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Cross-trait genetic analysis of asthma and eosinophils uncovers risk loci in African ancestry populations

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Abstract

Asthma disproportionately affects African ancestry populations, yet its genetic architecture remains poorly characterized due to persistent underrepresentation in genomic studies. We integrated genome-wide association study (GWAS) summary statistics for asthma and white blood cell traits in African ancestry cohorts. Genome-wide and local genetic correlations were assessed using linkage disequilibrium score regression, and cross-trait associations were identified using a conditional false discovery rate framework. We identified a robust positive genetic correlation between asthma and eosinophil counts, together with several ancestry-specific local signals. Cross-trait analysis identified 78 novel pleiotropic loci, including an African-specific locus upstream of CD36, complementing evidence from East Asian populations. We also identified an African-specific association at CD226 (rs8087187), independent of previously reported European associations. Flow cytometry in 19 patients with asthma and 19 healthy controls demonstrated increased CD226 expression in $CD4^+$ T cells from patients with asthma, supporting its functional relevance. Our findings reveal ancestry-specific genetic and immune mechanisms underlying asthma and highlight the importance of diverse populations in elucidating the genetic architecture of complex diseases.

Introduction

Asthma is a heterogeneous respiratory disorder with a strong heritable component and complex pathophysiology. Large-scale genome-wide association studies (GWAS) in European ancestry cohorts have identified hundreds of susceptibility loci, illuminating biological pathways related to immune regulation, airway remodeling, and allergic inflammation[1,2]. However, the genetic basis of asthma in African ancestry populations remains unclear, despite the disproportionately high burden and severity of disease in these groups[3] . Such disparities suggest that distinct ancestry-specific genetic architectures may contribute to asthma susceptibility. Previous studies have provided evidence for ancestry-dependent risk loci, indicating that broader genetic investigations in African ancestry populations are needed to capture the full landscape of asthma risk[4,5].

Eosinophil counts are a well-established biomarker of asthma pathophysiology, reflecting type 2 inflammation and predicting treatment response. Evidence from European cohorts has revealed shared genetic determinants between asthma and eosinophil traits, implying the potential of cross-trait analyses for identifying pleiotropic loci[6]. Inspired by these findings, our recent study in East Asian populations uncovered novel risk loci, including ancestry-specific associations, by jointly analyzing asthma and eosinophil GWAS data[7]. However, whether comparable shared genetic mechanisms exist in African ancestry populations remains largely unexplored.

To address this gap, we performed an integrative genetic analysis of asthma and eosinophil traits in individuals of African ancestry. By leveraging cross-trait statistical frameworks, we aimed to identify novel susceptibility loci, characterize ancestry-specific associations, and assess the degree of genetic sharing between asthma and eosinophil counts. This approach not only provides insights into the immunogenetic basis of asthma in African ancestry populations but also

contributes to a more inclusive understanding of asthma genetics across ancestries.

Methods

GWAS data

This study utilized GWAS summary statistics for asthma and multiple blood cell traits. Summary statistics for asthma GWAS datasets were obtained from the GWAS Catalog. The dataset[8] was comprised 12,093 asthma cases and 105,134 controls of African ancestry. This dataset is part of a large-scale investigation of the genetic architecture of 2,068 traits within the Million Veteran Program (MVP) programme[8].

GWAS summary statistics for blood cell phenotypes were extracted from the same MVP study[8], restricted to the African ancestry subset. Traits included inverse-normal transformed absolute counts (mean and maximum values) for neutrophils, monocytes, lymphocytes, eosinophils, and basophils. Sample sizes ranged from 45,860 to 90,448 across phenotypes and measurement modalities. All blood cell trait GWAS datasets used in this analysis are summarized in Supplementary Table S1.

Genetic correlation analysis

Genetic correlations between asthma and leukocyte traits were estimated using linkage disequilibrium score regression (LDSC) [9]. LDSC infers the correlation of causal effects between two traits (rg, ranging from -1 to 1) by exploiting the relationship between SNP effect sizes and their linkage disequilibrium patterns. Analyses were restricted to HapMap3 variants as recommended, using recomputed LD scores from African-ancestry samples in the 1000 Genomes

Project. Variants with imputation INFO < 0.9 were excluded. To account for potential sample overlap across datasets, LDSC applies an intercept adjustment, which inflates the intercept but does not bias the regression slope from which rg is estimated.

Local genetic correlation analysis

To investigate whether asthma shares local polygenic architecture with specific blood cell traits, we employed the LAVA framework, which performs local genetic correlation analysis across 2,495 approximately independent genomic regions defined by linkage disequilibrium (LD) structure[10]. Partitioning the genome in this manner allows for the detection of region-specific genetic overlap that may be obscured in global-level analyses.We first conducted univariate tests to estimate local SNP heritability (h^2_SNP) for each trait. Only regions with significant local heritability ($p < 0.05$) in both asthma and the respective blood cell trait were retained for downstream analysis. Bivariate tests were then performed to quantify local genetic correlations between asthma and each hematological phenotype within these regions. Multiple testing correction was applied using the Benjamini–Hochberg false discovery rate (FDR < 0.05) across all pairwise trait comparisons. All analyses were restricted to African ancestry summary statistics, using ancestry-matched LD reference panels provided with the LAVA package.

