nature portfolio

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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	The 5hmC-seq and RNA-seq data was collected on NovaSeq 6000 (Illumina). ChIP-seq data was collected on Illumina Hiseq2500. DxFLEX was used to collect flow cytometry data. PeakView 1.2 was used to collect metabolite data. ImageView was used to collect cell or tissue staining data.
Data analysis	Statistical analysis was performed using GraphPad Prism 7.0, including unpaired Student's t-tests, one-way ANOVA, two-way ANOVA, Kaplan-Meier method and correlation analysis. CytExpert for DxFLEX was used for flow cytometry analysis. IGV_2.12.2 was used for 5hmC-seq and CHIP-seq data analysis. GSEA_4.1.0 software and online DAVID Bioinformatics Resources were used for Gene Ontology 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 datasets generated and/or analyzed during the current study are publicly released and all available.

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	AML donors were: AML1: age: 64, gender: female; AML2: age: 43, gender: male; AML3: age: 32, gender: male; AML4: age: 28, gender: male; AML5: age: 45, gender: male; AML6: age: 47, gender: male; AML7: age: 51, gender: female; AML8: age:27, gender: male; AML9: age: 78, gender: male.
Reporting on race, ethnicity, or other socially relevant groupings	Participants were recruited from the First Affiliated Hospital of Zhejiang University School of Medicine, a tertiary hospital in Hangzhou. Ethnicity information was not collected as it was not a relevant variable for the aim of this study conducted within a homogeneous Han Chinese population.
Population characteristics	Bone marrow mononuclear cells were obtained from leukemia patients recruited from a tertiary hospital in Hangzhou, which serves both urban and rural populations.
Recruitment	All samples were obtained at the time of diagnosis or relapse with informed consent of the patients at the First Affiliated Hospital of Zhejiang University School of Medicine.
Ethics oversight	All patient samples were maintained and handled under the protocol approved by by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (Ethics File Approval No.: 2022-292).

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	For in vivo murine BMT and therapy models, 5-10 animals were included in each experimental group to form statistical significance. Sample sizes were determined according to our previous publications and others' reports.
Data exclusions	All data was included in statistical analysis without any exclusions.
Replication	All experiments were repeated for at least three times independently. All attempts at replication were successful.
Randomization	Randomization, allocation concealment and blind outcome assessment were conducted throughout all the experiments.
Blinding	The investigators were blinded to group allocation during data collection and analysis. Randomization, allocation concealment and blind outcome assessment were conducted throughout all the experiments.

Behavioural & social sciences study design

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

Study description	*Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).*
Research sample	*State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.*
Sampling strategy	*Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.*
Data collection	*Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.*

Timing	*Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Non-participation	*State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.*
Randomization	*If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.*

Ecological, evolutionary & environmental sciences study design

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

Study description	*Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.*
Research sample	*Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.*
Sampling strategy	*Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.*
Data collection	*Describe the data collection procedure, including who recorded the data and how.*
Timing and spatial scale	*Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Reproducibility	*Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.*
Randomization	*Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.*
Blinding	*Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.*

Did the study involve field work? ☐ Yes ☐ No

Field work, collection and transport

Field conditions	*Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).*
Location	*State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).*
Access & import/export	*Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).*
Disturbance	*Describe any disturbance caused by the study and how it was minimized.*

