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 Authors & Referees 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	Nano ITC Run 1.2.1(TA instruments)
Data analysis	Image J analysis software version 1.38e (NIH, Bethesda, MD, USA); GraphPad Prism 8.0 (GraphPad, San Diego, CA); Launch NanoAnalyze 1.2.1 (TA instruments)

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/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 other data are included within the article or Supplementary Information or available from the authors on request. The source data underlying Figures in the article and Supplementary Information are provided as a Source Data file.

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 study design

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

Sample size	In in vitro experiments, the sample size for each group was 3 or 4. In vivo, the number of mice in each group is six or seven. These sample sizes are sufficient for a statistical analysis.
Data exclusions	No data were excluded from the analysis.
Replication	The experiments were independently repeated multiple times, and statistical tests have been performed to ensure reproducibility. Information on statistical tests and reproducibility are described in the figure legends.
Randomization	Sample groups were allocated randomly.
Blinding	In all experiments, investigators were blinded to group identification during data collection and processing.

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 and 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
☐	☒ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used: Santa Cruz Biotechnology: Anti-GAPDH (Clone: G-9, cat no. sc-365062), Anti-IκBα (Clone: H-4, cat no. sc- 1643), Anti-MyD88 (Clone: E-11, cat no. sc-74532), Anti-ERK1/2 (Clone: C-9, cat no. sc-514302), Anti-p-ERK1/2 (Clone: 12D4, cat no. sc-81492), Anti-F4/80 (Clone: C-7, cat no. sc-377009), Anti-TGF-β(Clone: 3C11, cat no. sc-130348), Anti-Col 1 (cat no. sc-59772), Anti-TLR4 (Clone: 25, cat no. sc-293072), Anti-MD2 (Clone: J-12B, cat no. sc-80183), Anti-GLUT4 (Clone: IF8, cat no. sc-53566), Anti-Flag tags (Clone: G-8, cat no. sc-166384), Anti-HA tags (Clone: F-7, cat no. sc-7392), Anti-ANP (Clone: F-2, cat no. sc-515701), Anti-MyHC (Clone: B-5, cat no. sc-376157), Anti-MMP-2(Clone: 8B4, cat no. sc-13595), Anti-MMP-9(Clone: 6-6B, cat no. sc-12759), Anti-ICAM-1 (Clone: G-5, cat no. sc- 8439), Anti-VCAM-1 (Clone: E-10, cat no. sc-13160), Anti-α-actin (Clone: 1A4, cat no.sc-32251), Anti-CD68 (Clone: E-11, sc-17832), Anti-TNF-α (Clone: 52B83, cat no.sc-52746), and Anti-RAGE (Clone: E-1, cat no.sc-74473).
Cell Signaling Technology: Anti-JNK (cat no. 9252), Anti-p-JNK (Clone: G9, cat no. 9255), Anti-P38(cat no. 9212), Anti-p-P38 (Clone: D13E1, cat no. 8690).
AbCam: Anti-AGE antibody (cat no. ab23722).

Validation: Anti-GAPDH (Clone: G-9, cat no. sc-365062), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-IκBα (Clone: H-4, cat no. sc- 1643), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-MyD88 (Clone: E-11, cat no. sc-74532), Isotype: mouse IgG2b, κ, Application: Western Blotting, 1:200 dilution, and IP, 1:50 dilution.
Anti-ERK1/2 (Clone: C-9, cat no. sc-514302), Isotype: mouse IgG2a, κ, Application: Western Blotting, 1:200 dilution.
Anti-p-ERK1/2 (Clone: 12D4, cat no. sc-81492), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-F4/80 (Clone: C-7, cat no. sc-377009), Isotype: mouse IgG1, κ, Application: IF, 1:200 dilution.

