	1.07	0.80	1.43	6.34E-01	3.05E-03	1.59E-02	0.76	
MS4A3	11	rs571760	59824526	G/A	0.21	1.84	1.22	2.78	3.47E-03	1.23	0.91	1.65	1.76E-01	5.14E-03	2.52E-02	0.98	
MS4A3	11	rs479240	59830370	T/G	0.35	1.86	1.24	2.78	2.67E-03	1.12	0.82	1.51	4.75E-01	9.71E-03	4.03E-02	0.99	
BCAT1	12	rs16928083	24972244	T/G	0.17	1.56	1.03	2.37	3.75E-02	1.69	1.01	2.83	4.41E-02	1.22E-02	4.72E-02	0.01	
BCAT1	12	rs10505952	24974646	A/G	0.17	1.57	1.03	2.39	3.53E-02	1.80	1.06	3.04	2.83E-02	7.91E-03	3.62E-02	0.01	
BCAT1	12	rs7968607	24990454	A/G	0.16	1.61	1.05	2.48	3.02E-02	1.42	1.05	1.93	2.42E-02	6.00E-03	2.80E-02	0.01	
BCAT1	12	rs6487427	24992081	C/T	0.16	1.62	1.06	2.48	2.60E-02	1.37	0.98	1.90	6.34E-02	1.22E-02	4.72E-02	0.01	
BCAT1	12	rs9668094	25079296	G/C	0.26	1.74	1.17	2.58	6.28E-03	1.22	0.90	1.65	1.90E-01	9.23E-03	3.96E-02	0.68	
NFE2	12	rs73114552	54710793	T/C	0.18	1.97	1.30	2.99	1.39E-03	1.12	0.79	1.59	5.28E-01	6.01E-03	2.80E-02	0.08	
NFE2	12	rs12231393	54712773	C/T	0.22	1.87	1.25	2.80	2.18E-03	1.04	0.74	1.48	8.06E-01	1.29E-02	4.77E-02	0.37	
RNASE3	14	rs11156741	21356925	C/G	0.17	1.93	1.28	2.91	1.82E-03	1.03	0.77	1.37	8.62E-01	1.17E-02	4.65E-02	0.28	
EPB41L3	18	rs77751403	5480030	C/T	0.05	2.91	1.48	5.72	2.01E-03	1.30	0.77	2.19	3.32E-01	5.53E-03	2.67E-02	0.31	
EPB41L3	18	rs74980340	5480661	G/C	0.05	2.87	1.46	5.65	2.27E-03	1.18	0.69	2.01	5.40E-01	9.45E-03	3.99E-02	0.31	
CEACAM6	19	rs1971787	42267632	T/C	0.37	1.73	1.14	2.63	9.80E-03	1.31	0.90	1.91	1.60E-01	1.17E-02	4.65E-02	0.42	
CEACAM6	19	rs8106277	42267724	T/C	0.37	1.75	1.15	2.65	8.72E-03	1.42	0.98	2.05	6.48E-02	4.79E-03	2.40E-02	0.42	

