

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 was organized using R software (version 4.5.1)

Data analysis

All analyses were performed using SAS (version 9.4), R software (version 4.5.1), and GraphPad Prism (version 10.5.0).

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](#)

Average monthly temperatures in Central Park were obtained from the National Weather Service website. Anonymized clinical data are available upon request, subject to an internal review by N.G.B., P.C., D.L. and H.S. to ensure that the participants' anonymity and confidentiality are protected and completion of a data sharing agreement, and in accordance with The Rockefeller University and Memorial Sloan Kettering Cancer Center Institutional Review Board and Institutional Guidelines.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	Sex was determined based on self-report, and extracted from the institutional EHR.
Reporting on race, ethnicity, or other socially relevant groupings	Race/ethnicity were determined based on self-report. Race/ethnicity categories are presented as reported in the institutional EHR.
Population characteristics	Patients aged 18 or above with available FDG-PET/CT scan data from June 2009 to July 2024 at Memorial Sloan Kettering Cancer Center
Recruitment	Given the retrospective nature of the study no active recruitment was needed.
Ethics oversight	This retrospective case-control study followed institutional guidelines and was approved by the Institutional Review Boards of The Rockefeller University and Memorial Sloan Kettering Cancer Center (MSK). Due to its retrospective nature, requirement for informed consent was waived.

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

Life sciences study design

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

Sample size	No sample calculation was performed. Sample size was chosen based on independent preliminary studies
Data exclusions	On indirect calorimetry experiments done on WT mice treated with losartan vs control at 4°C, 3 mice were excluded due to technical issues with the metabolic cage airflow during the course of the experiment, leading to problematic O2 and CO2 recordings. This issues were independently confirmed by the company (Sable). On the indirect calorimetry experiment done on WT mice treated with losartan vs control at room temperature, 1 mouse was excluded due to outlier measurements in all parameters. ROUT testing confirmed this mouse was an outlier based on statistical testing.
Replication	Experimental findings were verified by biological replicates and by validation of at least two independent experiments.
Randomization	Samples/animals were randomly assigned when possible to control vs treatment groups.
Blinding	Experimenters were blinded by group allocation as much as possible when performing standardized sample processing.

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
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	anti-UCP1 (1:1000, Abcam Ab209483), anti-Cyclophilin B (1:1000, Abcam Ab 16045, anti-vinculin (1:1000, #4650)
Validation	Antibodies were validated per manufacturers website https://www.abcam.com/en-us/products/primary-antibodies/ucp1-antibody-epr20381-ab209483 , https://www.cellsignal.com/products/primary-antibodies/vinculin-antibody/4650?srsId=AfmBOop0g0mAMI46LmbFaW7LpCqymTJelV7a53f7rcSar4-S643WfaDE , https://www.abcam.com/en-us/products/primary-antibodies/cyclophilin-b-antibody-loading-control-ab16045

Eukaryotic cell lines

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

Cell line source(s)	Immortalized brown adipocytes were generated in the Cohen Lab. HEK293T cells used for lentiviral production were obtained from ATCC.
Authentication	Immortalized brown adipocytes were authenticated based on increased respiration and Ucp1 expression in response to norepinephrine.
Mycoplasma contamination	All cells were tested for mycoplasma contamination via PCR via and were negative.
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	C57Bl6/J wild-type (WT) at 12 weeks of age were used in this study.
Wild animals	N/A
Reporting on sex	Only male mice were used in this study.
Field-collected samples	N/A
Ethics oversight	Animal care and experimentation were performed according to procedures approved by the Institutional Animal Care and Use Committee at the Rockefeller University.

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	N/A
Study protocol	MSK IRB 17-581
Data collection	We collected pertinent clinical data for each patient as previously described in Becher et al, Nat Med, 2021. In brief, for cancer site, we included the specific cancer diagnostic code (ICD-0) listed closest to the index scan date (Supplementary Table 1). Data referring to cancer treatment were collected if administered within 90 days before the index scan and classified as previously4 (Supplementary Table 2). Pertinent ICD-9 and ICD-10 codes corresponding to cardiometabolic diseases (Supplementary Table 7), and all other codes were extracted up to 1 year after the index scan in patients from our PSM cohort. Codes were selected to represent non-pediatric, non-obstetric, adult disorders as explained below. For laboratory values, clinical indices, and imaging studies, we extracted available data up to 1 year after the index scan in our PSM cohort. Analyses were performed in BAT+ and BAT- patients with available values. To identify individual pharmacological agents associated with BAT presence, we extracted medications in the home medication list and/or medications with an active pharmacy prescription in the EHR from each patient belonging to our PSM cohort. We included only medications listed up one month before the index scan for each patient. We excluded pharmacological agents with unlikely systemic effects, such as those with topical, ophthalmic, nasal, and otic administration. Antimicrobials were excluded since they are generally prescribed in short courses. Medications classified as “as needed” (PRN) and herbal supplements were excluded. Medications with low frequency counts (present in less than 40 patients) were excluded. A final list of medications included in the analyses can be found in Supplementary Table 8. These medications were also grouped by general categories as described in Supplementary Table 8. Selection of diagnostic codes for unbiased associations with BAT To explore unbiased associations between BAT and other diseases, we extracted from the electronic health records (EHR) diagnostic codes (ICD-9 and ICD-10) listed up to 1 year after the index scan from patients belonging to our propensity score-matched (PSM)