Conditional False Discovery Rate (condFDR)

The condFDR framework extends standard false discovery rate (FDR) methodology by incorporating genetic information from a secondary phenotype to refine association signals in a primary trait [11]. In this study, asthma was the primary phenotype and eosinophil counts the

secondary. The method leverages the observation that true cross-trait associations tend to show enrichment across both traits beyond chance expectations. By conditioning on eosinophil associations, SNP-level test statistics for asthma are re-ranked, dynamically adjusting the significance threshold. Compared with conventional GWAS, condFDR increases power to detect variants jointly associated with both traits while maintaining control of false discoveries. A condFDR threshold of 0.05 was applied to identify significant pleiotropic loci.

Flow cytometry analysis

Peripheral blood samples (2 ml) were obtained from 19 patients with asthma and 19 healthy controls after written informed consent. Samples were diluted 1:1 with phosphate-buffered saline (PBS) and subjected to red blood cell lysis, followed by density gradient centrifugation to isolate peripheral blood mononuclear cells (PBMCs). After washing, Fc receptors were blocked on ice for 15 minutes (Fc Block, Absin, abs9477). Cells were then stained with fluorochrome-conjugated monoclonal antibodies: anti-CD3-FITC (Starter, S0B1765-20T, 1:100), anti-CD4-PE (BD Pharmingen, 753345, 1:200), anti-CD8-APC-Cy7 (Starter, S0B5449-20T, 1:200), anti-CD14-APC (Starter, S0B5194-20T, 1:100), anti-CD56-PE-Cy7 (Absin, abs1840595-25T, 1:100), and anti-CD226-BV421 (BD Pharmingen, 742493, 1:200). Staining was performed for 30 minutes at 4 °C in the dark. Flow cytometry was performed on a BD LSRFortessa cell analyzer, with data acquisition using FACSDiva software. Data analysis was conducted in FlowJo (v10.8.1). Major immune subsets, including lymphocytes, monocytes, and granulocytes, were gated based on size, granularity, and scatter properties before evaluating CD226 expression. The study protocol was approved by the Institutional Ethics Committee of the Affiliated Yantai Yuhuangding Hospital of

Qingdao University (2024-910). All methods were performed in accordance with the relevant guidelines and regulations.

Results

Genetic correlation between asthma and white blood cell traits

We first estimated SNP-based heritability and cross-trait genetic correlations using LD score regression (LDSC). Asthma showed a modest heritability on the observed scale (h^2 = 0.02, SE = 0.0042). Eosinophil traits demonstrated moderate heritability (maximum count: h^2 = 0.11, SE = 0.012; mean count: h^2 = 0.14, SE = 0.014), confirming substantial genetic control of these traits in individuals of African ancestry.

Our analyses demonstrated robust positive genetic correlations between asthma and eosinophil counts (maximum: rg = 0.30, $P = 1\times10^{-3}$; mean rg = 0.33, $P = 2\times10^{-4}$), consistent with previous evidence in European and Asian populations[6,7]. The stronger correlations compared with other white blood cell traits reinforce the key role of eosinophils in asthma and support joint analytical approaches to identify pleiotropic risk loci in African populations (Figure 1).

Local genetic correlation between asthma and eosinophils

We next conducted local genetic correlation analyses focusing on asthma and two measures of eosinophil counts: the maximum and mean values. In total, 74 genomic regions reached statistical significance (FDR < 0.05), demonstrating that the genetic overlap between these traits is driven by specific regions rather than being uniformly distributed across the genome (Figure 2). Notably, several genetically correlated regions encompass key asthma-risk loci previously identified in multi-ancestry GWAS, including the *IL18R1*/*IL1RL1* locus at 2q12.1 and the *TSLP* gene region at

5q22.1. In addition to these known loci, we observed novel regions with significant local correlations that were not captured in previous studies, suggesting new pleiotropic contributors to asthma susceptibility mediated through eosinophilic biology. Importantly, the results were concordant across both maximum and mean eosinophil analyses, supporting the robustness of these shared signals (Figure 2 and Table S2-3).