CEACAM6	19	rs10418434	42267864	T/C	0.37	1.73	1.14	2.63	9.80E-03	1.33	0.91	1.94	1.40E-01	1.04E-02	4.26E-02	0.42
CEACAM6	19	rs10408842	42270588	T/C	0.37	1.71	1.13	2.60	1.09E-02	1.63	1.12	2.36	1.04E-02	1.14E-03	7.01E-03	0.41
CEACAM6	19	rs10413359	42271006	C/T	0.37	1.7	1.12	2.58	1.22E-02	1.33	0.91	1.94	1.40E-01	1.26E-02	4.77E-02	0.40
CEACAM6	19	rs2116943	42273489	C/T	0.37	1.71	1.13	2.60	1.09E-02	1.45	1.00	2.1	5.06E-02	4.69E-03	2.39E-02	0.41
CEACAM6	19	rs7258008	42274159	C/A	0.36	1.72	1.14	2.61	1.06E-02	1.64	1.13	2.37	8.87E-03	9.64E-04	6.35E-03	0.40
CEACAM6	19	rs10403840	42274895	G/T	0.37	1.72	1.14	2.61	1.04E-02	1.36	0.94	1.98	1.03E-01	8.33E-03	3.75E-02	0.41
CEACAM6	19	rs2701	42275099	A/G	0.37	1.64	1.09	2.48	1.90E-02	1.61	1.11	2.33	1.28E-02	2.27E-03	1.20E-02	0.36
CEACAM3	19	rs7251960	42306043	T/C	0.40	2.58	1.65	4.03	3.12E-05	1.54	1.03	2.31	3.50E-02	1.61E-05	8.90E-04	0.03
CEACAM3	19	rs7251336	42306326	A/G	0.41	2.56	1.64	4.00	3.34E-05	1.58	1.06	2.38	2.66E-02	1.33E-05	8.90E-04	0.02
CEACAM3	19	rs7251783	42306436	G/A	0.41	2.42	1.56	3.76	8.69E-05	1.58	1.06	2.38	2.66E-02	3.23E-05	8.90E-04	0.02
CEACAM3	19	rs7251799	42306477	G/A	0.41	2.42	1.56	3.76	8.69E-05	1.58	1.06	2.38	2.66E-02	3.23E-05	8.90E-04	0.02
CEACAM3	19	rs10418100	42306894	C/A	0.41	2.44	1.57	3.79	8.01E-05	1.63	1.09	2.44	1.82E-02	2.11E-05	8.90E-04	0.03
CEACAM3	19	rs10419827	42306984	T/C	0.41	2.44	1.57	3.79	8.01E-05	1.63	1.09	2.44	1.82E-02	2.11E-05	8.90E-04	0.03
CEACAM3	19	rs34819714	42307316	C/G	0.41	2.44	1.57	3.79	8.01E-05	1.65	1.10	2.48	1.51E-02	1.76E-05	8.90E-04	0.03
CEACAM3	19	rs10426020	42308031	G/A	0.39	2.30	1.5	3.54	1.51E-04	1.62	1.06	2.45	2.46E-02	5.01E-05	8.90E-04	0.03
CEACAM3	19	rs10426049	42308080	G/C	0.39	2.28	1.48	3.51	1.74E-04	1.61	1.07	2.44	2.25E-02	5.26E-05	8.90E-04	0.03
CEACAM3	19	rs10426243	42308145	G/T	0.39	2.23	1.45	3.43	2.42E-04	1.67	1.12	2.51	1.27E-02	4.21E-05	8.90E-04	0.02
CEACAM3	19	rs10401370	42308164	T/G	0.39	2.16	1.41	3.31	3.78E-04	1.68	1.12	2.52	1.21E-02	6.07E-05	9.60E-04	0.08
CEACAM3	19	rs10401528	42308183	T/G	0.38	2.19	1.43	3.35	2.92E-04	1.68	1.12	2.52	1.21E-02	4.78E-05	8.90E-04	0.09
CEACAM3	19	rs8113283	42308287	A/G	0.38	2.19	1.43	3.35	2.92E-04	1.68	1.12	2.52	1.21E-02	4.78E-05	8.90E-04	0.09
CEACAM3	19	rs8113720	42308440	G/C	0.39	2.23	1.45	3.41	2.36E-04	1.68	1.12	2.52	1.21E-02	3.92E-05	8.90E-04	0.09
CEACAM3	19	rs8113538	42308500	A/C	0.38	2.19	1.43	3.35	2.92E-04	1.68	1.12	2.52	1.21E-02	4.78E-05	8.90E-04	0.09
CEACAM3	19	rs8113813	42308535	G/T	0.38	2.19	1.43	3.35	2.92E-04	1.68	1.12	2.52	1.21E-02	4.78E-05	8.90E-04	0.09
CEACAM3	19	rs8113641	42308552	C/T	0.38	2.19	1.43	3.35	2.92E-04	1.68	1.12	2.52	1.21E-02	4.78E-05	8.90E-04	0.09
CEACAM3	19	rs8113741	42308603	C/T	0.39	2.17	1.42	3.32	3.58E-04	1.63	1.09	2.44	1.71E-02	7.98E-05	1.13E-03	0.08
CEACAM3	19	rs10408367	42309686	A/G	0.38	2.19	1.43	3.35	3.07E-04	1.63	1.09	2.44	1.82E-02	7.34E-05	1.10E-03	0.08
CEACAM3	19	rs10416824	42310388	T/C	0.38	2.20	1.42	3.40	3.80E-04	1.39	0.93	2.06	1.07E-01	4.52E-04	4.07E-03	0.12
CEACAM3	19	rs1811564	42310919	A/G	0.38	2.14	1.39	3.29	5.47E-04	1.61	1.07	2.40	2.10E-02	1.42E-04	1.89E-03	0.12
CEACAM3	19	rs2199829	42313557	T/C	0.38	2.12	1.38	3.26	6.52E-04	1.58	1.06	2.38	2.66E-02	2.08E-04	2.34E-03	0.11

