

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

Data 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 numerical source data for graphs and charts are available as Supplementary data. Label-free quantification mass spectrometry (LFQ-MS) data have been deposited at PRIDE and are publicly available with accession numbers PXD045910 and PXD052976.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	<input type="text" value="n/a"/>
Population characteristics	<input type="text" value="n/a"/>
Recruitment	<input type="text" value="n/a"/>
Ethics oversight	<input type="text" value="n/a"/>

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](https://www.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	<input type="text" value="For assessment of physiological parameters at least 10 animals were used (required sample size estimated for the following parameters: difference between groups - 25%, measuring error - 20%), for other analyses at least 4 animals were used."/>
Data exclusions	<input type="text" value="The outlier values were excluded based on the ROUT method (Q = 2%)."/>
Replication	<input type="text" value="Each experiment represents at least 3 biological replicates, for physiological parameters at least 10 animals were used."/>
Randomization	<input type="text" value="The animals of the same genotype were randomly assigned to each experimental group. Blood and tissue collections as well as metabolomic and proteomic analyses were also randomized."/>
Blinding	<input type="text" value="Blinding was not performed in the study."/>

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	<input type="checkbox"/>	Included in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/>	Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/>	Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Dual use research of concern

Methods

n/a	<input type="checkbox"/>	Included in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/>	ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/>	MRI-based neuroimaging

Antibodies

Antibodies used

Primary antibodies/catalog #/company:
 Total OXPHOS antibody cocktail_Mouse/ab110412/Abcam
 Anti-LC3B_Rabbit/ab48394/Abcam
 Anti-Citrate Synthase/ab129095/Abcam
 Anti-Actin_Mouse/#MAB1501/Merck
 Anti-Actin (Ab-1) IgM_Mouse/#CP01-1EA/Calbiochem

Secondary antibodies/catalog #/company:
 Alexa Fluor 680 Donkey anti-mouse IgG/#A10038/Life Technologies
 Alexa Fluor 680 Donkey anti-rabbit IgG/#A10043/Life Technologies
 IRDye 800 Donkey anti mouse IgG/#926-32212/LI-COR
 IRDye 800 Goat anti-mouse IgM/#926-32280/LI-COR

Validation

All the antibodies were validated by the manufactures.
 Total OXPHOS antibody cocktail - application - WB
 Anti-LC3B (Abcam) - application WB, immunofluorescence
 Anti Citrate Synthase (Abcam) - application WB, immunofluorescence, immunohistochemistry, flow cytometry
 Anti-Actin (Merck) - application WB, immunofluorescence, immunohistochemistry
 Anti-Actin (Calbiochem) - application WB, Immunofluorescence

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	In-house prepared primary fibroblasts from SHR and mtF344 rats.
Authentication	n/a
Mycoplasma contamination	All cell lines were negative for mycoplasma.
Commonly misidentified lines (See ICLAC register)	n/a

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	Male of inbred spontaneously hypertensive rats (SHR; SHR/OlaIpcv strain) and F344 (F344/Crl), and strains derived from SHR with the mitochondrial genome of inbred strains F344 and Brown Norway (no. of backcrossing with SHR males >50) as described in Pravenec et al., Genome Res 2007 (doi:10.1101/gr.6548207) and Houstek et al., Physiol Genomics 2014 (doi:10.1152/physiolgenomics.00069.2014).
Wild animals	n/a
Reporting on sex	Only males were used, we plan to perform the studies on females as well.
Field-collected samples	The study did not involve collected samples from the field.
Ethics oversight	Animal experiments were approved by the Institutional Animal Care and Use Committee and the Committee for Animal Protection of the Czech Academy of Sciences (Approval Number: 58/2021) in agreement with the Animal Protection Law of the Czech Republic, which is fully compatible with the guidelines of the European Community Council directives 2010/63/EU.

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