nature research

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Reporting Summary

Nature Research 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 Research 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	CFX ConnectTM Real-Time System (Bio-Rad); High Speed Spinning Disk Confocal Microscope (Dragonfly);ZEISS LSM 710 NLO &DuoScan System; BD FACSVerse; ZEN 3.1 for Vert.A1 (ZEISS)
Data analysis	GraphPad Prism 8; ArchR 1.0.1; base R 3.6.3; bedGraphToBigWig 4; bedtools 2.29.0; bismark 0.22.3; bowtie2 2.3.5; Cellranger 3.1.0; Cellranger ATAC 1.2.0; clusterProfiler 3.14.3; ComplexHeatmap 2.2.0; data.table 1.12.8; deeptools 3.3.1; DESeq 1.38.0; DESeq2 1.26.0; FastQC 0.11.8; featureCounts 2.0.0; ggplot2 3.3.2; homer 4.10.3; IDR 2.0.4.2; irlba 2.3.3; MACS2 2.2.5; picard 2.18.21; samtools 1.9; scater 1.14.0; scran 1.14.1; Seurat 3.2.3; SingleCellExperiment 1.8.0; STAR 2.7.3a; tidyverse 1.3.0; Trimmomatic 0.39 The detailed data analysis procedures were provided in the method.

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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data is available in the main text or the supplementary materials. Raw and processed next-generation sequencing datasets have been deposited at the NCBI Gene Expression Omnibus (GEO) under accession number GSE178325 (single-cell RNA-seq data), GSE178324 (single-cell ATAC-seq data), GSE176381 (bulk RNA-seq data), GSE178323 (bulk ATAC-seq data), GSE178966 (WGBS data). The public datasets we used can be accessed under accession number GSE143753 (human limb

bud data), GSE106269 (axolotl data), GSE165901 (frog data), GSE135985 (mouse data), GSE83765 (human naïve pluripotency stem cell data), GSE36552 (human embryo data) from GEO, and E-MTAB-3929 (human embryo data) from ArrayExpress.

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 human chemical reprogramming, we repeated the reprogramming protocols on more than ten samples including human embryonic fibroblasts, adult human adipose derived mesenchymal stromal cells and adult human dermal fibroblasts from different donors. Similar results/findings were observed. These results suggest our sample size is sufficient. Sample size numbers for each experiment can be found in the figure legend.
Data exclusions	No data were exclued from the analyses.
Replication	All experiments presented here been repeated several times with similar results, the number of repeated experiments is indicated in the figure legends.
Randomization	No randomization methods were used only for animals used for experiments that were randomly allocated.
Blinding	We did not considered blinding required in the experiments in this study.

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
☐	☒ 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

Antibodies Company Cat. NO. Dilution
Rabbit polyclonal anti-LIN28A Invitrogen Cat# PA1-096; RRID: AB_2539865 1:200
Rabbit monoclonal anti-Lin28A Abcam Cat# ab124765; RRID: AB_10975201 1:500
Mouse monoclonal anti-SALL4 Abcam Cat# ab57577; RRID: AB_2183366 1:200
Rabbit monoclonal anti-FOXA2 Cell Signaling Technology Cat# 8186S; RRID: AB_10891055 1:200
Goat monoclonal anti-SOX17 R&D Cat# AF1924; RRID: AB_355060 1:200
Mouse monoclonal anti-EpCAM Invitrogen Cat# MA5-12436; RRID: AB_10981962 1:200
Mouse monoclonal anti-OCT4 BD Biosciences Cat# 611203; RRID: AB_398737 1:200
Rabbit monoclonal anti-OCT4 Invitrogen Cat# MA5-14845; RRID: AB_10979606 1:200

