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Corresponding author(s): Hai-Yan Zhou

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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	BD FACS Diva software v9.0 and BD Canto II/Aria system(flow cytometry), Applied Biosystem 7900HT Real-Time PCR System (qPCR), Oxymax-CLAMS and Oxymax Systems (metabolic cages), OLYMPUS CX41-32RFL microscope system and Leica SP8 confocal microscope system(immunofluorescence).
Data analysis	FlowJo V10 (flow cytometry),GraphPad Prism 8 .0 (data analysis), ImageJ 1.44 (imaging analysis), featureCounts software, Seurat V3.1.2, R package clusterProfiler (Version 3.5.1).

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 RNA-Seq data and RIP-Seq data produced in this paper have been deposited in the Sequence Read Archive database with the BioProject accession number

PRJNA852952 (https://www.ncbi.nlm.nih.gov/bioproject/PRJNA852952/). The accession numbers for published dataset used in this paper are GSM4331816 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSM4331816], GSM4331817 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSM4331817] and GSE25324 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE25324]. The data for Genotype Tissue Expression (GTEx) database are acquired from GEPIA2 [http://gepia2.cancer-pku.cn/]. The Tlr4 and Ager expression profiles are aquired from BioGPS [http://biogps.org].All other data supporting the findings of this study are available within the paper and its Supplementary Information. Source data are provided with this paper.

Human research participants

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

Reporting on sex and gender	9 young male participants (aged from 16-32) and 13 older male participants (aged from 56-69, male) .
Population characteristics	Human peripheral blood cells were colloceted from people defined healthy status based on no prior history of cadiovascular diseas, liver disease, diabetes or immunological disorders and divided into two categories based on age: Young:aged from 16-32; Older: aged from 56-69.
Recruitment	The patients were randomly recruited at Xiangya Hospital of Central South University. There is no potential self-selection bias or other biases.
Ethics oversight	The collection and use of human blood samples were approved by the Committee of Clinical Ethics at Xiangya Hospital of Central South University and the protocols followed were compliant with the ethical principles of the Helsinki Declaration. Written informed consents were obtained from all human donors.

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	Sample size was not predetermined but we performed experiments with group sizes based on existing published literature of similar experiments. For animal experiments, n≥4 was chosen based on the previous publications in the field (Meilian Liu et al., 2014, Cell metabolism). For experiments other than those involving animals, n≥3 was chosen based on the previous publications in the field (Tuo Deng et al., 2013, Cell metabolism) and also because this size is necessary to calculate statistical significances.
Data exclusions	In qPCR data, samples were rarely excluded when the RNA quality was poor or the expression of the house keeping genes (internal controls) in a particular sample differed from the average of the other samples by more than 2 Ct value. The exclusion criteria (the expression of the house keeping genes) was pre-established.
Replication	All experimental findings were reliably reproduced for three times and all replication attempts were successful.
Randomization	The samples used in this study were randomly assigned to control or experimental groups.
Blinding	Investigators were blinded to group allocation during data collection of histological specimens and metabolic tests. In experiments without subjective estimation like flow cytometry and qPCR, investigators were unblinded during data collection since no bias would be introduced by the investigators.For all experiments, investigators were blinded during data 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