Anti-TGF-β(Clone: 3C11, cat no. sc-130348), Isotype: mouse IgG1, κ, Application: IF, 1:50 dilution, and Western Blotting, 1:200 dilution.
Anti-Col 1 (cat no. sc-59772) Isotype: mouse IgG1, κ, Application: Western IF, 1:50 dilution, Blotting, 1:200 dilution.
Anti-TLR4 (Clone: 25, cat no. sc-293072),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution, and IP, 1:50 dilution.
Anti-MD2 (Clone: J-12B, cat no. sc-80183),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution, ELISA, 1:500 dilution, and IP, 1:50 dilution.
Anti-GLUT4 (Clone: IF8, cat no. sc-53566),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-Flag tags (Clone: G-8, cat no. sc-166384), Isotype: mouse IgG2b, κ, Application: Western Blotting, 1:200 dilution, and IP, 1:50 dilution.
Anti-HA tags (Clone: F-7, cat no. sc-7392), Isotype: mouse IgG2a, κ, Application: Western Blotting, 1:200 dilution, and IP, 1:50 dilution.
Anti-ANP (Clone: F-2, cat no. sc-515701),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-MyHC (Clone: B-5, cat no. sc-376157),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution, and IF, 1:50 dilution.
Anti-MMP-2(Clone: 8B4, cat no. sc-13595)), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-MMP-9(Clone: 6-6B, cat no. sc-12759),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-ICAM-1(Clone: G-5, cat no. sc- 8439), Isotype: mouse IgG2a, κ, Application: Western Blotting, 1:200 dilution.
Anti-VCAM-1 (Clone: E-10, cat no. sc-13160),), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-α-actin (Clone: 1A4, cat no.sc-32251) Isotype: mouse IgG2a, κ, Application: IF, 1:100 dilution.
Anti-CD68(Clone: E-11, sc-17832). Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution, and IHC, 1:50 dilution.
Anti-TNF-α (Clone: 52B83, cat no.sc-52746), Isotype: mouse IgG1, κ, Application: IHC, 1:50 dilution.
Anti-RAGE (Clone: E-1, cat no.sc-74473), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-JNK (cat no. 9252), Rabbit polyclonal antibodies, Application: Western Blotting, 1:1000 dilution.
Anti-p-JNK (Clone: G9, cat no. 9255), Isotype: mouse IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-P38(cat no. 9212), Rabbit polyclonal antibodies, Application: Western Blotting, 1:1000 dilution.
Anti-p-P38(Clone: D13E1, cat no. 8690), Isotype: rabbit IgG1, κ, Application: Western Blotting, 1:200 dilution.
Anti-AGE antibody (cat no. ab23722), Rabbit polyclonal antibodies, Application: Western Blotting, 1:1000 dilution, ELISA, 1:5000 dilution.
All antibodies used in this study are commercially available and validated by manufacturers. All validations are provided on the product details page of each commercially available antibody.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	H9C2 cell line was obtained from the Shanghai Institute of Biochemistry and Cell Biology (Shanghai, China)
Authentication	H9C2 cell line was authenticated by PCR assays with species-specific primer in Shanghai Institute of Biochemistry and Cell Biology, China.
Mycoplasma contamination	Cell lines were tested to be mycoplasma-negative by the standard PCR method.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell line was used.

Palaeontology

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.

Animals and other organisms

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

Laboratory animals	Male C57BL/6 mice (18-22 g), 1-3 day old neonatal SD rat(8-12 g) and male SD rat(200-220 g) were obtained from Animal Center of Wenzhou Medical University (Wenzhou, China). MD2-/- mice on C57BL/6 background were purchased from Riken BioResource Center (Tokyo, Japan). Male db/db (C57BLKS/J-leprdb/eprdb) mice and male db/m littermate were purchased from Model Animal Research Center of Nanjing University (Nanjing, China) 6-week old male C57BL/6 (WT) and MD2-/- (MD2KO) mice were used for made diabetic by a single dose intraperitoneal injection of streptozotocin and bone marrow transplantation

	experiment. 8-week old male db/m and db/db mice were used for type 2 model of diabetes. neonatal SD rats were used for isolated primary cardiomyocytes. All of the mice were bred and maintained in specific pathogen-free (SPF) barrier facility at Animal Center of Wenzhou Medical University (Wenzhou, China)
Wild animals	The study did not involve wild animals.
Field-collected samples	Study did not involve samples collected from the field.
Ethics oversight	All animals received humane care according to the National Institutes of Health (USA) guidelines. All animal care and experimental procedures were approved by the Wenzhou Medical University Animal Policy and Welfare Committee.

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	The information of healthy subjects and diabetic patients are shown in the Supplementary Table S1.
Recruitment	8 apparently healthy subjects without diabetes, 7 diabetic patients without cardiomyopathy, and 9 diabetic patients exhibiting reduced ejection fraction (EF%), and without the indication of other cardiac diseases were recruited from the hospital clinic and community, based on an a priori protocol. All subjects were screened for the echocardiographic exam. DCM candidates were excluded if they were pregnant, had a self-reported history of symptomatic micro- or macrovascular complications of diabetes (including nephropathy, neuropathy, retinopathy, peripheral vascular disease, ischemic heart disease, and stroke) or other significant comorbidities including malignancy, renal failure, or significant psychiatric illness. In addition, All samples were de-identified and corresponding clinical information was collected by an honest broker. There was no potential self-selection bias or other biases that may impact results.
Ethics oversight	Approval for this study was granted by the Human Research Ethics Committees of Wenzhou Medical University, Wenzhou, China. All subjects gave written, informed consent to participate in the study and research was carried out in accordance with the Declaration of Helsinki (2008) of the World Medical Association.

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 ICMJEguidelines for publication of clinical research and a completedCONSORT 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.*

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	Cells were incubated with LPS-FTIC or D-glucose, and then harvested, washed and measured in basic DMEM media
Instrument	Flow cytometry was performed on FACS Calibur(BD)
Software	Data was analyzed using FlowJo 10.0
Cell population abundance	No post-sorting analysis was done
Gating strategy	Cells were gated based on their forward scatter (FSC) and side scatter (SSC) using gate R1. The fluorescence intensity of FITC was shown in gate R1

☒ 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.