nature portfolio

Corresponding author(s): Xing Guo

Last updated by author(s): Jun 15, 2022

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	Beckman Optima XE-90; Biorad Gene Pulser Xcell; Malvern Zetasizer Nano ZS90; Transmission electron microscopy (JEM-2100F); Enzyme marker (Biotek ELX800); Fluorescence microscope (Axio Observer Z1, Zeis, Germany); Confocal microscope (A1R+, Nikon); Microplate reader (Varioskan LUX, Thermo Fisher Scientific, USA); Laser speckle contrast imaging system (RFLSI Ⅲ, RWD); In vivo imaging system (IVIS Spectrum); Small animal 7T magnetic resonance scanning system (Bruker, BioSpec 70/30USR); Microscope slide scanner (PANNORAMIC MIDI, 3DHISTECH); Ortho fluorescence microscope (Beijing Shiji Kexin Scientific Instrument Co., Ltd); Chemiluminescence imager (Monna, QuickChemi 5100); Two-photon confocal microscopy (A1RMP+, Nikon); NanoDrop 2000 spectrophotometer (Thermo Scientific, USA); Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, USA); TruSeq Stranded mRNA LT Sample Prep Kit (Illumina, San Diego, CA, USA); RNA extraction reagent (TRIcom, Tianmu Biological).
Data analysis	SMART 3.0 behavioral recording system (Panlab, Spain); FlowJo (version 10.4.0); CytExpert (version 2.0); ImageJ software (version 2.0.0); LivingImage (version 4.5.2); Zen (version 2.3); Origin (version 2021); GraphPad Prism (version 8.0).

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 authors declare that all the data supporting the findings of this study are available within the article, the Supplementary Information and Source Data file.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	No human research performed.
Population characteristics	No human research performed.
Recruitment	No human research performed.
Ethics oversight	No human research 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	Simple sizes of 3-10 biologically independent samples or animals per group were used for in vitro and in vitro studies, respectively, as indicated for specific experiments in figure legends. We adhered to sample size requirements necessary for determining statistical significance with reference to the numbers used in recent relevant publications.
Data exclusions	No data were excluded from the analyses.
Replication	All experiments have at least 3 biologically independent replicates, the number of which is indicated in figure legends.
Randomization	Mice are allocated randomly to each treatment group.
Blinding	Behavioral tests were performed by an investigator blinded to the experimental groups.

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[ ]	[x] MRI-based neuroimaging

Antibodies

Antibodies used

CD11b (1:100 for Flow, ab24874, Abcam);
CD206 (1:100 for Flow, MA5-16872, eBioscience);
CD80 (1:100 for Flow, ab93507, Abcam);
IBA-1 (1:100 for Flow, ab178846, Abcam);
CD16/32 (1:100 for Flow, 1:200 for IF, ab171202, Abcam);
CD45 (1:100 for Flow, ab269346, Abcam);
Ly6G (1:100 for Flow, 1:200 for IF, ab25377, Abcam);
H3cit (1:800 for WB, 1:1000 for IF, ab219407, Abcam);
STING (1:800 for WB, ab288157, Abcam);
VE-Cadherin (1:800 for WB, ab205336, Abcam);
Claudin-5 (1:800 for WB, ab131259, Abcam);
Occludin (1:800 for WB, ab216327, Abcam);
ZO-1 (1:800 for WB, ab276131, Abcam);
CD206 (1:100 for IF, ab64693, Abcam);
GFAP (1:1000 for IF, ab7260, Abcam);
Alexa fluor 488 conjugated donkey anti-rabbit (1:1000 for IF, R37118, Invitrogen);
Alexa Fluor 647-conjugated goat anti-rat IgG (1:1000 for IF, ab150159, Abcam);
Alexa Fluor 488-conjugated goat anti-rat IgG (1:1000 for IF, ab150157, Abcam);
Alexa Fluor 488-conjugated goat anti- rabbit IgG (1:1000 for IF, GB25303, Servicebio);
Alexa Fluor 647-conjugated goat anti- rabbit IgG (1:1000 for IF, GB27303, Servicebio).