Goat polyclonal anti-SOX2 R&D Cat# AF2018; RRID: AB_355110 1:200
Rabbit polyclonal anti-NANOG Abcam Cat# ab21624; RRID: AB_446437 1:200
Mouse monoclonal anti-TRA-1-60 Millipore Cat# MAB4360; RRID: AB_2119183 1:100
Mouse monoclonal anti-TRA-1-81 Millipore Cat# MAB4381; RRID: AB_177638 1:100
Mouse polyclonal anti-SSEA-4 Santa Cruz Cat# sc-21704; RRID: AB_628289 1:100
Rabbit polyclonal anti-SOX2 Abcam Cat# ab97959; RRID: AB_2341193 1:800
Rabbit monoclonal anti-FOXG1 Abcam Cat# ab196868; RRID: AB_2892604 1:100
Rabbit monoclonal anti-NESTIN Abcam Cat# ab105389; RRID: AB_10859398 1:200
Rabbit monoclonal anti-PAX6 Abcam Cat# ab195045; RRID: AB_2750924 1:500
Goat polyclonal anti-GATA4 R&D Cat# AF2606; RRID: AB_2232177 1:400
Goat plyclonal anti-T R&D Cat# AF2085; RRID: AB_2200235 1:200
Goat plyclonal anti-SOX1 R&D Cat# AF3369; RRID: AB_2239879 1:200
Mouse monoclonal anti-TUJ1 BioLegend Cat# 801201; RRID: AB_2313773 1:200
7-AAD BD Biosciences Cat# 559925; RRID: AB_2869266 1:1500
PE/Cyanine7 anti-human CD144 BioLegend Cat# 348516; RRID: AB_2687022 1:1500
PE anti-human CD31 BioLegend Cat# 303106; RRID: AB_314332 1:1500
FITC anti-human CD34 BioLegend Cat# 343504; RRID: AB_1731852 1:1500
PE anti-human CD5 BioLegend Cat# 300608; RRID: AB_314094 1:1500
APC anti-human CD4 BioLegend Cat# 300514; RRID: AB_314082 1:1500
PE/Cyanine7 anti-human CD8b Invitrogen Cat# 25-5273-42 RRID: AB_11219680 1:1500
Alexa Fluor 488-AffiniPure Donkey Anti-Mouse IgG (H+L) Jackson Immuno Research Cat# 715-545-150; RRID:AB_2340846 1:200
Alexa Fluor 488-AffiniPure Donkey Anti-Rabbit IgG (H+L) Jackson Immuno Research Cat# 711-545-152; RRID:AB_2313584 1:200
Alexa Fluor 488-AffiniPure Donkey Anti-Goat IgG (H+L) Jackson Immuno Research Cat# 705-545-147; RRID:AB_2336933 1:200
Cy3-AffiniPure Donkey Anti-Rabbit IgG (H+L) Jackson Immuno Research Cat# 711-165-152; RRID:AB_2307443 1:200
Cy3-AffiniPure Donkey Anti-Mouse IgG (H+L) Jackson Immuno Research Cat# 715-165-150; RRID:AB_2340813 1:200
Cy3-AffiniPure Donkey Anti-Goat IgG (H+L) Jackson Immuno Research Cat# 705-165-147; RRID:AB_2307351 1:200
Alexa Fluor 647 Donkey Anti-Goat IgG (H+L) Jackson Immuno Research Cat# 705-605-147; RRID:AB_2340437 1:200
Alexa Fluor 647 Donkey Anti-Mouse IgG (H+L) Jackson Immuno Research Cat# 715-605-150; RRID:AB_2340862 1:200
Alexa Fluor 647 Donkey Anti-Rabbit IgG (H+L) Jackson Immuno Research Cat# 711-605-152; RRID:AB_2492288 1:200