CEACAM3	19	rs3795022	42313803	T/C	0.38	2.12	1.38	3.26	6.52E-04	1.63	1.09	2.44	1.82E-02	1.47E-04	1.89E-03	0.11
CEACAM3	19	rs734107	42313921	G/T	0.39	2.11	1.37	3.27	7.56E-04	1.39	0.93	2.06	1.07E-01	8.45E-04	5.71E-03	0.14
CEACAM3	19	rs899662	42315281	G/T	0.38	2.12	1.38	3.26	6.52E-04	1.59	1.06	2.38	2.56E-02	2.00E-04	2.34E-03	0.11
CEACAM3	19	rs2008808	42315300	G/T	0.38	2.19	1.42	3.38	4.18E-04	1.42	0.95	2.11	8.66E-02	4.06E-04	3.78E-03	0.12
CEACAM3	19	rs2008798	42315406	A/G	0.38	2.19	1.42	3.38	4.18E-04	1.38	0.93	2.05	1.13E-01	5.15E-04	4.41E-03	0.12
CEACAM3	19	rs10419111	42315813	C/T	0.37	2.14	1.39	3.29	5.14E-04	1.33	0.90	1.99	1.56E-01	8.37E-04	5.71E-03	0.08
CEACAM3	19	rs8110199	42316236	G/A	0.38	2.19	1.42	3.38	4.18E-04	1.35	0.91	2.00	1.42E-01	6.34E-04	4.51E-03	0.12
CEACAM3	19	rs2199830	42317003	G/A	0.38	2.19	1.42	3.38	4.18E-04	1.35	0.91	2.00	1.42E-01	6.34E-04	4.51E-03	0.12
CEACAM3	19	rs8099934	42317279	C/T	0.38	2.19	1.42	3.38	4.18E-04	1.35	0.91	2.00	1.42E-01	6.34E-04	4.51E-03	0.12
CEACAM3	19	rs8100182	42317451	C/T	0.38	2.19	1.42	3.38	4.18E-04	1.35	0.91	2.00	1.42E-01	6.34E-04	4.51E-03	0.12
CEACAM3	19	rs10401928	42317651	A/C	0.38	2.13	1.38	3.28	6.03E-04	1.53	1.02	2.28	3.81E-02	2.68E-04	2.78E-03	0.11
CEACAM3	19	rs10407619	42317872	A/G	0.38	2.19	1.42	3.38	4.18E-04	1.35	0.91	2.00	1.42E-01	6.34E-04	4.51E-03	0.12
CEACAM3	19	rs10410918	42318486	T/C	0.38	2.12	1.38	3.26	6.52E-04	1.53	1.02	2.28	3.81E-02	2.88E-04	2.88E-03	0.11
CEACAM3	19	rs6508998	42319560	T/C	0.38	2.12	1.38	3.26	6.52E-04	1.51	1.01	2.25	4.52E-02	3.37E-04	3.25E-03	0.11
CEACAM3	19	rs4480913	42320394	G/A	0.38	2.13	1.38	3.28	6.03E-04	1.53	1.02	2.28	3.81E-02	2.68E-04	2.78E-03	0.11
CEACAM3	19	rs28821622	42321344	T/C	0.39	2.15	1.40	3.31	4.71E-04	1.54	1.03	2.31	3.45E-02	1.96E-04	2.34E-03	0.10
CEACAM3	19	rs6508999	42322547	G/A	0.40	2.07	1.33	3.21	1.19E-03	1.35	0.91	2.00	1.42E-01	1.63E-03	9.18E-03	0.16
CEACAM3	19	rs6509000	42322577	G/C	0.40	1.98	1.28	3.07	2.13E-03	1.51	1.01	2.25	4.52E-02	9.87E-04	6.35E-03	0.15
CEACAM3	19	rs28824227	42323491	G/A	0.40	2.07	1.33	3.21	1.19E-03	1.35	0.91	2.00	1.42E-01	1.63E-03	9.18E-03	0.16
CEACAM3	19	rs10407206	42323636	A/G	0.40	2.01	1.3	3.11	1.69E-03	1.55	1.04	2.32	3.11E-02	5.72E-04	4.51E-03	0.15
CEACAM3	19	rs10407797	42323681	G/T	0.40	2.07	1.33	3.21	1.19E-03	1.35	0.91	2.00	1.38E-01	1.60E-03	9.18E-03	0.16
CEACAM3	19	rs8106505	42324088	A/G	0.40	1.99	1.29	3.09	1.99E-03	1.49	1.00	2.23	4.98E-02	1.01E-03	6.35E-03	0.19
CEACAM3	19	rs10414823	42324599	C/T	0.40	2.05	1.32	3.18	1.40E-03	1.35	0.91	2.00	1.42E-01	1.89E-03	1.04E-02	0.20
CEACAM3	19	rs12979253	42325196	A/G	0.40	2.04	1.31	3.17	1.49E-03	1.55	1.04	2.31	3.20E-02	5.22E-04	4.41E-03	0.20