Methods

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

Antibodies

Antibodies used

Immunofluorescence Staining: Cd11b (BioLegend, 101245, 1:100), CD3 (BioLegend, 100203, 1:50), S100A8 (Proteintech, 15792-1-AP, 1:200), TH (GeneTex, GTX634481, 1:200), TH (Beyotime, AF2185, 1:100), TUBB3 (Cell Signaling Technology, 4466S, 1:200), EGFP (Servicebio, GB11602, 1:500), CD31 (Servicebio, GB12063, 1:200). Secondary antibodies: Alexa Fluor 488 conjugated anti-Rabbit (Invitrogen, A21206, 1:200) , Alexa Fluor 555 conjugated anti-Rabbit (Invitrogen, A21428, 1:200), Alexa Fluor 555 conjugated anti-mouse (Invitrogen, A31570, 1:200).
Immunoblot : RBM3 (Proteintech, 14363-1-AP, 1:1000), PGC1a (4A8) (Santa Cruz Biotechnology, sc-517380, 1:500), UCP1 (Abcam, ab10983, 1:1000), P21 (Abcam, ab109520, 1:1000), P16 (Sigma-Aldrich, SAB4500072, 1:1000), Tubulin (Proteintech, 11224-1-AP, 1:5000), S100A8 (Proteintech, 15792-1-AP, 1:1000), S100A9 (Proteintech, 26992-1-AP, 1:1000), p-p38 (Cell Signaling Technology, 4511S, 1:1000), p38 (Cell Signaling Technology, 8690S, 1:1000), p-ERK (Cell Signaling Technology, 4370S, 1:1000), ERK (Cell Signaling Technology, 4695S, 1:1000), GAPDH (Origene, TA802519, 1:5000), NRP1(A-12) (Santa Cruz Biotechnology, sc-5307, 1:500), EPHA7 (Affinity Biosciences, AF0627, 1:1000), TH (Beyotime, AF2185, 1:1000), Phospho-TH (Ser40) (Cell Signaling Technology, 2791S, 1:1000), TUBB3(Cell Signaling Technology, 4466S, 1:1000), phosphor-Histone H2A.X (Ser139) (Sigma, 05-636, 1:1000), PCNA (Boster, BM0104, 1:10000).
Flow cytometry: Zombie Aqua™ Fixable Dye (BioLegend, 423102, 1000), anti-mouse CD16/32 (BioLegend, 101320, 1:100), Alexa Fluor 555 conjugated anti-Rabbit (Invitrogen, A21428, 1:200), Alexa Fluor 647 conjugated anti-Rabbit (Invitrogen, A32795, 1:200), APC-Cy7-anti-mouse-CD45 (Biolgend, 103116, 1:100), FITC-anti-human/mouse-CD11b (BioLegend, 101206, 1:200), Percp-Cy5.5-anti-mouse-CD3 (Biolgend, 100328, 1:100), PE-anti-human-CD45 (BioLegend, 304007, 1:20), FITC anti-mouse Lineage Cocktail with Isotype Ctrl (BioLegend, 133302, 1:1000), APC-Sca-1(BioLegend, 108111, 1:100), BV421 anti-mouse c-kit (BioLegend, 105827, 1:20), anti-human/mouse-S100A8 (Proteintech, 15792-1-AP, 1:200), S100A9 (Proteintech, 26992-1-AP, 1:200), Biotin anti-human CD3 Antibody (BioLegend, 317319, 1:20), Percp/Cyanine5.5 Streptavidin (BioLegend, 405214, 1:400), PE-anti-mouse-CD62L (BioLegend, 104407, 1:200), PE-anti-mouse-CXCR2 (BioLegend, 149303, 1:200), APC anti-mouse-CXCR4 (BioLegend, 146507, 1:200).
Immunohistochemistry: Anti-UCP1 (ab10983,abcam, 1:500)

Validation

For immunofluorescence Staining: Cd11b (BioLegend, 101245), CD3 (BioLegend, 100203), S100A8 (Proteintech, 15792-1-AP), TH (GeneTex, GTX634481), TH (Beyotime, AF2185, 1:100), TUBB3 (Cell Signaling Technology, 4466S), EGFP (Servicebio, GB11602, 1:500), CD31 (Servicebio, GB12063), Alexa Fluor 488 conjugated anti-Rabbit (Invitrogen, A21206), Alexa Fluor 555 conjugated anti-Rabbit (Invitrogen, A21428), Alexa Fluor 555 conjugated anti-mouse (Invitrogen, A31570) were validated by the companies and by users.
For immunoblot : RBM3 (Proteintech, 14363-1-AP), PGC1a (4A8) (Santa Cruz Biotechnology, sc-517380), UCP1 (Abcam, ab10983), P21 (Abcam, ab109520), P16 (Sigma-Aldrich, SAB4500072), Tubulin (Proteintech, 11224-1-AP), S100A8 (Proteintech, 15792-1-AP), S100A9 (Proteintech, 26992-1-AP), p-p38 (Cell Signaling Technology, 4511S), p38 (Cell Signaling Technology, 8690S), p-ERK (Cell Signaling Technology, 4370S), ERK (Cell Signaling Technology, 4695S), GAPDH (Origene, TA802519), NRP1(A-12) (Santa Cruz Biotechnology, sc-5307), EPHA7 (Affinity Biosciences, AF0627), TH (Beyotime, AF2185), Phospho-TH (Ser40) (Cell Signaling Technology, 2791S), TUBB3(Cell Signaling Technology, 4466S), phosphor-Histone H2A.X (Ser139) (Sigma, 05-636), PCNA (Boster, BM0104) were validated by the companies and by users.
For flow cytometry: Zombie Aqua™ Fixable Dye (BioLegend, 423102), anti-mouse CD16/32 (BioLegend, 101320), Alexa Fluor 555 conjugated anti-Rabbit (Invitrogen, A21428), Alexa Fluor 647 conjugated anti-Rabbit (Invitrogen, A32795), APC-Cy7-anti-mouse-CD45 (Biolgend, 103116), FITC-anti-human/mouse-CD11b (BioLegend, 101206), Percp-Cy5.5-anti-mouse-CD3 (Biolgend, 100328), PE-anti-human-CD45 (BioLegend, 304007), FITC anti-mouse Lineage Cocktail with Isotype Ctrl (BioLegend, 133302), APC-Sca-1(BioLegend, 108111), BV421 anti-mouse c-kit (BioLegend, 105827), anti-human/mouse-S100A8 (Proteintech, 15792-1-AP), S100A9 (Proteintech, 26992-1-AP), Biotin anti-human CD3 Antibody (BioLegend, 317319), Percp/Cyanine5.5 Streptavidin (BioLegend, 405214), PE-anti-mouse-CD62L (BioLegend, 104407), PE-anti-mouse-CXCR2 (BioLegend, 149303), APC anti-mouse-CXCR4 (BioLegend, 146507) were validate by the companies and by users.
For immunohistochemistry: Anti-UCP1 (ab10983,abcam) were validated by the company and by users.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

