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Last updated by author(s): Nov 5, 2021

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 *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	Erythrocytes in the blood were lysed using FACSlyse solution (BD Pharmingen San Diago, CA). Multi-parameter analysis and flow cytometric cell sorting were performed on a FACS Aria II (BD Biosciences San Jose, CA) and analyzed with FlowJo software (Tree Star, Inc., Ashland, OR, USA).
Data analysis	Statistical analyses were done with Prism GraphPad software v5.0, and the exact tests used are indicated within the appropriate text.

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

All data generated or analyzed during this study that are not included in this published article and its supplementary information files are available from the corresponding authors on reasonable request.

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 method was used to pre-determine the sample size. For the animal experiment, 4-6 biological replicates were performed.
Data exclusions	No data exclusions
Replication	All experiments were reliably reproduced and results are represented as the means ± SEM as appropriate, which is indicated in figure legends.
Randomization	Experimental mice were age- and sex-matched and all experiments included littermate controls, without randomization process.
Blinding	The investigators were blinded to the genotype of the animals during the experimental procedure.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Fluorochrome-conjugated mAbs specific to mouse F4/80 (clone BM8), CD115 (clone AFS98), Ly6C (HK 1.4), Ly6A/E (clone D7), CD117 (clone 2B8), CD135 (clone A2F 10), CD34 (clone RAM34), CD207 (clone 4C7), I-A/I-E (clone M5/114.15.2), and the corresponding isotype controls were purchased from BioLegend (San Diego, CA, USA.). CD3e (clone 145-2c 11), CD19 (clone 1D3), and a lineage cocktail with an isotype control (561317) were purchased from BD Pharmingen (San Diago, CA).
Validation	1. Fluorochrome-conjugated mAb specific to mouse F4/80 (clone BM8), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤ 0.25 µg per 106 cells in 100 µl. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/apc-anti-mouse-f4-80-antibody-4071 2. Fluorochrome-conjugated mAbs specific to mouse CD115 (clone AFS98), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤ 0.25 µg per 106 cells in 100 µL volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/purified-anti-mouse-cd115-csf-1r-antibody-6214 3. Fluorochrome-conjugated mAbs specific to mouse Ly6C (HK 1.4), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤ 0.25 µg per 106 cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/apc-anti-mouse-ly-6c-antibody-6047 4. Fluorochrome-conjugated mAbs specific to mouse Ly6A/E (clone D7), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤0.25 µg per million cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/apc-anti-mouse-ly-6a-e-sca-1-antibody-225

5. Fluorochrome-conjugated mAbs specific to mouse CD117 (clone 2B8), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤0.06 µg per million cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/purified-anti-mouse-cd117-c-kit-antibody-77

6. Fluorochrome-conjugated mAbs specific to mouse CD135 (clone A2F 10), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤ 1.0 µg per 106 cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/apc-anti-mouse-cd135-antibody-6284

7. Fluorochrome-conjugated mAbs specific to mouse CD34 (clone RAM34), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤1.0 µg per million cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/pe-anti-mouse-cd34-antibody-13484

8. Fluorochrome-conjugated mAbs specific to mouse CD207 (clone 4C7), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤1.0 µg per million cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/purified-anti-mouse-human-cd207-langerin-antibody-8537

9. Fluorochrome-conjugated mAbs specific to mouse I-A/I-E (clone M5/114.15.2), application statement in manufacturer's website as following: Each lot of this antibody is quality control tested by immunofluorescent staining with flow cytometric analysis. For flow cytometric staining, the suggested use of this reagent is ≤ 0.25 µg per million cells in 100 µl volume. It is recommended that the reagent be titrated for optimal performance for each application. https://www.biolegend.com/en-us/search-results/purified-anti-mouse-i-a-i-e-antibody-368

10. Fluorochrome-conjugated mAbs specific to mouse CD3e (clone 145-2c11), application statement in manufacturer's website as following: Flow cytometry (Routinely Tested). https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv737-hamster-anti-mouse-cd3e.612771

11. Fluorochrome-conjugated mAbs specific to mouse CD19 (clone 1D3), application statement in manufacturer's website as following: Flow cytometry (Routinely Tested). https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv737-rat-anti-mouse-cd19.612781

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Tg(Csf1r-Mer-iCre-Mer)1Jwp mice (Jax#019098), R26R-EYFP mice (Jax#006148), W/Wv mice (Jax#100410), mT/mG mice (Jax#007676), Cx3cr1<tm2.1(cre/ERT2)Jung>/J mice (Jax#020940), Fgd5ZsGr.CreERT2 mice (Jax#027789), B6 ACTb-EGFP mice (Jax#003291) were purchased from the Jackson Laboratory. Stop-Cas9 mic (#T002249) were purchased from NanJing Biomedical Research Institute of Nanjing University (China). Wildtype C57BL/6 mice were obtained from the Institute of Laboratory Animal Science Chinese Academy of Medical Science. CCR2- mice (Jax#004999) were kindly provided by Dr. Li Tang (Beijing Institute of Lifeomics). Unless otherwise stated, mice were used at 6-12 weeks of age. Experimental mice were age- and sex-matched.
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	All animal procedures performed in this study were approved by the Institutional Animal Care and Use Committee of Capital Medical University.

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

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	Erythrocytes in the blood were lysed using FACSlyse solution (BD Pharmingen San Diago, CA). The isolated cells were surface stained in FACS buffer (PBS w/o Ca2+ Mg2+ supplemented with 0.5% BSA and 5 mM EDTA) for 30 min on ice.
Instrument	Multi-parameter analysis and flow cytometric cell sorting were performed on a FACS Aria II (BD Biosciences San Jose, CA).
Software	Multi-parameter analysis and flow cytometric cell sorting were analyzed with FlowJo software (Tree Star, Inc., Ashland, OR,

USA).

Cell population abundance

For absolute F4/80+ cell counts, total NPCs isolated from each mouse were stained and sorted separately, and the cell number was counted with flow cytometry during FACS.

Gating strategy

1. Gating strategy of Kupffer cells. Dot plots are gated on viable single liver non-parenchymal cells. Kupffer cells are defined as F4/80 + cells. All Kupffer cells are CD45+ /CD11b+/ Ly6C- cells.

2. Gating strategy of bone marrow hematopoietic stem cells. 7-AAD + dead cells and doublets were excluded from the analysis and sorting. Dot plots are gated on all bone marrow cells, then on Lineage - cells, and then on Sca-1 + and c-kit + cells. Hematopoietic stem cells are defined as Linneg /Sca-1+/ c-kit+ /CD34- /CD135- cells.

3. Gating strategy of blood MO. Dot plots are gated on blood cells in monocyte region. MO are defined as CD115 + cells.

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