Cross-trait GWAS analysis between asthma and eosinophils

Building on the strong genetic correlation identified by LDSC analysis, we used a conditional false discovery rate (condFDR) framework to pinpoint loci shared between asthma and eosinophilic traits. Analysis was based on GWAS summary statistics for asthma and two measures of eosinophil counts including maximum and mean absolute values. Joint analysis of asthma with maximum eosinophil counts identified 68 asthma-associated loci, 54 of which are novel and not in LD ($R^2 < 0.05$) with previously reported asthma risk variants; 46 of these fall within genomic regions not previously implicated in asthma (Figure 3 and Table S4). Similarly, analysis of mean eosinophil counts revealed 69 loci, including 53 novel associations and 43 located in regions without prior asthma-linked signals (Figure 3 and Table S5).

Among the newly identified loci, *JAK1* at 1p31.3 emerged as a compelling candidate. *JAK1* encodes a kinase in the JAK–STAT signaling pathway, which mediates cytokine receptor signaling and plays a central role in type 2 inflammation and asthma pathogenesis. Another novel signal was identified near *CD36*, where the risk allele (rs7808977) occurs at a higher frequency in African ancestry populations (gnomAD: 0.249) compared with European populations (0.081). Evidence from whole blood eQTLs in African ancestry cohorts further supports a potential regulatory role of

this locus and highlights its ancestry-specific relevance to asthma susceptibility (Table S6)[12].

We also identified a signal near *CD226*, where the risk allele rs8087187 shows striking population differences (gnomAD: 0.078 in Europeans vs. 0.748 in Africans). Because of its low frequency in Europeans, no significant eQTLs were observed in GTEx; however, whole blood data from African ancestry cohorts revealed significant eQTL effects at this locus (Table S6)[12]. These findings suggest that *CD226*, an immune co-stimulatory receptor, may contribute to asthma susceptibility in African populations through ancestry-specific regulatory mechanisms. Single-cell transcriptomic profiling of airway mucosa further demonstrated that *CD226* expression was significantly increased in $CD4^+$ T cells, epithelial cells, mononuclear phagocytes, and NK cells in asthma (Figure S1)[13].

Flow cytometric analysis of CD226 expression in peripheral blood immune cells

We next examined the expression of CD226 in peripheral blood immune cell subsets from asthma patients and healthy controls using flow cytometry. A total of 19 patients with asthma and 19 non-allergic healthy volunteers were included in the analysis. Standard gating strategies were applied, beginning with FSC versus SSC to distinguish monocytes and lymphocytes, followed by CD3, CD4, CD8, CD56, and CD14 markers to identify $CD4^+$ T cells, $CD8^+$ T cells, NK cells, and monocyte lineage populations, respectively. Within each gated population, the proportion of $CD226^+$ cells was quantified (Figure S2).

The overall proportions of $CD4^+$ T cells, $CD8^+$ T cells, NK cells, and monocyte lineage populations did not differ significantly between asthma patients and controls, indicating that total immune cell composition was comparable across groups (Figure 4A). However, asthma patients

exhibited altered CD226 expression within these subsets. The frequency of $CD226^+$ cells was significantly increased in $CD4^+$ T cells, while differences in $CD8^+$ T cells, NK cells, and monocyte populations were less pronounced (Figure 4B). These findings indicate that CD226 is differentially regulated in T cell subsets during asthma, and may contribute to immune dysregulation in disease pathogenesis.

Discussion

Despite the disproportionate burden and severity of asthma among African ancestry populations, their genetic architecture remains poorly characterized due to limited cohort sizes and underrepresentation in genomic studies. In this study, we jointly analyzed asthma and eosinophil traits and identified ancestry-relevant signals that remain undetected in European-focused research. These findings emphasize the need to expand asthma genetics into diverse populations and illustrate how integrative approaches can advance both biological understanding and clinical translation.

Consistent with previous studies in European and Asian populations, our analyses confirmed substantial genetic sharing between asthma and eosinophil traits, with several well-known loci such as *IL18R1*/*IL1RL1* and *TSLP* showing concordant local correlations across ancestries. These findings reinforce the central role of type 2 immune pathways in asthma pathophysiology regardless of genetic background. At the same time, we also observed ancestry-specific patterns, as certain genomic regions exhibited significant local correlations only in African ancestry populations. Importantly, the HLA locus, a well-established asthma risk region in Europeans and East Asians [1,2,7], did not reach significance in our African ancestry analyses, suggesting that this

224 canonical association may have reduced or distinct effects in African populations . From a clinical
225 perspective, such differences demonstrate the importance of considering ancestry when
226 interpreting genetic findings and developing precision medicine strategies for asthma.

