

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ | 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ | 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

Data analysis

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 raw data of CyTOF in this paper have been deposited in the OMIX, China National Center for Bioinformatics / Beijing Institute of Genomics, Chinese Academy of Sciences (<https://ngdc.cncb.ac.cn/omix>; accession no. OMIX006334). The raw data of RNA-seq reported in this paper have been deposited in the Genome Sequence Archive (Genomics, Proteomics & Bioinformatics 2021) in National Genomics Data Center (Nucleic Acids Res 2022), China National Center for Bioinformatics / Beijing Institute of Genomics, Chinese Academy of Sciences (GSA: CRA016019) that are publicly accessible at <https://ngdc.cncb.ac.cn/gsa>. The raw data of single-cell

RNA-seq have been deposited in the Genome Sequence Archive at the National Genomics Data Center, China National Center for Bioinformation / Beijing Institute of Genomics, Chinese Academy of Sciences (GSA: CRA025173) and are publicly accessible at <https://ngdc.cncb.ac.cn/gsa>. All data in this article are provided in source data file or available upon reasonable request from the corresponding authors.

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	We did not select based on sex and gender in the cohort of 1068 serum samples (male : female = 553 : 515).
Reporting on race, ethnicity, or other socially relevant groupings	We did not select based on race, ethnicity, or other socially relevant groupings.
Population characteristics	We did not select based on population characteristics.
Recruitment	We collected data without any bias in the recruitment process. These people were excluded: (1) people during pregnancy; (2) people suffered from congenital or hereditary anemia, HIV, end-stage kidney disease, cirrhosis, blood cancer, BM transplant and splenectomy, or other severe motor and/or mental disturbance; (3) people that predicted lifespan were lower than 1 years.
Ethics oversight	The detection and analysis of clinical samples in this study were under the ethical approval of the Fourth Affiliated Hospital Zhejiang University School of Medicine (K2022171). Registration and giving informed written consent were performed.

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	No statistical methods were used to pre-determine sample size, but the sample sizes are similar to those in previously published works in the field.
Data exclusions	Outliers were excluded from the analyses.
Replication	All experimental groups contained at least three biological replicates.
Randomization	Allocations were random.
Blinding	Investigators were blinded to group allocation during data collection and analysis.

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

1. CD45-APC, eBioscience, 17-0454-811, 104 (1:50 for Flow Cyt)
2. CD45-FITC, Biolegend, 103107, 30-F11 (1:50 for Flow Cyt)
3. CD11b-FITC, Biolegend, 101205, M1/70 (1:50 for Flow Cyt)
4. CD3e-FITC, Invitrogen, 11-0031-82, 145-2C11 (1:50 for Flow Cyt)
5. CD3e-APC/Cy7, Biolegend, 100221, 17A2 (1:50 for Flow Cyt)
6. CD19-APC/Cy7, Biolegend, 115529, 6D5 (1:50 for Flow Cyt)
7. CD19-PE, Biolegend, 115507, 6D5 (1:50 for Flow Cyt)
8. Ly6G-APC/Cy7, Biolegend, 127623, 1A8 (1:50 for Flow Cyt)
9. Ly6G-APC, Biolegend, 127613, 1A8 (1:50 for Flow Cyt)
10. NK1.1-APC, Biolegend, 156505, S17016D (1:50 for Flow Cyt)
11. NK1.1-APC/Cy7, Biolegend, 108723, PK136 (1:50 for Flow Cyt)
12. CD170-APC/Cy7 (SiglecF), Biolegend, 155531, S17007L (1:50 for Flow Cyt)
13. NEU1, Santa Cruz, sc-166824, F-8 (1:1000 for WB)
14. Tubulin, CST, 2144 (1:3000 for WB)
15. Anti-mouse HRP, Jackson Immuno Research, 115-035-003 (1:5000 for WB)
16. Anti-rabbit HRP, Abclonal, AS014 (1:5000 for WB)
17. IL-1b, R&D Systems, MAB401 (5 mg/kg for Neutralization)
18. IL-6, R&D Systems, MAB406 (2 mg/kg for Neutralization)
19. MIP-1a, R&D Systems, AF-450 (2 mg/kg for Neutralization)
20. Elastin, Sigma, E4013, BA-4 (5 mg/kg for Neutralization)

Validation

All the antibodies in this study are commercially available and have been applied and validated in multiple published research studies.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

Bone marrow-derived macrophages were isolated from femurs and tibias from wild-type or LysM-Cre/Neu1-flox male mice. bone marrow was flushed with culture medium using a 1 ml syringe for acquiring bone marrow-derived macrophages. BMDMs were cultured and purified in low-glucose Dulbecco's modified Eagle's medium (L-DMEM, C11885500BT, Gibco, USA) containing 10% FBS and M-CSF (CB34, Novoprotein, China).

Authentication

None of the cell lines used were authenticated.

Mycoplasma contamination

Cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines (See [ICLAC](#) register)

No commonly misidentified lines used.

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals

Wild type C57BL/6J mice (12, 40, 60, 65, 68, 70-week-old); P16-3MR mice (12, 60-week-old); Rag1 gene knockout mice (8, 30-week-old); LysM-IDTR mice (24-week-old); LysM-Cre/Neu1-flox mice (12-week-old); Neu1 gene knockout mice (12-week-old); Yorkshire pigs (24-week-old); NDG-hIL15 mice (24-week-old).

Wild animals

I declare that the study did not involve wild animals.

Reporting on sex

Male animals were primarily used to verify the findings.

Field-collected samples

I declare that the study did not involve samples collected from the field.

Ethics oversight

Animal experiments were conducted with the approval of the Zhejiang University Experimental Animal Welfare and Ethics Committee (ZJU20230096 for mice experiments, ZJU20240053 for pig experiments).

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration

No clinical trial.

Study protocol

Note where the full trial protocol can be accessed OR if not available, explain why.

Data collection	<i>Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.</i>
Outcomes	<i>Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.</i>

Plants

Seed stocks	<i>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.</i>
Novel plant genotypes	<i>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.</i>
Authentication	<i>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, mosaicism, off-target gene editing) were examined.</i>

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	<i>Sample was collected from mouse peripheral blood or spleen. Blood or spleen samples were collected and red blood cells were lysed. Cells were resuspended and stained with antibodies for 60 min on ice in dark. Wash cells with PBS and resuspend in PBS for flow cytometry analysis.</i>
Instrument	<i>The flow cytometry analyzer (Cytoflex, Beckman, USA) was used.</i>
Software	<i>Data was analyzed with the Flowjo software (v10.8.1).</i>
Cell population abundance	<i>Cells were stained as follows: B cell (CD45+, CD19+), T cell (CD45+, CD3E+), neutrophil (CD45+, CD11B+, LY6G+), monocyte/macrophage (CD45+, CD11B+, LY6G-, CD3E-, CD19-, NK1.1-, SiglecF-).</i>
Gating strategy	<i>Live cells were gated with FSC/SSA, and doublets were excluded based on FSC-H/FSC-A. Immune cells were stained as CD45+ and subset cells were further defined based on multiple markers as follows: B cell (CD45+, CD19+), T cell (CD45+, CD3E+), neutrophil (CD45+, CD11B+, LY6G+), monocyte/macrophage (CD45+, CD11B+, LY6G-, CD3E-, CD19-, NK1.1-, SiglecF-).</i>

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