Validation

The antibodies used in the study were all purchased from reputable commercial sources. All antibodies are widely used and validated by the providers or previous publications. Below are the manufacturer's links to the antibody information and relevant citations.
CD11b (ab24874, Abcam)(https://www.abcam.cn/fitc-cd11b-antibody-m170-ab24874.html);
CD206 (MA5-16872, eBioscience)(https://www.thermofisher.cn/cn/zh/antibody/product/CD206-Antibody-clone-MR5D3-Monoclonal/MA5-16872);
CD80 (ab93507, Abcam) (https://www.abcam.cn/pe-cd80-antibody-16-10a1-ab93507.html);
IBA-1 (ab178846, Abcam)(https://www.abcam.cn/iba1-antibody-epr16588-ab178846.html);
CD16/32 (ab171202, Abcam)(https://www.abcam.cn/cd16cd32-antibody-93-low-endotoxin-azide-free-ab171202.html);
CD45 (ab269346, Abcam)(https://www.abcam.cn/pe-cd45-antibody-em-05-ab269346.html);
Ly6G (ab25377, Abcam)(https://www.abcam.cn/ly6g--ly6c-antibody-rb6-8c5-ab25377.html);
H3cit (ab219407, Abcam)(https://www.abcam.cn/histone-h3-citrulline-r17-antibody-epr20358-120-ab219407.html);
STING (ab288157, Abcam)(https://www.abcam.cn/sting-antibody-epr25090-107-ab288157.html);
VE-Cadherin (ab205336, Abcam)(https://www.abcam.cn/ve-cadherin-antibody-epr18229-ab205336.html);
Claudin-5 (ab131259, Abcam)(https://www.abcam.cn/claudin-5-antibody-epr7583-ab131259.html);
Occludin (ab216327, Abcam)(https://www.abcam.cn/occludin-antibody-epr20992-ab216327.html);
ZO-1 (ab276131, Abcam)(https://www.abcam.cn/zo1-tight-junction-protein-antibody-blr092g-ab276131.html);
CD206 (ab64693, Abcam)(https://www.abcam.cn/mannose-receptor-antibody-ab64693.html);
GFAP (ab7260, Abcam)(https://www.abcam.cn/gfap-antibody-ab7260.html);
Alexa fluor 488 conjugated donkey anti-rabbit (R37118, Invitrogen)(https://www.thermofisher.cn/cn/zh/antibody/product/Donkey-anti-Rabbit-IgG-H-L-Secondary-Antibody-Polyclonal/R37118);
Alexa Fluor 647-conjugated goat anti-rat IgG (ab150159, Abcam)(https://www.abcam.cn/goat-rat-igg-hl-alexa-fluor-647-ab150159.html);
Alexa Fluor 488-conjugated goat anti-rat IgG (ab150157, Abcam)(https://www.abcam.cn/goat-rat-igg-hl-alexa-fluor-488-ab150157.html);
Alexa Fluor 488-conjugated goat anti- rabbit IgG (GB25303, Servicebio)(https://www.servicebio.cn/goodsdetail?id=273);
Alexa Fluor 647-conjugated goat anti- rabbit IgG (GB27303, Servicebio)(https://www.servicebio.cn/goodsdetail?id=4191).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

RAW264.7 and BV-2 were obtained from the Chinese Academy of Sciences. Neutrophils were extracted from the bone marrow of healthy adult C57BL/6 mice.

Authentication	RAW264.7 and BV-2 cell lines were used for less than 1 month since purchase and neutrophils for less than 24 hours from extraction. No further authentication test was performed.
Mycoplasma contamination	All cell were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None of the cell lines used in this research are listed in the database of commonly misidentified cell lines.

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	Male C57BL/6 mice (8-12 weeks, 25-30 g) were obtained from Beijing Huafukang Biotechnology Co., Ltd. The animals were hosted in SPF barrier environment at 25 ℃ with a 12h dark/light cycle and have access to food and water.
Wild animals	No wild animals were used in this study.
Reporting on sex	No sex- and gender-based analyses have been performed.
Field-collected samples	No Field-collected samples used.
Ethics oversight	All animal experiments were conducted under protocols approved by the Institutional Animal Care and Use Committee of Southwest Jiaotong Universtiy.

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	For neutrophil identification, cells extracted from the mouse bone marrow were added to erythrocyte lysis solution and washed to collect the neutrophil suspension for further analysis. For brain tissues, the sample is chopped to small pieces, digested by collagenase and then mechanically processed to form single cell suspensions through 40 um cell strainer for flow cytometry analysis.
Instrument	BD FACS Ariall (BD Bioscience).
Software	FlowJo (version 10.4.0)
Cell population abundance	Neutrophils were confirmed to be >90%.
Gating strategy	Cells were gated by forward scattering height (FSC-H) and lateral scattering height (SSC-H). Macrophage surface marker positive events were gated using CD11b-FITC (1:100, Abcam), CD206-PE (1:100, eBioscience) and CD80-PE (1:100, Abcam) versus fluoresecence height; Microglia were labeled with IBA-1-FITC (1:100, Abcam), CD206-PE (1:100, eBioscience) and CD16/32-PE (1:100, Abcam); and neutrophils were labeled with CD45-PE (1:100, Abcam), CD11b-FITC (1:100, Abcam) and Ly6G-APC (1:100, Abcam).

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

Magnetic resonance imaging

Experimental design

Design type	Structural (T2WI) imaging.
Design specifications	T2WI were acquired to evaluate the infarct volume.
Behavioral performance measures	No behavioral performance measures.

Acquisition

Imaging type(s)	Stuctural Magnetic Resonance Imaging
Field strength	7T (Bruker, BioSpec 70/30USR)
Sequence & imaging parameters	The T2-weighted series used are as follows: TR=2,500.0 ms, TE =35.0 ms, flip angel = 90.0°, NEX = 4, FOV = 3.00 cm, matrix = 256, section thickness = 1.00 mm, scan = 20, echo =1/1.
Area of acquisition	Whole brain

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	No preprocessing performed.
Normalization	Not used.
Normalization template	Not used.
Noise and artifact removal	Not used.
Volume censoring	Not used.

Statistical modeling & inference

Model type and settings	No modeling performed.
Effect(s) tested	Not used.

Specify type of analysis: ☒ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)	Not relevent.
Correction	Not used.

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☐	☒ Graph analysis
☒	☐ Multivariate modeling or predictive analysis

Graph analysis	The infarct volume was calculated through ImageJ software according to T2WI.