227 Our cross-trait analyses further revealed both shared and ancestry-specific loci in African
228 ancestry populations. For example, *JAK1* emerged as a novel locus that has not been reported in
229 previous asthma studies, further supporting and enriching the genetic evidence for the JAK–STAT
230 signaling pathway in asthma susceptibility[14,15]. We also identified a signal near *CD36* that was
231 absent in European cohorts. Notably, in our previous study, we reported an East Asian–specific
232 missense variant in *CD36* linked to asthma[7], with supporting evidence from mouse models[16]. The
233 present finding of a noncoding regulatory signal upstream of *CD36*, enriched in African
234 populations, deepens our understanding of how variation at this locus may influence asthma risk
235 in a population-specific manner. Finally, we identified an African-specific signal at *CD226*.
236 Although *CD226* locus (rs1788103) has previously reached genome-wide significance in trans-
237 ethnic meta-analyses, those associations were largely driven by European samples[1]. Notably, the
238 variant (rs8087187) we report here is independent from previously described signals based on
239 linkage disequilibrium, suggesting that *CD226* may be subject to distinct regulatory mechanisms
240 across ancestries. Supporting these findings, single-cell transcriptomic profiling showed elevated
241 *CD226* expression across multiple immune and structural cell types in asthmatic airways[13], while
242 flow cytometry further demonstrated increased expression in peripheral blood $CD4^+$ T cells from
243 patients. These observations are consistent with previous reports and provide convergent genetic
244 and functional evidence for *CD226* in asthma pathogenesis[17,18].

245 Our study identifies both shared and ancestry-specific asthma risk loci in African ancestry

populations, providing convergent genetic and functional evidence for their role in disease pathogenesis. These results not only extend current knowledge beyond European-focused studies but also highlight the importance of including diverse populations to improve mechanistic insight and inform precision prevention and treatment strategies in asthma.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Institutional Ethics Committee of the Affiliated Yantai Yuhuangding Hospital of Qingdao University (approval number: 2024-910). All participants provided written informed consent to participate in this study. This study used GWAS data from prior research. Ethical approvals and consents were obtained in the original studies.

Consent for publication

Not applicable. This manuscript does not contain any identifiable individual person's data.

Availability of data and materials

The GWAS summary statistics analyzed in this study were obtained from the VA Million Veteran Program (MVP) and are publicly available through the database of Genotypes and Phenotypes (dbGaP) under accession number phs002453 (https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs002453). The data can also be explored through the MVP PheWeb browser (https://phenomics.va.ornl.gov/web/). The processed flow cytometry data supporting the

findings of this study are included in the article and its Supplementary Information. Additional de-identified flow cytometry data are available from the corresponding author upon reasonable request, subject to applicable ethical and participant privacy restrictions. Details of each GWAS are provided in Supplementary Table S1.

Competing interests

The authors declare that they have no competing interests.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this manuscript, the author(s) used ChatGPT (OpenAI) to assist with manuscript writing, language editing, and translation between Chinese and English. The author(s) reviewed and revised the AI-generated output as necessary and take full responsibility for the content of the published article.

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References

1. Tsuo, K. *et al.* Multi-ancestry meta-analysis of asthma identifies novel associations and highlights the value of increased power and diversity. *Cell Genom* **2**, 100212 (2022).
2. Han, Y. *et al.* Genome-wide analysis highlights contribution of immune system pathways to the genetic architecture of asthma. *Nat Commun* **11**, 1776 (2020).
3. Keet, C.A. *et al.* Neighborhood poverty, urban residence, race/ethnicity, and asthma: Rethinking the inner-city asthma epidemic. *J Allergy Clin Immunol* **135**, 655-62 (2015).
4. Chang, X. *et al.* Genetic architecture of asthma in African American patients. *J Allergy Clin Immunol* **151**, 1132-1136 (2023).
5. Daya, M. *et al.* Association study in African-admixed populations across the Americas recapitulates asthma risk loci in non-African populations. *Nat Commun* **10**, 880 (2019).
6. Li, B. *et al.* Shared genetic architecture of blood eosinophil counts and asthma in UK Biobank. *ERJ Open Res* **9**(2023).
7. Zhi, L. *et al.* Multi-trait genetic analysis of asthma and eosinophils uncovers pleiotropic loci in East Asians. *Nat Commun* **16**, 5081 (2025).
8. Verma, A. *et al.* Diversity and scale: Genetic architecture of 2068 traits in the VA Million Veteran Program. *Science* **385**, eadj1182 (2024).
9. Bulik-Sullivan, B.K. *et al.* LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat Genet* **47**, 291-5 (2015).
10. Werme, J., van der Sluis, S., Posthuma, D. & de Leeuw, C.A. An integrated framework for local genetic correlation analysis. *Nat Genet* **54**, 274-282 (2022).
11. Smeland, O.B. *et al.* Discovery of shared genomic loci using the conditional false discovery rate approach. *Hum Genet* **139**, 85-94 (2020).
12. Kachuri, L. *et al.* Gene expression in African Americans, Puerto Ricans and Mexican Americans reveals ancestry-specific patterns of genetic architecture. *Nat Genet* **55**, 952-963 (2023).
13. Alladina, J. *et al.* A human model of asthma exacerbation reveals transcriptional programs and cell circuits specific to allergic asthma. *Sci Immunol* **8**, eabq6352 (2023).
14. Xin, Y. *et al.* Emu-miR-10a-5p in Echinococcus multilocularis-derived-extracellular vesicles alleviates airway inflammation in mice with allergic asthma by inhibiting macrophage M2a polarization through LIF-mediated JAK1-STAT3 signaling. *Front Immunol* **16**, 1577349 (2025).
15. Lai, Y. *et al.* Lingganwuweijiangxin Decoction suppresses allergic airway inflammation in Guinea pigs with cough variant asthma by regulating the treg/Th17 balance and the JAK1/STAT6 signaling pathway. *J Asthma* **62**, 1280-1295 (2025).
16. Patel, P.S. & Kearney, J.F. CD36 and Platelet-Activating Factor Receptor Promote House Dust Mite Allergy Development. *J Immunol* **199**, 1184-1195 (2017).
17. Zhang, Y. *et al.* CD226 implicated in Akt-dependent apoptosis of CD4(+) T cell contributes to asthmatic pathogenesis. *Cell Death Dis* **15**, 705 (2024).
18. Sakano, Y. *et al.* Blocking CD226 regulates type 2 innate lymphoid cell effector function and alleviates airway hyperreactivity. *J Allergy Clin Immunol* **153**, 1406-1422.e6 (2024).