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
[x]	[ ] Plants

Methods

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

Antibodies

Antibodies used

Antibodies for TET1 (GeneTex, GTX627420) and IgG (Cell Signaling Technology, 2729) were used for chromatin immunoprecipitations. PE/Cyanine7-anti-mouse CD117 (c-Kit) antibody (Biolegend, 105814), Brilliant Violet 605™ anti-mouse Ly-6A/E (Sca-1) antibody (Biolegend, 108134), APC anti-mouse CD150 (SLAM) antibody (Biolegend, 115910), PE anti-mouse CD135 antibody (Biolegend, 135306), Brilliant Violet 421™ anti-mouse CD34 antibody (Biolegend, 152208), FITC anti-mouse Lineage Cocktail (Biolegend, 133302), Brilliant Violet 605™ anti-human CD45 antibody (Biolegend, 304042), anti-mouse CD45 antibody (BD Biosciences,553081), anti-mouse CD45.1-PerCP/Cyanine5.5 (eBioscience, 45-0453-82), anti-mouse CD45.2-Brilliant Violet 510 (Biolegend, 109838), anti-Mac-1-Brilliant Violet 605 (eBioscience, 63-0112-82), and anti-human CD33-PerCP/Cyanine5.5 (eBioscience, 45-0338-42) were used for flow cytometry analysis. Primary antibodies anti-TET1 (Santa Cruz, sc-293186,1:1000), anti-GCLC (Santa Cruz, sc-390811,1:1000), anti-β-Actin (ABclonal, AC026,1:100000), anti-GSTP1 (ABclonal, A19061,1:1000), anti-FSP1 (ABclonal, A22278,1:10000), anti-GPX4 (Cell Signaling Technology, 52455,1:1000), anti-DHODH (Proteintech, 14877-1-AP,1:2000), anti-GCH1 (Proteintech, 28501-1-AP,1:1000), anti-GAPDH (Santa Cruz, sc-47724,1:1000), anti-ZIP14 (Thermo Fisher Scientific, PA5-21077,1:1000), anti-FTL (Abcam, ab69090,1:1000), anti-FTH (Abcam, ab65080,1:1000), and anti-FPN (Abcam, ab78066,1:1000) were used for western blotting analysis. Primary antibody anti-5hmC (Active Motif, 39769,1:5000) was used for dot blotting analysis.

Validation

The above antibodies are shown to fit for ChIP, flow cytometry or blotting analysis on each manufacturer's website, or cited by previous publications.
WB:
https://www.scbt.com/zh/p/tet1-antibody-4f4
https://www.scbt.com/zh/p/gamma-gcsc-antibody-h-5
https://abclonal.com.cn/catalog/AC026
https://abclonal.com.cn/catalog/A19061
https://abclonal.com.cn/catalog/A22278
https://www.cellsignal.cn/products/primary-antibodies/gpx4-antibody/52455
https://www.ptgcn.com/Products/DHODH-Antibody-14877-1-AP.htm
https://www.ptgcn.com/products/GCH1-Antibody-28501-1-AP.htm
https://www.scbt.com/zh/p/gapdh-antibody-0411
https://www.thermofisher.cn/cn/zh/antibody/product/ZIP14-Antibody-Polyclonal/PA5-21077
https://www.abcam.cn/products/primary-antibodies/ferritin-light-chain-antibody-ab69090
https://www.abcam.cn/products/primary-antibodies/ferritin-heavy-chain-antibody-ab65080
https://www/abcam.cn/products/primary-antibodies/slc40a1-antibody-ab78066
ChIP:
https://www.genetex.cn/Product/Detail/TET1-antibody-GT1462/GTX627420
https://www.cellsignal.cn/products/primary-antibodies/normal-rabbit-igg/2729
Dot blot:
https://www.activemotif.com/actalog/details/39768.html
Flow cytometry:
https://www.biolegend.com/en-gb/products/pecyanine7-anti-mouse-cd117-c-kit-antibody-2900?GroupID=BLG1945
https://www.biolegend.com/fr-ch/products/brilliant-violet-605-anti-mouse-ly-6a-e-sca-1-antibody-8664?GroupID=BLG2524
https://www.biolegend.com/en-gb/products/pe-cyanine7-anti-mouse-cd150-slam-antibody-3056?GroupID=BLG4214
https://www.biolegend.com/en-gb/products/pe-anti-mouse-cd135-antibody-6173?GroupID=BLG7934
https://www.biolegend.com/en-gb/products/brilliant-violet-421-anti-mouse-cd34-antibody-14036?GroupID=BLG15506
https://www.biolegend.com/en-gb/products/fitc-anti-mouse-lineage-cocktail-with-isotype-ctrl-5803?GroupID=BLG10793
https://www.biolegend.com/en-gb/products/brilliant-violet-605-anti-human-cd45-antibody-8521?GroupID=BLG5926
https://www.bdbiosciense s.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-rat-anti-mouse-cd45.553081?tab=product_details
https://www.thermofisher.cn/cn/zh/antibody/product/CD45-1-Antibody-clone-A20-Monoclonal/45-0453-82
https://www.biolegend.com/en-gb/products/brilliant-violet-510-anti-mouse-cd45-2-antibody-7998?GroupID=BLG1934
https://www.thermofisher.cn/cn/zh/antibody/product/CD11b-Antibody-clone-M1-70-Monoclonal/63-0112-82
https://www.thermofisher.cn/zh/antibody/product/CD33-Antibody-clone-WM-53-WM53-Monoclonal/45-0338-42