Models adjusted by age, sex, medication use, BMI, PC1-PC2 in TCCAS

Models adjusted by age, sex, race, treatment groups, BMI, PC1-PC10 in CAMP

CHR: chromosome; BP: base pair; OR: odds ratio; L95: lower 95% confidence interval of OR; U95: upper 95% confidence interval of OR

†Effect allele/referent allele; MAF: minor allele frequency on TCCAS cohort.

Table S6. Summary of rs7251960 and RSV latent infection on pulmonary function variables

		rs7251960	N	Q1	Q2	Q3	mean	SD
FEV1	RSV(-)	CC	136	1.38	1.82	2.35	1.90	0.78
		CT/TT	257	1.24	1.78	2.28	1.83	0.74
PEF	RSV(-)	CC	136	2.76	3.41	4.81	3.78	1.64
		CT/TT	257	2.41	3.36	4.52	3.69	1.73
	RSV(+)	CC	12	2.57	3.74	4.39	3.48	1.40
		CT/TT	22	2.43	2.96	4.55	3.68	1.94

		rs7251960	N	Q1	Q2	Q3	mean	SD
FEV1	RSV(-)	CC	136	1.38	1.82	2.35	1.90	0.78
		CT	196	1.23	1.81	2.32	1.84	0.75
	RSV(+)	CC	12	1.20	1.83	2.12	1.67	0.63
		CT	16	1.13	1.43	2.28	1.58	0.66
PEF	RSV(-)	CC	136	2.76	3.41	4.81	3.78	1.64
		CT	196	2.40	3.38	4.67	3.70	1.71
	RSV(+)	CC	12	2.57	3.74	4.39	3.48	1.40
		CT	16	2.43	2.57	4.26	3.38	1.68
		TT	6	2.85	4.38	6.09	4.46	2.52