Figures

Figure 1. Genetic correlations between asthma and leukocyte traits. (A) Genetic correlations between asthma and maximum absolute counts of five leukocyte traits. (B) Genetic correlations between asthma and mean absolute counts of the same leukocyte traits. Estimates (rg) and 95% confidence intervals are shown.

Figure 2. Local genetic correlations between asthma and eosinophil counts across the genome in African ancestry populations. Red and pink circles represent correlations with maximum and mean eosinophil counts, respectively, while diamonds mark previously reported asthma loci in European (blue) and African (brown) populations.

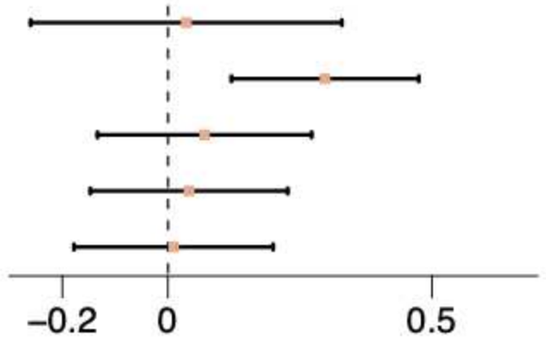
Figure 3. Circular Manhattan plot of significant loci associated with asthma in African populations. (A) Circular plot illustrating significant loci across the genome (chr1–chr22). From outer to inner rings: (i) condFDR results for asthma and eosinophil maximum counts, (ii) condFDR results for asthma and eosinophil mean counts, (iii) single-trait GWAS of asthma (iv) single-trait GWAS of eosinophil maximum counts, and (v) single-trait GWAS of eosinophil mean counts. (B–D) Regional association plots for representative loci, illustrating fine-mapping results and linkage disequilibrium patterns surrounding key variants. The y-axis indicates −log10(*p*-value), and the color of each point reflects LD (r^2) with the lead SNP.

Figure 4. Flow cytometric analysis of CD226 expression in peripheral blood immune cells. (A) Quantification of the proportion of $CD4^+$ T cells, $CD8^+$ T cells, NK cells, and myeloid nuclear

phagocyte (MNP) cells among total peripheral blood mononuclear cells from asthma patients and healthy controls. (B) Proportion of $CD226^+$ cells within each immune subset ($CD4^+$ T cells, $CD8^+$ T cells, NK cells, and MNP cells) in asthma patients versus controls. Flow cytometry was performed on samples from 19 asthma patients and 19 non-allergic healthy volunteers. Data are shown as mean ± SD. Statistical significance was assessed using two-sided unpaired Student's t-test (*$P < 0.05$; ns, not significant).

A

Trait1	Trait2	rg(95%CI)	P value
Asthma	Basophil count	0.03 (−0.26,0.32)	0.81
	Eosinophil count	0.29 (0.12,0.47)	1.00×10^{-3}
	Lymphocyte count	0.07 (−0.13,0.27)	0.50
	Monocyte count	0.04 (−0.14,0.22)	0.67
	Neutrophil count	0.01 (−0.17,0.19)	0.91



B

Trait1	Trait2	rg(95%CI)	P value
Asthma	Basophil count	0.03 (−0.22,0.29)	0.79
	Eosinophil count	0.33 (0.16,0.51)	2.00×10^{-4}
	Lymphocyte count	0.08 (−0.11,0.28)	0.38
	Monocyte count	0.05 (−0.12,0.23)	0.51
	Neutrophil count	0.0035 (−0.18,0.19)	0.97