Validation

All the antibodies used in this study are commercially available and validated for use in IF staining or flow cytometry. Data are available on the manufacturer's websites.
Rabbit polyclonal anti-LIN28A, Cat# PA1-096: https://www.thermofisher.cn/cn/zh/antibody/product/LIN28A-Antibody-Polyclonal/PA1-096
Rabbit monoclonal anti-Lin28A, Cat# ab124765: https://www.abcam.com/lin28a-antibody-epr4640-ab124765.html
Mouse monoclonal anti-SALL4, Cat# ab57577: https://www.abcam.com/sall4-antibody-6e3-ab57577.html
Rabbit monoclonal anti-FOXA2, Cat# 8186S: https://www.cellsignal.com/products/primary-antibodies/foxa2-hnf3b-d56d6-xp-rabbit-mab/8186
Goat monoclonal anti-SOX17, Cat# AF1924: https://www.rndsystems.com/cn/products/human-sox17-antibody_af1924
Mouse monoclonal anti-EpCAM, Cat# MA5-12436: https://www.thermofisher.cn/cn/zh/antibody/product/EpCAM-Antibody-clone-323-A3-Monoclonal/MA5-12436
Mouse monoclonal anti-OCT4, Cat# 611203: https://www.bdbiosciences.com/en-eu/products/reagents/microscopy-imaging-reagents/immunofluorescence-reagents/purified-mouse-anti-oct3-4.611203
Rabbit monoclonal anti-OCT4, Cat# MA5-14845: https://www.thermofisher.cn/cn/zh/antibody/product/OCT4-Antibody-clone-T-631-9-Monoclonal/MA5-14845
Goat polyclonal anti-SOX2, Cat# AF2018: https://www.rndsystems.com/cn/products/human-mouse-rat-sox2-antibody_af2018
Rabbit polyclonal anti-NANOG, Cat# ab21624: https://www.abcam.com/nanog-antibody-ab21624.html
Mouse monoclonal anti-TRA-1-60, Cat# MAB4360: https://www.merckmillipore.com/CN/zh/product/Anti-TRA-1-60-Antibody-clone-TRA-1-60,MM_NF-MAB4360?ReferrerURL=https%3A%2F%2Fcn.bing.com%2F&bd=1
Mouse monoclonal anti-TRA-1-81, Cat# MAB4381: https://www.merckmillipore.com/CN/zh/product/Anti-TRA-1-81-Antibody-clone-TRA-1-81,MM_NF-MAB4381
Mouse polyclonal anti-SSEA-4, Cat# sc-21704: https://www.scbt.com/p/ssea-4-antibody-813-70/
Rabbit polyclonal anti-SOX2, Cat# ab97959: https://www.abcam.com/SOX2-antibody-ab97959.html
Rabbit monoclonal anti-FOXG1, Cat# ab196868: https://www.abcam.com/foxg1-antibody-epr18987-ab196868.html
Rabbit monoclonal anti-NESTIN, Cat# ab105389: https://www.abcam.com/nestin-antibody-sp103-ab105389.html
Rabbit monoclonal anti-PAX6, Cat# ab195045: https://www.abcam.com/pax6-antibody-epr15858-ab195045.html
Goat polyclonal anti-GATA4, Cat# AF2606: https://www.rndsystems.com/cn/products/human-gata-4-antibody_af2606
Goat polyclonal anti-T, Cat# AF2085: https://www.rndsystems.com/cn/products/human-mouse-brachyury-antibody_af2085
Goat polyclonal anti-SOX1, Cat# AF3369: https://www.rndsystems.com/cn/products/human-mouse-rat-sox1-antibody_af3369
Mouse monoclonal anti-TUJ1, Cat# 801201: https://www.biolegend.com/en-us/search-results/purified-anti-tubulin-beta-3-tubb3-antibody-11580?GroupID=GROUP686
7-AAD, Cat# 559925: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/7-aad.559925
PE/Cyanine7 anti-human CD144, Cat# 348516: https://www.biolegend.com/en-us/products/pe-cyanine7-anti-human-cd144-ve-cadherin-antibody-14432?GroupID=BLG8915
PE anti-human CD31, Cat# 303106: https://www.biolegend.com/en-us/products/pe-anti-human-cd31-antibody-882
FITC anti-human CD34, Cat# 343504: https://www.biolegend.com/en-us/products/fitc-anti-human-cd34-antibody-6032
PE anti-human CD5, Cat# 300608: https://www.biolegend.com/en-us/products/pe-anti-human-cd5-antibody-871
APC anti-human CD4, Cat# 300514: https://www.biolegend.com/en-us/products/apc-anti-human-cd4-antibody-823
PE/Cyanine7 anti-human CD8b, Cat# 25-5273-42: https://www.thermofisher.cn/cn/zh/antibody/product/CD8b-Antibody-clone-SIDI8BEE-Monoclonal/25-5273-42
Alexa Fluor 488-AffiniPure Donkey Anti-Mouse IgG (H+L), Cat# 715-545-150: https://www.jacksonimmuno.com/catalog/products/715-545-150
Alexa Fluor 488-AffiniPure Donkey Anti-Rabbit IgG (H+L), Cat# 711-545-152: https://www.jacksonimmuno.com/catalog/products/711-545-152

