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Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	GWAS summary statistics of asthma in East Asians were downloaded from GBMI study,and summary statistics Japanese were obtained from studies of BioBank Japan through GWAS Catalog. Summary statistics of the largest GWAS for hematological traits were obtained from GWAS Catalog.RNA sequencing data from GSE201955 was downloaded from the GEO database.
Data analysis	The article utilized LDSC v1.0.1 to estimate the genetic correlation between asthma and hematological traits, employed S-LDSC to assess the enrichment of cell-type-specific SNP heritability, and conducted bidirectional Mendelian randomization analysis using the R package "TwoSampleMR" v0.6.4. Local genetic correlation analysis was carried out using ρ-HESS v0.5.3. Multi-trait GWAS meta-analysis for asthma and various hematological traits was performed using MTAG. GWAS analysis of Chinese individuals was conducted using PLINK 1.9. The differential expression of CD36 was evaluated using the two-sided Wilcoxon rank-sum test.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The datasets analyzed in this study are obtained from publicly available sources. Summary statistics for the BioBank Japan (BBJ) dataset were accessed via the GWAS Catalog (https://www.ebi.ac.uk/gwas/summary-statistics) under their data usage policies. Data from the Global Biobank Meta-analysis Initiative (GBMI) were used in accordance with their access guidelines (https://www.globalbiobankmeta.org/resources). Additional genotype and phenotype data from the Chinese replication cohort are not publicly available due to participant privacy restrictions. Access can be requested from the corresponding author (changxiao@sdfmu.edu.cn) and requires ethical approval and a data use agreement. Summary statistics for genome-wide significant loci generated in this study are provided in the Supplementary Data.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	In this study, the sex of participants in the Chinese cohort was determined through self-reporting. During the multivariable logistic regression analysis to investigate the association between genetic variations and asthma diagnosis status in Chinese individuals, sex was included as a covariate.
Reporting on race, ethnicity, or other socially relevant groupings	In our manuscript, we specifically used "ethnicity" as a categorization variable to focus our genetic analysis on East Asians. This demographic focus was utilized to explore the genetic basis of asthma in a population that is underrepresented in global asthma studies.Ethnicity was used not as a proxy for other variables such as socioeconomic status, but as a means to directly study genetic variations unique to East Asians. This approach is essential because genetic markers and their association with diseases can significantly vary between populations due to evolutionary backgrounds and environmental interactions.
Population characteristics	See above
Recruitment	A total of 1,100 asthmatic patients were recruited from The First Affiliated Hospital of Shandong First Medical University. Patients diagnosed with asthma were identified based on the criteria outlined in the 2023 GINA Report (Global Strategy for Asthma Management and Prevention).Additionally, asthmatic patients from the CAS cohort who are currently undergoing asthma treatment were included based on healthcare and lifestyle questionnaires. A total of 2,506 control subjects were selected from the CAS cohort based on questionnaire information indicating no history of allergies or respiratory diseases.
Ethics oversight	This study was approved by the Institutional Review Boards of The First Affiliated Hospital of Shandong First Medical University, Beijing Institute of Genomics (Chinese Academy of Sciences) and Beijing Zhongguancun Hospital.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	In this study, the determination of sample size was not explicitly detailed regarding whether pre-statistical methods calculations were performed. The asthma GWAS analysis involved 18,549 cases and 322,655 controls for the East Asian population, and 13,015 cases and 162,933 controls for the Japanese population. Additionally, in the GWAS analysis of Chinese individuals, 1,100 asthmatic patients were recruited from The First Affiliated Hospital of Shandong First Medical University, and 2,506 control subjects without a history of allergies or respiratory diseases were selected from the CAS cohort of the Chinese Academy of Sciences in Beijing. These sample sizes were chosen based on existing large bioinformatics databases and available data from preliminary studies, providing sufficient statistical power to explore the association between asthma and related genetic markers.
Data exclusions	In the GWAS analysis, individuals with a genotype call rate less than 95%, gender mismatch, possible contamination, or not belonging to the target population (such as non-East Asians or Japanese) were excluded. Additionally, SNPs that did not meet Hardy-Weinberg equilibrium tests were also excluded. These exclusion criteria were pre-established to ensure the quality and reliability of the analysis data.
Replication	The study follows standard bioinformatics workflows to ensure the reproducibility and robustness of the findings.

Randomization

Since this study primarily involved observational genetic analysis rather than experimental interventions, samples/organisms/participants were not randomly assigned to experimental groups. All data originated from existing bioinformatics databases, hence this issue is not applicable to our study.

Blinding

During the data collection and analysis process, as the study's nature was primarily based on analyses of existing databases, the researchers were aware of the group allocations, and blinding was not a requirement. Moreover, the analysis relied on objective genetic data, which minimized the possibility of subjective bias.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

APC anti-human CD36
Supplier: Biolegend
Catalog number: 336207
Clone name: 5-271
Lot number: B348761

Pacific Blue anti-human CD294 (CRTH2)
Supplier: Biolegend
Catalog number: 350129
Clone name: BM16
Lot number: B314227

FITC anti-human CD4
Supplier: Biolegend
Catalog number: 317407
Clone name: OKT4
Lot number: B374224

Validation

Antibodies are commercially available and validated in the literature as cited on the manufacturers' websites (listed below), as well as by the manufacturers data sheets.
APC anti-human CD36（336207）: https://www.biolegend.com/en-us/products/apc-anti-human-cd36-antibody-5421#antigenDetails.
Pacific Blue anti-human CD294(CRTH2) (350129): https://www.biolegend.com/en-us/products/pacific-blue-anti-human-cd294-crth2-antibody-16162.
FITC anti-human CD4 (317407): https://www.biolegend.com/en-us/products/fitc-anti-human-cd4-antibody-3653.

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Two milliliters (ml) of human peripheral blood were collected using an anticoagulant tube and diluted with phosphate-buffered saline (PBS) at a 1:1 ratio. Ficoll-Paque PLUS (Cytiva, 17144002) was added into a 15 ml centrifuge tube. Diluted peripheral blood was carefully layered onto the Ficoll along the tube wall, and after centrifugation, the middle white membrane layer containing Peripheral Blood Mononuclear Cells (PBMCs) was collected. PBMCs were washed and resuspended in PBS. Cells were then stained with monoclonal antibodies specific to CD4 (Biolegend, clone: OKT4, 317407), CD36 (Biolegend, clone: 5-271, 336207), and CRTH2 (Biolegend, clone: BM16, 350129).
Instrument	flow cytometry analysis was performed utilizing the BD-FACSAria Fusion platform.
Software	FACSDiva (BD) for cell acquisition and FlowJo software (FlowJo,LLC) version 10 for analysis.
Cell population abundance	PBMCs were freshly isolated using density gradient centrifugation from heparinized peripheral blood.
Gating strategy	Monocytes, granulocytes, lymphocytes are gated based on cell shape, size, and cell granularity. ILC2-rich cells are then identified in lymphocytes by CD4- and CRTH2+.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

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