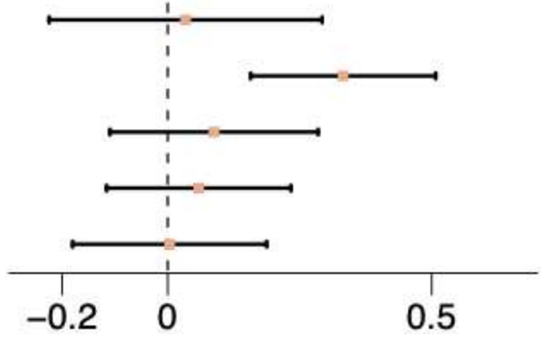


Fig2

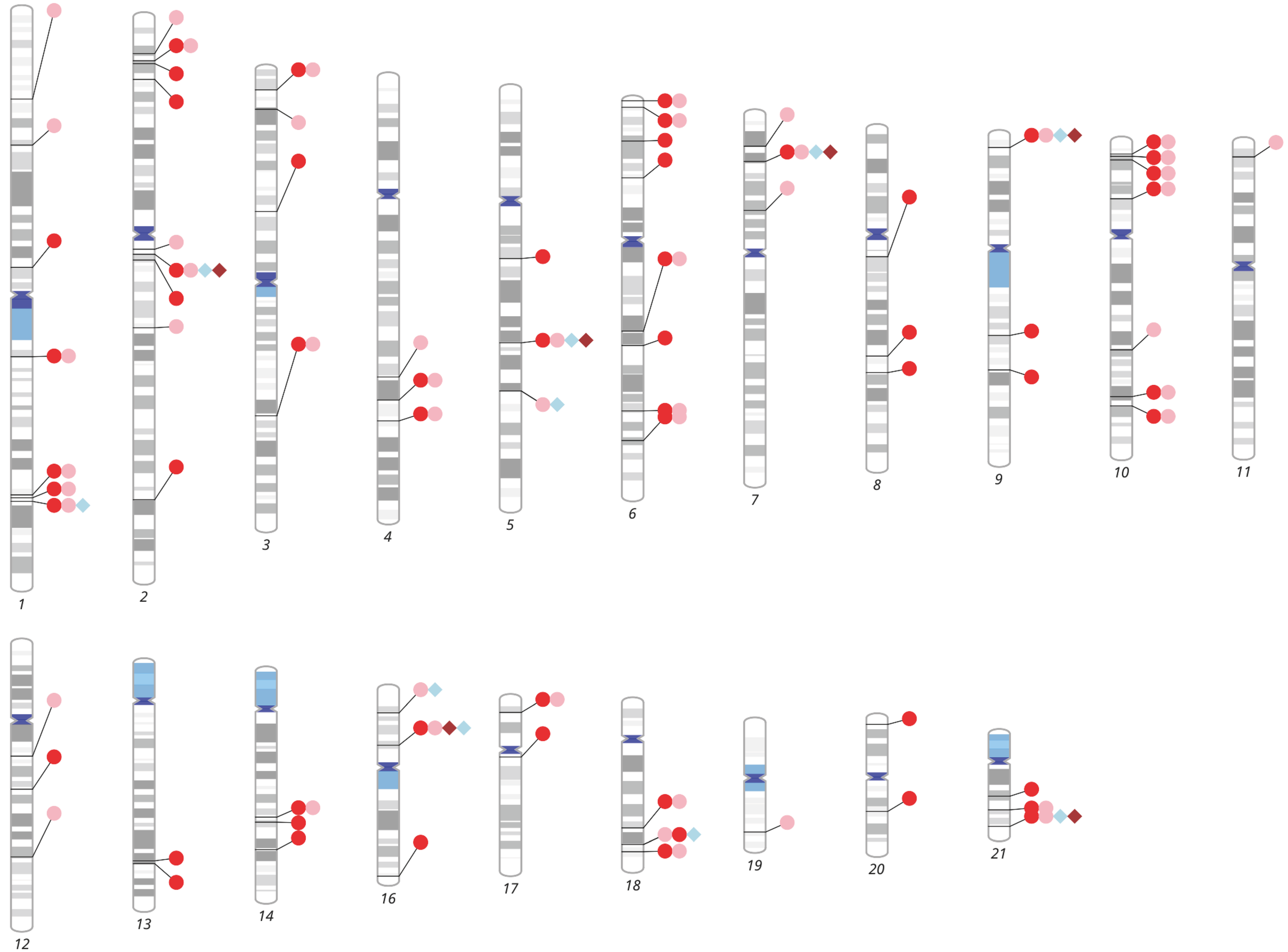