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	THP1 (TIB-202), U937 (CRL-1593.2) and MV4;11 (CRL-9591) cells were obtained from America Type Culture Collection (ATCC) and cultured in RPMI-1640 medium (Gibco, Grand Island, NY, USA), supplemented with 10% FBS (Vistech) and penicillin-streptomycin. HEK293T (ATCC, CRL-3216) were maintained in DMEM medium (Gibco) supplemented with 10% FBS and penicillin-streptomycin. MOLM13 (ACC554) and NB4 (ACC207) cells were obtained from German Collection of Microorganisms and Cell Cultures (DSMZ) and cultured in RPMI-1640 medium, supplemented with 10% FBS and penicillin-streptomycin. Kasumi-1 (SCSP-5015), HL60 (TCHu23), K562 (TCHu191) and 786-O (SCSP-5059) cells were obtained from the Cell Resource Center, Shanghai Academy of Health Sciences (Shanghai, China) and cultured in RPMI-1640 medium, supplemented with 10% FBS and penicillin-streptomycin. HepG2 cells (SCSP-510) were purchased from the Cell Resource Center, Shanghai Academy of Health Sciences (Shanghai, China) and cultured in DMEM medium, supplemented with 10% FBS and penicillin-streptomycin. Jurkat (1101HUM-PUMC000075), Daudi (1101HUM-PUMC000134), CA46 (1101HUM-PUMC000366), HCC827 (1101HUM-PUMC000478), NCI-H292 (1101HUM-PUMC000233) and A549 (1101HUM-PUMC000002) cells were purchased from the National Science and Technology Infrastructure, the National Biomedical Cell-Line Resource (NSTI-BMCR) and cultured in RPMI-1640 medium, supplemented with 10% FBS and penicillin-streptomycin. B16-F10 (1101HUM-PUMC000473) and A375 (1101HUM-PUMC000126) cells (NSTI-BMCR) were cultured in DMEM medium, supplemented with 10% FBS and penicillin-streptomycin. HLF (CBP60589) cells were purchased from COBIOER Biosciences (Nanjing, China) and cultured in DMEM medium supplemented with 10% FBS and penicillin-streptomycin. HT1080 (C1052) cells were purchased from WHELAB Biotechnology (Shanghai, China) and cultured in MEM medium (Gibco) supplemented with 10% FBS and penicillin-streptomycin. MIA PaCa-2 (CL-0627), PaTu 8988t (CL-0579), ACHN (CL-0021) cells were purchased from Procell Life Science & Technology (Wuhan, China) and cultured in DMEM medium supplemented with 10% FBS and penicillin-streptomycin. ASPC-1 cells (CL-0027) were purchased from Procell Life Science & Technology (Wuhan, China) and cultured in RPMI-1640 medium supplemented with 10% FBS and penicillin-streptomycin. The NFE2L2 knockout THP1 cell line (RAW 264.7) was purchased from Ubigene Biosciences (Shanghai, China).
Authentication	Cell lines were authenticated by use of STR profiling upon purchasing and right before the completion of the research project.
Mycoplasma contamination	Mycoplasma contamination was tested once per month for all cell lines. All cells were tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

Palaeontology and Archaeology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.*
Specimen deposition	*Indicate where the specimens have been deposited to permit free access by other researchers.*
Dating methods	*If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

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

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	6-8-weeks-old C57BL/6 (CD45.2) mice, B6.SJL (CD45.1) mice, NOD/ShiLtJGpt-Prkdcem26Cd52Il2rgem26Cd22/Gpt (NSG) mice and Mx1-Cre+/-Tet1flox/flox mice were used in the study.
Wild animals	The study does not include any wild animals.
Reporting on sex	Both males and females were included.
Field-collected samples	No field collected samples were included in the study.
Ethics oversight	All experiments were carried out according to the ethical standards of the Committee on Experimental Animal Care & Ethics of Zhejiang University. As for the leukemic models, according to the animal protocol approved by the institutional (i.e., the Laboratory Animal Center of Zhejiang University) committee board, mice were euthanized when they met the one of the points listed below: 1)

Weight loss: >20% weight loss; 2) Tumor burden: with hunched posture and ruffled fur, WBC > 50,000/ul, pale ears and feet, decreased motion, especially severe symptoms such as posterior paralysis.