Q1: 25th percentile; Q2: 50th percentile; Q3: 75th percentile; SD: standard deviation

Table S7. ENCODE analysis of rs7251960 potential regulatory mechanisms underlying eQTL for *CEACAM3*

SNP	Promoter histone marks	Enhancer histone marks	DNase	Proteins bound	Motifs changed
rs7251960	BLD (Primary neutrophils from peripheral blood, primary B cells from cord blood, monocytes-CD14+ RO01746 Primary cells)	hESC Derived CD56+ Ectoderm Cultured Cells, Adipose Derived Mesenchymal Stem Cell Cultured Cells, Primary monocytes from peripheral bold, Primary B cells from peripheral blood, Primary hematopoietic stem cells, Primary hematopoietic stem cells short term culture, Primary Natural Killer cells from peripheral blood, Primary hematopoietic stem cells G-CSF-mobilized Female, Primary hematopoietic stem cells G-CSF-mobilized Male, Adipose Nuclei, Esophagus, Placenta, Fetal Thymus, Rectal Mucosa Donor 31, GM12878 Lymphoblastoid Cells	Primary monocytes from peripheral blood, Primary B cells from peripheral blood, Primary T cells from cord blood, Primary Natural Killer cells from peripheral blood, Primary hematopoietic stem cells G-CSF-mobilized Female, Primary YY1 hematopoietic stem cells G-CSF-mobilized Male, GM12878 Lymphoblastoid Cells, Monocytes-CD14+ RO01746 Primary Cells, NHDF-Ad Adult Dermal Fibroblast Primary Cells	CEBPB, COMP1, Gsc, Otx2, Pou2f2, YY1	

Table S8. DeepSEA analyses of rs7251960 in *CEACAM3* identify top 10 potential alterations (sorted by E-value) in transcription factor activities

Chromatin Feature	Cell type	Treatment	E-value	Effect (\log_2 FC) (C allele as reference)	Difference (T allele - C allele)
YY1	GM12892	None	0.000441	0.59734	0.05612
YY1	GM12891	None	0.000459	0.66804	0.032434
YY1	GM12878	None	0.000522	0.65988	0.08005
PAX5-N19	GM12878	None	0.000774	0.90228	0.044407
Pou2f2	GM12891	None	0.00085	0.9377	0.018917
p300	GM12878	None	0.000868	1.0102	0.010871
IRF4	GM12878	None	0.000902	0.8146	0.04814
PAX5-C20	GM12878	None	0.000928	0.72718	0.037238
ATF2	GM12878	None	0.00107	0.90614	0.052002
BCL11A	GM12878	None	0.001084	0.92902	0.049382

FC: fold change

E is short for 'Expect', and E-value is defined as the expected proportion of SNPs with larger predicted effect (from reference allele to alternative allele) for this chromatin feature. The predicted effect magnitude is measured as the product of relative and absolute change, i.e. $|\log(p_{\text{ref}}/(1-p_{\text{ref}}))-\log(p_{\text{alt}}/(1-p_{\text{alt}}))| * |p_{\text{ref}}-p_{\text{alt}}|$. E-value is computed based on the empirical distributions of predicted effects for 1000 Genomes SNPs (<http://deepsea.princeton.edu/help/>).