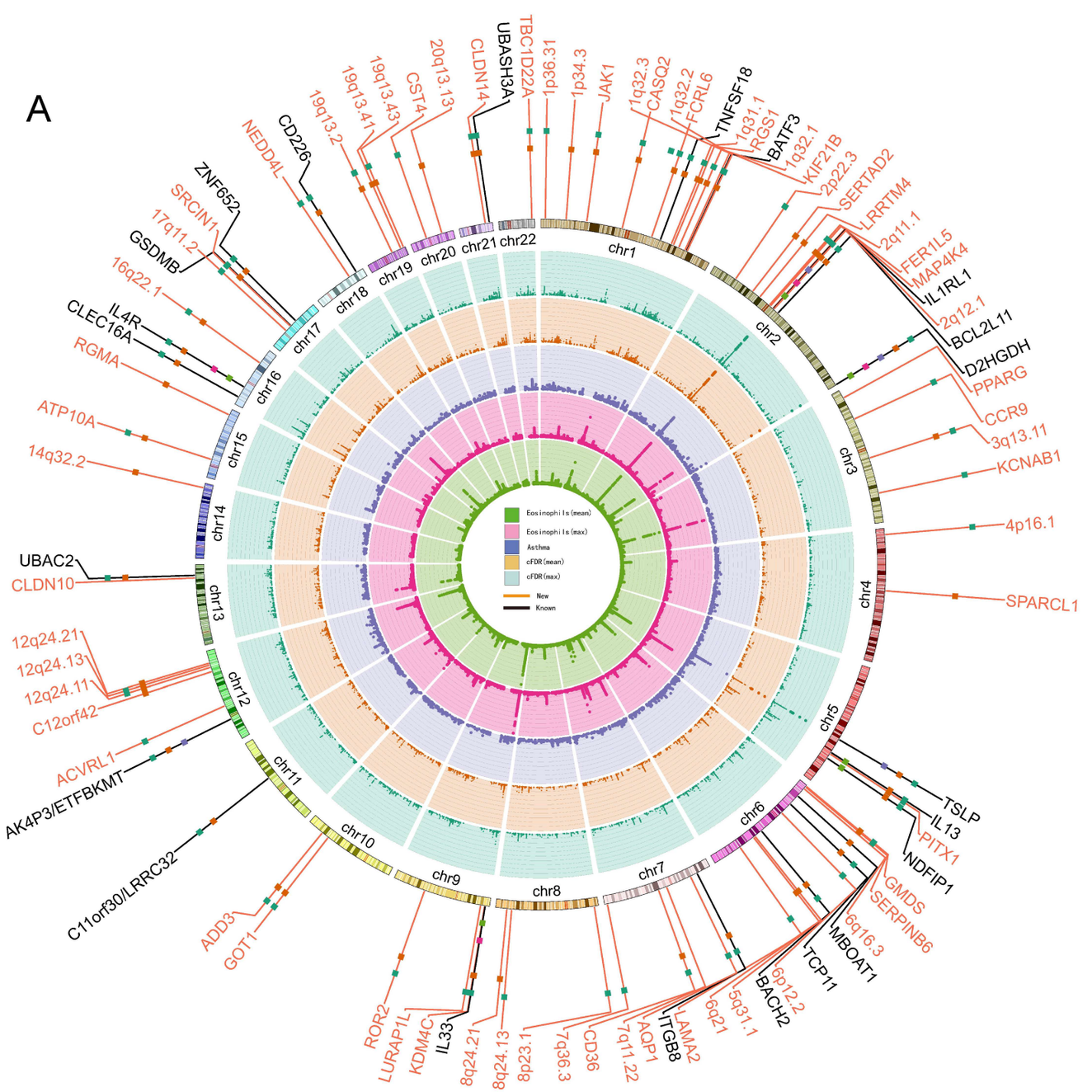
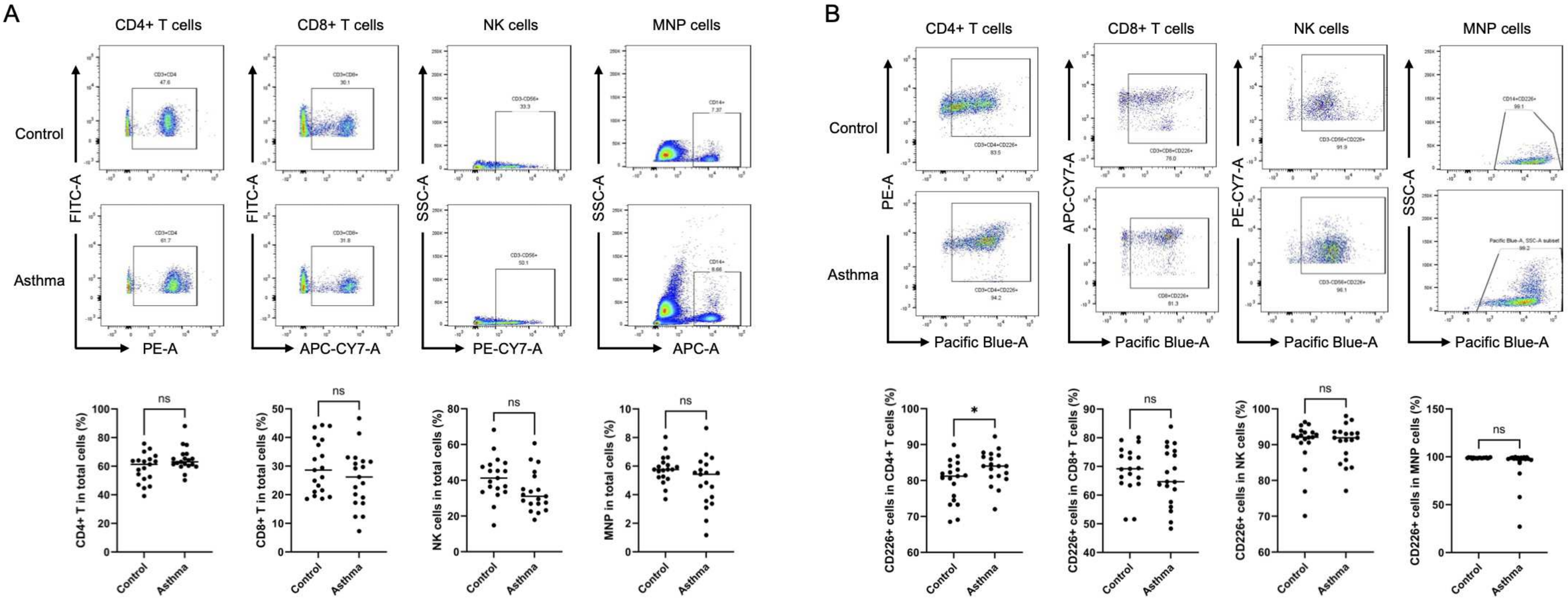

