

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 AxioVision 4.9.1, NIS-Elements.

Data analysis MassHunter, Excel 365, GraphPad Prism 7, JMP v15.1, SPSS v24, ImageJ 1.45 and R v4.1.1

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](#)

Microarray data generated in this study are publicly available in the NCBI Gene Expression Omnibus repository under the accession number GSE192361. Additional data used in this work are available using GEO numbers detailed in the paper under the section Data Availability.

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	Human omics data were retrospectively analyzed from previously described independent patient cohorts (see references in the Results section). For animal experiments, the number of mice was based on previous experience. No sample size calculation was therefore performed.
Data exclusions	No data were excluded
Replication	Experimental findings were repeated multiple times in independent experiments as indicated in the figure legends
Randomization	Experiments in wild-type and knockout animals were not randomized as mice were identified by genotyping. In other experiments, samples/mice treated with siRNA/drugs/diets, were randomly assigned to each group.
Blinding	For the mouse studies, the investigators were not blinded as they handled the phenotyping and sacrifice of the mice. However, the investigators were blinded for sample processing and samples were processed in random order.

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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input 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 type="checkbox"/>	<input checked="" type="checkbox"/> Human research participants
<input type="checkbox"/>	<input checked="" type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involved 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	All antibodies used in this study are detailed in Supplementary Table 2 including catalogue numbers and manufacturers.
Validation	All antibodies used in this study were commercially available and validation data can be found on the respective manufacturers' websites. Key findings were validated by siRNA knockdown experiments.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	For Ckb floxed animals, age and housing conditions are detailed in Rahbani et al (PMID 33597756). For HFD and phosphocreatine injection studies, C57BL/6J male mice were used and were sacrificed at 10-12 weeks of age. Animals were housed at the KM-B animal facility at the Karolinska Institutet in ventilated cages (4 animals/cage) with a 12 hour light/12 hour dark cycle (lights on 06:00–18:00) in a temperature-controlled (20-24°C, 50 % humidity) facility with ad libitum access to food and water. Animals were handled following the European Union laws and guidelines for animal care. Health inventories were performed on a regular basis (every 3 months) and follow the guidelines of the Federation of European Laboratory Animal Science Associations.
Wild animals	No wild animals were included in the study.
Field-collected samples	No field-collected samples were used in this study.

Ethics oversight

Ethical permits were obtained from the regional ethics board as detailed in the manuscript.

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

Clinical characteristics of the four cohorts are detailed in Supplementary Table 1.

Recruitment

No new patients/research subjects were recruited for this study.

Ethics oversight

All studies based on existing human data sets were approved by the regional ethics board of the Stockholm County Council. Informed written consent was obtained from all participants. A compensation of approximately 100 EUR was given to participants undergoing fine needle biopsies according to Swedish guidelines and the approved ethical permits.

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

NCT01727245 (cohort 1 and 4) and NCT01785134 (cohort 3)

Study protocol

The intervention (bariatric surgery) is described at [clinicaltrials.gov](#)

Data collection

All subjects were investigated in the morning after an overnight fast at the Karolinska University Hospital, Huddinge. Subcutaneous white adipose tissue biopsies from the periumbilical area were obtained by needle biopsies. One part of the tissue was rinsed and snap frozen in liquid nitrogen and stored at -80°C until analysis. One part was rinsed and fixed in PFA for immunohistochemistry. Details on additional analyses are provided in the paper including relevant references.

Outcomes

Primary and secondary outcome measures for each study are detailed at [clinicaltrials.gov](#).