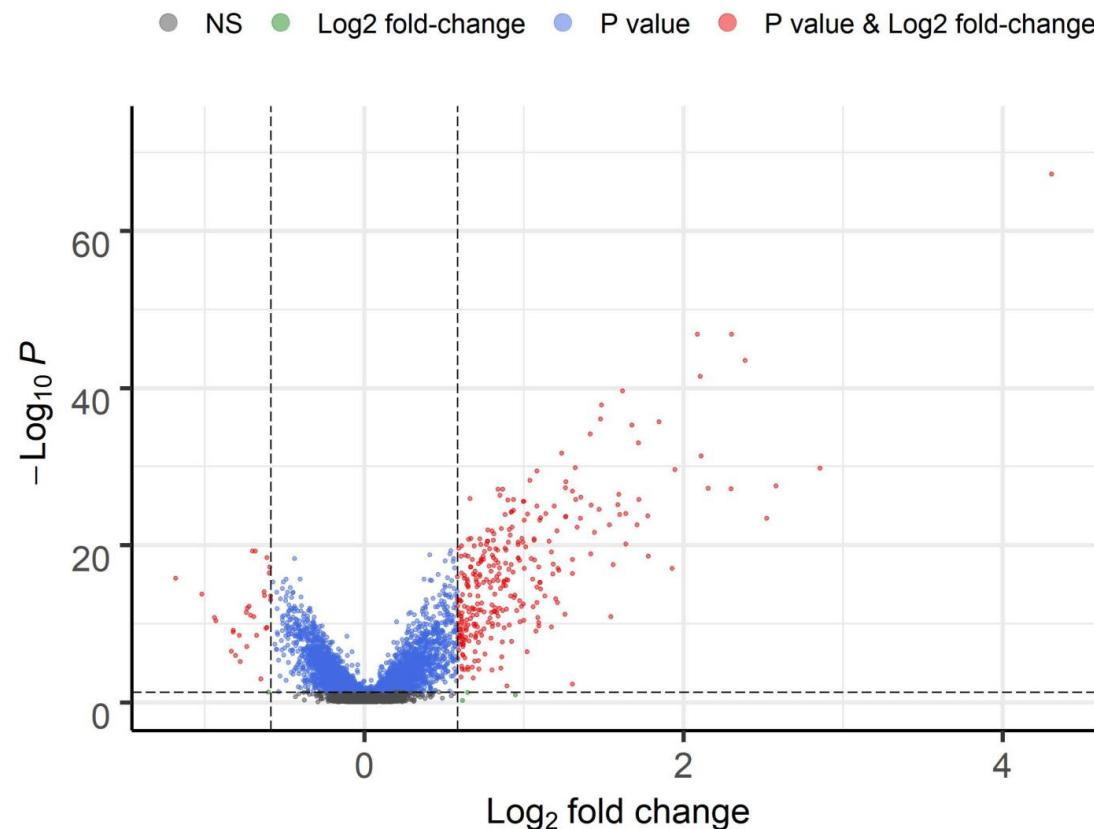


Figure S1. Volcano plot of RSV-related genes for meta-analysis.

Volcano plot shows changes in gene expression of RSV infection. Each circle represents one gene, and a total of 9,031 genes are plotted. The log₂ fold change in the indicated RSV infection versus non-RSV infection is represented on the x-axis. The y-axis shows the log₁₀ of the adjusted p-value. An adjusted p-value of 0.05 and a |log₂ fold change| of 0.585 (fold change of 1.5) are indicated by dash lines.