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Significant region
Known asthma locus
Eosinophis (max)
Eosinophis (mean)
Asthma-EUR
Asthma-AFR

Fig3


A
UBASH3A
TBC1D22A
1p36.31
1p34.3
JAK1
1q32.3
CASQ2
1q32.2
FCRL6
TNFSF18
1q31.1
RGS1
BATF3
1q32.1
KIF21B
2p22.3
SERTAD2
LRRTM4
2q11.1
FER1L5
MAP4K4
IL1RL1
2q12.1
BCL2L11
D2HGDH
PPARG
CCR9
3q13.11
KCNAB1
4p16.1
SPARCL1
TSLP
IL13
PITX1
NDFIP1
GMDS
SERPINB6
6q16.3
MBOAT1
TCP11
BACH2
6p12.2
5q31.1
6q21
LAMA2
AQP1
7q11.22
CD36
7q36.3
8p23.1
8q24.13
8q24.21
IL33
KDM4C
LURAP1L
ROR2
ADD3
GOT1
C11orf30/LRRC32
AK4P3/ETFBKMT
ACVRL1
C12orf42
12q24.11
12q24.13
12q24.21
CLDN10
UBAC2
14q32.2
ATP10A
RGMA
CLEC16A
IL4R
16q22.1
GSDMB
17q11.2
SRCIN1
ZNF652
NEDD4L
CD226
19q13.2
19q13.41
19q13.43
CST4
20q13.13
CLDN14
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chr21
chr22
Eosinophils (mean)
Eosinophils (max)
Asthma
cFDR (mean)
cFDR (max)
New
Known
B
Plotted SNPs
rs6588104
RAVER2
JAK1
LINC01359
Position on chr1 (Mb)
C
Plotted SNPs
rs7792680
GNAI1
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GNAT3
CD36
Position on chr7 (Mb)
D
Plotted SNPs
rs8087187
DOK6
CD226
RTTN
Position on chr18 (Mb)
Recombination rate (cM/Mb)


A
CD4+ T cells
CD8+ T cells
NK cells
MNP cells
Control
Asthma
FITC-A
PE-A
FITC-A
APC-CY7-A
SSC-A
PE-CY7-A
SSC-A
APC-A
CD4+ T in total cells (%)
CD8+ T in total cells (%)
NK cells in total cells (%)
MNP in total cells (%)
ns
ns
ns
ns
Control
Asthma
B
CD4+ T cells
CD8+ T cells
NK cells
MNP cells
Control
Asthma
PE-A
APC-CY7-A
PE-CY7-A
SSC-A
Pacific Blue-A
Pacific Blue-A
Pacific Blue-A
Pacific Blue-A
CD226+ cells in CD4+ T cells (%)
CD226+ cells in CD8+ T cells (%)
CD226+ cells in NK cells (%)
CD226+ cells in MNP cells (%)
*
ns
ns
ns
Control
Asthma

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable2.docx
- SupplementaryFigures.docx