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Last updated by author(s): Apr 22, 2021

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	LC/MS data was collected using Thermo Scientific Xcalibur software 4.3.73.11. GC/MS data was collected with
Data analysis	Peak picking analysis of raw LC/MS files was completed using El-MAVEN (v0.12.0) and of raw GC/MS files by Agilent MassHunter Quantitative Analysis (v9.0). Natural abundance correction was completed using Polly by Elucidata (https://elucidata.io/) for LC/MS data and using the web tool fluxfix.science for GC/MS data.

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 generated or analyzed during this study are included in this published article (and its supplementary information files).

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	3 C57BL/6 mice injected with saline (Ctrl) abd 3 C57BL/6 mice injected with Phenformin for tail vein infusion. All mice from the same litter and of the same age
Data exclusions	No data was excluded
Replication	biological replicates
Randomization	N/A comparison of Phenformin treatment vs control
Blinding	N/A comparison of Phenformin treatment vs control

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	Also See Table 3 FITC KLRG1 (ThermoFisher) 11-5893-82 2F1 PE CD8 1/300 (ThermoFisher) 12-0081-85 53-6.7 PECy7 CD44 1/300 (ThermoFisher) 25-0441-82 IM7 APC Thy1.1 1/300 (ThermoFisher) 17-0900-82 HIS51 APCCy7 Viability 1/1000 (ThermoFisher) 65-0865-14 BV421 CD127 1/100 (Biolegend) 135024 A7R34 BV605 CD4 1/300 (Biolegend) 100548 RM4-5
Validation	Validated by manufacturer

Animals and other organisms

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

Laboratory animals	C57BL/6J Purchased from Jackson Lab, Aged 6-8 weeks Females
Wild animals	NA
Field-collected samples	NA
Ethics oversight	IACUC Approval (18-12-035)

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	Mouse Splenocytes
Instrument	Beckman Coulter CytoFLEX S (A four laser, 14-color benchtop analyzer (4 violet, 2 blue, 4 yellow-green, 3 red)
Software	FlowJo v10.7.1
Cell population abundance	Full Gating shown in figure 5
Gating strategy	Shown in figure 5

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