C3H10T1/2 preadipocytes and PC12 cell lines were both perchased from Procell Life Science & Technology Co. Ltd.(Wuhan, China).

Authentication

The cell line was authenticated by lipid accumulation on adipocyte differentiation, cell morphology by microscopy, and thermogenic gene expression by qPCR analyses.

Mycoplasma contamination

The cell lines were tested negative for mycoplasma contamination.

Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell line was 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	Mus musculus Wild-type mice, C57BL/6J background, 2-, 8-or 15-month-old male mice were used. Tlr4-knockout mice (Tlr4-/-), C57BL/6J background, 8 week-old male mice were used. Tlr4 flox/flox mice, C57BL/6J background, 8 week-old male mice were used. Adpn-Cre mice, C57BL/6J background, 8 week-old male mice were used to cross with Tlr4 flox/flox mice. S100a8-Cre-EGFP mice, C57BL/6J background, 2-month-old male mice were used. NOD-SCID mice, BABL/c background, 2-month-old male mice were used. Mice were bred under specific-pathogen-free conditions at the Laboratory Animal Research Center of Central South University at a controlled temperature (22-24°C) and humidity (50-60%), with a 12 h dark/light cycle (07:00 to 19:00 light on), with standard food and water provided ad libitum.
Wild animals	This study does not involve wild animals.
Reporting on sex	Male mice were used since estrogen affects bone and adipose metabolism.
Field-collected samples	This study does not involve field-collected samples.
Ethics oversight	Animal experiments were approved by the Animal Ethics Committee and followed the Guidelines for the Care and Use of Laboratory Animals at Xiangya Hospital of Central South 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	Adipose tissues were carefully excised, minced, and digested with 1.5 g/L type 2 collagenase (Sigma-Aldrich) for 25 min at 37°C, with shaking to get single cells. Cells were Digested cells were filtered with a 100 µm nylon screen, washed, and centrifuged for 5 min to pellet the stromal vascular fractions (SVFs) from floating mature adipocytes. Single bone marrow cells were collected from the femur and tibia. To detect the expression of surface molecules, cells were first incubated with an anti-Fc receptor (Biolegend, San Diego, CA) to reduce nonspecific binding of antibodies, followed by incubation with the indicated antibodies for 20-30 min at 4°C.
Instrument	BD Canto II (BD Biosciences, San Jose, USA); BD Aria (BD Biosciences, San Jose, USA)
Software	Data were collected using BD FACS Diva software and were analyzed by FlowJo V10 (BD Biosciences, San Jose, USA).
Cell population abundance	No post-sorting analysis was done.
Gating strategy	Preliminary FSC/SSC gates of the starting cell population of SVFs were set according to the FSC/SSC gates of lymphocytes in the bone marrow samples. Dead cells and doublets were removed by dead-cell dye staining and FSC-A/FSC-H gating, respectively. Positive and negative populations were selected by single-positive control samples and isotype-matched negative control samples.

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