Alexa Fluor 488-AffiniPure Donkey Anti-Goat IgG (H+L), Cat# 705-545-147: https://www.jacksonimmuno.com/catalog/products/705-545-147
Cy3-AffiniPure Donkey Anti-Rabbit IgG (H+L), Cat# 711-165-152: https://www.jacksonimmuno.com/catalog/products/711-165-152
Cy3-AffiniPure Donkey Anti-Mouse IgG (H+L), Cat# 715-165-150: https://www.jacksonimmuno.com/catalog/products/715-165-150
Cy3-AffiniPure Donkey Anti-Goat IgG (H+L), Cat# 705-165-147: https://www.jacksonimmuno.com/catalog/products/705-165-147
Alexa Fluor 647 Donkey Anti-Goat IgG (H+L), Cat# 705-605-147: https://www.jacksonimmuno.com/catalog/products/705-605-147
Alexa Fluor 647 Donkey Anti-Mouse IgG (H+L), Cat# 715-605-150: https://www.jacksonimmuno.com/catalog/products/715-605-150
Alexa Fluor 647 Donkey Anti-Rabbit IgG (H+L), Cat# 711-605-152: https://www.jacksonimmuno.com/catalog/products/711-605-152

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Human embryonic fibroblasts, human adipose-derived stromal cells and human adult dermal fibroblasts were derived from tissues of donors. Human ES cell lines H1 and H9 were obtained from WiCell.
Authentication	Human embryonic fibroblasts, human adipose-derived stromal cells and human adult dermal fibroblasts were authenticated in house by q-PCR, RNA-seq and STR analysis. H1 and H9 were obtained directly from the WiCell and authenticated by q-PCR, RNA-seq and STR analysis
Mycoplasma contamination	All cultured cells were tested negative for mycoplasma contamination by PCR.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study.

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).*
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 organisms

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

Laboratory animals	Mice was used in this study. The two-to-three-month-old male immunodeficient NPG mice that purchased from Beijing Vitalstar Biotechnology Company.The mice were housed with a 12-h light/12-h dark cycle between 06:00 and 18:00 in a temperature-controlled room (22±1°C) with 40–60% humidity. Water and food were accessible at all times.
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	All of the mouse experiments performed were approved by the Institutional Animal Care and Use Committee of Peking University

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	As stated in the method, human skin and adipose tissues were obtained from participants of different ages and gender (supplementary table 2).
Recruitment	The human skin and adipose tissues were obtained from the donors (ranging from 1 to 91 years) without skin and adipose related disease. No other biases are present. All the tissues were obtained with informed written consent.
Ethics oversight	Human embryonic fibroblasts (HEFs) were isolated from embryonic dermis tissues that obtained with informed written consent and approval by the Clinical Research Ethics Committee of China-Japan Friendship Hospital (Ethical approval No. 2009-50). Adult human adipose derived mesenchymal stromal cells (hADSCs) and human adult skin fibroblasts (hASFs) were

isolated from adult tissue that obtained with informed written consent and approval by the Institute of Ethics Committee Review Board in Peking University (IRB 00001052-19070).

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	*Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.*
Study protocol	*Note where the full trial protocol can be accessed OR if not available, explain why.*
Data collection	*Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.*
Outcomes	*Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.*

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

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.*	*For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.*
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

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 cell marker detection, cultured cells were digested with accutase (Millipore, Cat: SCR005) at 37 °C for 5 min, diluted with an equal volume of PBS (Corning, Cat: 21-040-CV), centrifuged at 1,800 rpm for 3 min to obtain cell pellets, and resuspended with PBS containing 0.5% BSA (Sigma, Cat: A1470–100G) to form single-cell suspension. Next, the indicated antibodies were added and incubated with the cells for 15 min in the dark at room temperature. Then, the cells were washed three times with PBS, were suspended in 300 µl of PBS, and then were filtered through a 40 µm nylon cell strainer for analysis. Single-cell suspensions of chemically reprogrammed cells at the end of each stage were dissociated by 0.25% Trypsin-EDTA at 37 oC for 15-20 min followed by filtration through 40 µm cell strainers. FACS analyses were performeded with the BD Cytofix/ Cytoperm™ Fixation/Permeablization Kit according to the manufacturer's instructions. Flow cytometry was performed using CytoFlEX S (BeckMan Coulter). Antibody details are provided in the Supplementary Table 7.
Instrument	FACSVerse (BD) CytoFlEX S (BeckMan Coulter)
Software	FlowJo-V10
Cell population abundance	Purity was computer determined by the software.
Gating strategy	Because of the various sizes of the dissociated cells analyzed, the majority of starting cells were included in FSC/SSC gates. The boundary between positive and negative is defined according the negative controls.

☒ 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 (See Eklund et al. 2016) *Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.*

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.*