cohort. To select the codes for extraction, we grouped ICD-9 and ICD-10 codes based on their 3 first letters/digits. ICD-10 codes belonging to general groupings: A, B, C, D, E, F, G, H, I, J, K, L, M, N, R were included since they group the medical pathologies most likely to be found in a non-pediatric, non-obstetric, adult cancer population. A similar rationale was used for the selection of ICD-9 codes. A total of 1,157 ICD-10 codes and 626 ICD-9 codes were queried for extraction from the EHR.

After the code extraction was performed, to avoid redundancy, we merged ICD-9 codes with their corresponding ICD-10 codes based on a manual review of each code. The nomenclature of the ICD-10 code was maintained for downstream analysis in cases where an ICD-10 and ICD-9 code were merged. ICD-9 codes that did not have a corresponding ICD-10 code were maintained with their nomenclature. This left us with a total of 1,209 codes between individual ICD-9 and merged ICD-9/ICD-10 codes.

To further filter diagnostic codes for analyses, we excluded codes with low frequencies (present in less than 40 patients) and those referring to a cancer diagnosis (Supplementary Table 1) given all patients had a cancer site assigned already. This left us with a final list of 511 diagnostic codes. Given the large number of codes, we initially performed a screening analysis utilizing a univariable logistic regression analysis to identify unadjusted associations of the 511 with the presence of BAT. 104 codes were significantly associated with BAT status in this analysis. Subsequently, we analyzed each of these 104 codes using a multivariable regression analysis to assess their individual association with BAT, while controlling for age, sex, BMI, ambient temperature, self-reported race and ethnicity, smoking history, family history of cardiovascular disease, cancer site, cancer stage, cancer treatment, and general groups of outpatient medications (Extended Data Fig. 5a).

Outcomes

The association between BAT and age/BMI/temperature was assessed by a Pearson's correlation coefficient. Prevalence of BAT in men and women was compared using a chi-squared test.

To assess whether BAT status was a predictor of cardiometabolic diseases in the PSM cohort, we used multivariable logistic regression adjusting for age, sex, BMI, ambient temperature, self-reported race and ethnicity, smoking history, family history of cardiovascular disease, cancer site, cancer stage, cancer treatment, and general groups of outpatient medications. BAT metabolic activity (total and depot-specific) was calculated as the product of Standardized Uptake Value (SUV) mean and BAT volume (mL) and stratified into tertiles. The association of BAT activity with cardiometabolic diseases was assessed via a multivariable logistic regression adjusted age, sex, BMI, and outdoor temperature with BAT- patients or BAT patients in tertile 1 (lowest BAT metabolic activity) as reference. The correlation of BAT activity with age and outside temperature was calculated with Pearson correlation coefficient after logarithmic transformation. The association of BAT activity with SAT area, VAT area, SAT/VAT ratio, and other clinical continuous variables was calculated with linear regression after logarithmic transformation.

The association of BAT status and an expanded set of 511 ICD codes was assessed via univariable logistic regression to identify crude associations. ICD codes significantly associated with BAT were then individually analyzed through multivariable logistic regression analysis adjusting for age, sex, BMI, ambient temperature, self-reported race and ethnicity, smoking history, family history of cardiovascular disease, cancer site, cancer stage, cancer treatment, and general groups of outpatient medications. For overrepresentation analysis (ORA), the 511 codes were grouped by organ system.

Unpaired t-tests were used to compare lab values, imaging studies, and clinical indices in BAT+ vs BAT- patients. Variance equality was assessed via an F-test. When variances were equal, standard t-tests assuming equal variances were used; otherwise, t-tests with unequal variance adjustments were applied. For adjusted analyses, general linear models (GLMs) were used to estimate least square means, adjusting for age, sex, BMI, self-reported race and ethnicity, ambient temperature, cancer site, cancer stage, and cancer treatment. Post-hoc pairwise comparisons were performed using Tukey's HSD method. Categorical variables were compared using Fisher's exact test.

Associations between BAT and individual medications were assessed through multivariable logistic regression adjusted for age, sex, BMI, temperature, ethnicity, race, smoking history, family history of cardiovascular disease, cancer sites, cancer stage, cancer treatment, and cardiovascular diagnoses. For in vitro and in vivo proof-of-concept experiments, group comparisons were conducted using unpaired t-tests. To account for multiple comparisons, P values were corrected using the Benjamini-Hochberg false discovery rate (FDR) method, and adjusted P values are reported as such where applicable. Metabolic cage data were analyzed, and statistical significance was calculated either using 2-way ANOVA for hourly data or unpaired t-test for 24hr cumulative, light, and dark cycle. All analyses were performed using SAS (version 9.4), R software (version 4.5.1), and GraphPad Prism (version 10.5.0). All reported P values are two-sided, and statistical significance was defined as $\alpha < 0.05$.

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.