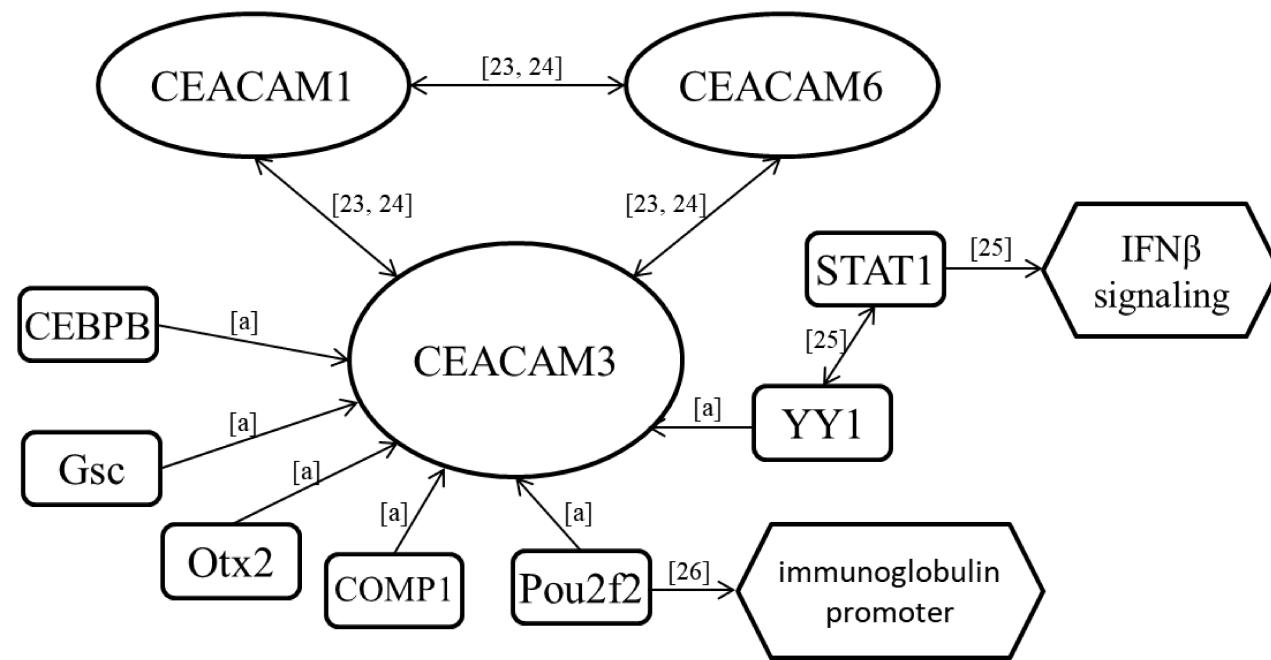


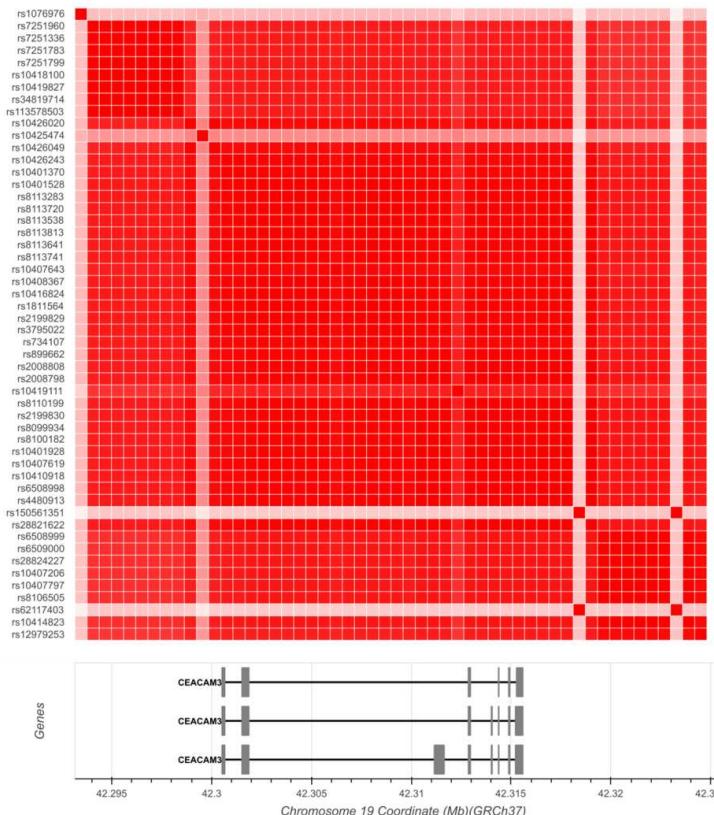
Figure S2. Summary of CEACAM3 and associated regulatory genes of RSV and asthma.