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	N/A
Study protocol	N/A
Data collection	N/A
Outcomes	N/A

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☐	☐	Public health
☐	☐	National security
☐	☐	Crops and/or livestock
☐	☐	Ecosystems
☐	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☐	☐	Demonstrate how to render a vaccine ineffective
☐	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☐	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☐	☐	Increase transmissibility of a pathogen
☐	☐	Alter the host range of a pathogen
☐	☐	Enable evasion of diagnostic/detection modalities
☐	☐	Enable the weaponization of a biological agent or toxin
☐	☐	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☒ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE240527
Files in database submission	Raw data, files for bw and excel format were submissed.
Genome browser session (e.g. UCSC)	https://genome.ucsc.edu/

Methodology

Replicates	Replicate samples were sequenced for each group.
Sequencing depth	The sequencing depth was 60M reads per replicate, at a 50 base read length.
Antibodies	Antibodies for TET1 (GeneTex, GTX627420) and IgG (Cell Signaling Technology, 2729) were used for chromatin immunoprecipitations.
Peak calling parameters	Peak calling was performed with STAR (2.5.3a) with default parameters.
Data quality	The library was qualified with Qubit ssDNA kit. Sequencing was conducted by Beijing Genomics Institution (BGI, Shenzhen, China) and was implemented on the platform of Illumina Hiseq2500. Clean Reads Q20 Rate >97%, Mapping Rate >96%.
Software	Peak calling was performed with STAR (2.5.3a) with default parameters. Peaks were annotated with UCSC human genome GRCh38 by using Bedtools (2.25.0), HOMER (Hypergeometric Optimization of Motif EnRichment) (4.10). RSeQC (2.6) was used for peak distribution analysis.

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 lipid peroxidation analysis: 5×105 AML cells per well were seeded into 24-well dishes and treated with a indicated doses of RSL3, Fer-1 or DMSO for 24 hours. At the end of the treatments, cells were incubated with 2 μM BODIPY 581/591 C11 (D3861, Thermo Fisher Scientific) at 37 °C for 25 minutes. Stained cells were transferred into 1.5 ml EP tubes and washed twice with PBS. Then the cells were loaded for flow cytometry analysis. For cell sorting: 3×106 cells were harvested and washed with cold PBS. After blocking in PBS with 0.1% BSA at room temperature for 10 minutes, cells were stained with the following antibodies: anti-CD117 (c-KIT, Biolegend), anti-Ly-6A/E (Sca-1, Biolegend), anti-CD150 (SLAM, Biolegend), anti-CD135 (Flk-2, Biolegend), anti-CD34 (Biolegend) and/or FITC anti-mouse Lineage Cocktail (Biolegend). Mouse BM cells were prepared as follows: femora and tibiae were isolated and gently crushed in RPMI-1640 medium with 2% FBS). Red blood cells (RBCs) were lysed using Ammonium-Chloride-Potassium (ACK) lysing buffer for 8 minutes on ice. Cells were harvested and washed in cold PBS. After blocking in PBS with 0.1% BSA at room temperature for 10 minutes, cells were stained with the indicated antibodies.
Instrument	DeFLEX flow cytometer
Software	CytExpert for DxFLEX software
Cell population abundance	At least 10,000 cells were analyzed for each sample.
Gating strategy	FSC and SSC were used to eliminate debris, dead cells and clumps or doublets, and to find out viable, single cell events. All the gated cells were then included in the following analysis.

☒ 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	*Indicate task or resting state; event-related or block design.*

Design specifications

Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.

Behavioral performance measures

State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)

Specify: functional, structural, diffusion, perfusion.

Field strength

Specify in Tesla

Sequence & imaging parameters

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.

Area of acquisition

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software

Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

Normalization

If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.

Normalization template

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.

Noise and artifact removal

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

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

Statistic type for inference

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

(See Eklund et al. 2016)

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

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

Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.