CEACAM3, expressed together with CEACAM6 and CEACAM1, has been recognized to internalize CEACAM-binding pathogens in the absence of opsonizing antibodies or complement factors.^{23,24} We found several transcription factors (CEBPB, COMP1, Gsc, Otx2, Pou2f2 and YY1) potentially regulated CEACAM3 by HaploReg analysis. YY1 dynamically regulates antiviral innate responses during viral infection.²⁵ In the absence of infection, YY1 interacts with STAT1 to avoid an exacerbated and uncontrolled IFN- β signaling. During the viral infection, YY1 expression is gradually downregulated, facilitating IFN- β signaling to inhibit viral infection. Pou2f2 (POU class 2 homeobox 2; OTF2) induced transcription of an immunoglobulin promoter *in vitro*, and has been reported as a B cell-specific transcription factor.²⁶

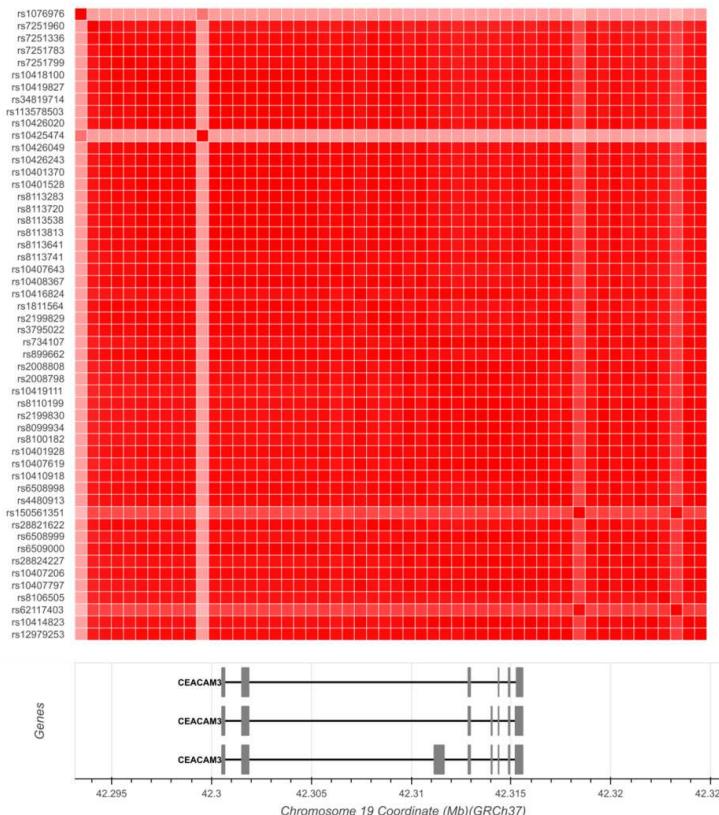
[]: number indicates reference; [a]: current study.

CEACAM3: Carcinoembryonic antigen-related cell adhesion molecules 3; CEACAM6: Carcinoembryonic antigen-related cell adhesion molecules 6; Pou2f2: POU class 2 homeobox 2; YY1: Yin Yang 1; STAT1: Signal transducer and activator of transcription 1; COMP1: cooperates with myogenic proteins 1; Otx2: Orthodenticle Homeobox 2; Gsc: Goosecoid Homeobox; CEBPB: CCAAT Enhancer Binding Protein Beta.

(A)



(B)

**Figure S3. LD plots of SNPs in *CEACAM3* gene**

The LD plots of *CEACAM3* gene are from (A) Han Chinese in Beijing (CHB) and Southern Han Chinese (CHS) and (B) Ad Mixed American (AMR). LD plots are drawn from LDlink website (<https://ldlink.nci.nih.gov/?tab=ldmatrix>).