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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

Anthropometric measurements were obtained under a 12-hour fasting condition by trained dietitians. Waist and hip circumferences were measured using a non-stretchable SECA 201 measuring tape with 0.1 cm precision. Height was measured with a SECA stadiometer, and weight was measured with a SECA mBCA 514 calibrated body composition analyzer. Body mass index (BMI) was calculated as weight (kg) divided by height (m2). Body composition analysis was performed with dual-energy X-ray absorptiometry (DXA) (GE Healthcare, CoreScan software version).
Systolic and diastolic blood pressure were measured by trained personnel while the participant was seated and at rest. Immediately following blood pressure measurement, venous blood samples were drawn by trained nurses. HbA1c plasma concentration was measured using high-performance liquid chromatography (HPLC) (variant II Turbo, BIORAD). Fasting insulin levels were determined by chemiluminescence immunoassay (Beckman Coulter Access 2). Plasma total cholesterol, triglycerides, and HDL-cholesterol were measured using colorimetric assays (Unicel DxC 600 Syncron Clinical System Beckman Coulter). LDL-cholesterol was calculated using the Martin's equation. Plasma glucose concentration was measured with an automated glucose analyzer (Yellow Springs Instruments, OH, USA). Subcutaneous adipose tissue (SAT) biopsies and blood samples were taken between 7:00 and 8:00 hours.
Total RNA from approximately 20 mg of SAT tissue was extracted using 500 µL of TRIzol (Invitrogen) and quantified by UV spectroscopy (NanoDrop, Thermo Fisher Scientific). RNA quality was assessed with a RIN > 7.0 using the Bioanalyzer RNA 6000 (Agilent). Next, 150 ng of RNA was used for transcriptome analysis using the Clariom D Human microarray (Applied Biosystems) on a GeneChip 3000 scanner, performed by the INMEGEN Microarray Analysis Unit. Raw data was normalized, and gene expression values were obtained using the Transcriptome Analysis Console (TAC) 4.0 software (Thermo Fisher Scientific).
The analysis of Expression (Gene + Exon) with SST-RMA summarization method was employed to compare gene expression levels between groups S1 (NW vs. OW), S2 (NW vs. PD), and S3 (NW vs. T2D) using ANOVA with eBayes correction 120. The differentially expressed coding genes among groups were identified based on the criteria of P< 0.05 and |log2(Fold Change) |>1.1. The transcriptomic data are available at

Gene Expression Omnibus GSE249298

Data analysis

Means ± standard error (SEM) were calculated, and different statistical tests were used. A t-test analysis was employed to compare two independent groups, a one-way ANOVA test followed by a post-hoc Tukey-Kramer test was applied to compare three or more independent groups, or Dunnet´s post-hoc when comparing a control group, provided that the variable data was normally distributed (Shapiro-Wilk P>0.05) and homoscedastic (Bartlett's test P>0.05). If the data did not meet the assumptions of ANOVA, the Kruskal-Wallis with Wilcoxon post-hoc test (non-normal and homoscedastic data) or Welch's ANOVA test with post-hoc Games-Howell test (for normal and heteroscedastic data) were used. The analyses were conducted using the 'moments', 'rstatix', and 'plotrix' packages for R. Plots were obtained using GraphPad Prism 9.0. Factor analysis of mixed data (FAMD) was performed to analyze the association between quantitative (gene expression) and qualitative variables (diagnosis and sex). The FAMD was conducted using FactoMineR, and factoextra. The analysis of Expression (Gene + Exon) with SST-RMA summarization method was employed to compare gene expression levels between groups S1 (NW vs. OW), S2 (NW vs. PD), and S3 (NW vs. T2D) using ANOVA with eBayes correction 120. The differentially expressed coding genes among groups were identified based on the criteria of P< 0.05 and |log2(Fold Change) |>1.1. The transcriptomic data are available at Gene Expression Omnibus GSE249298

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

Provide your data availability statement here.

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	Factor analysis of mixed data (FAMD) was performed to analyze the association between quantitative (gene expression) and qualitative variables (diagnosis and sex). The FAMD was conducted using FactoMineR, and factoextra
Reporting on race, ethnicity, or other socially relevant groupings	Social relevant characteristics such as race and ethnicity, socioeconomic status, etc were not considered in this study
Population characteristics	Sixty-two females and twenty-six males (43.5 ± 23.5 years) were recruited. Sample sizes were not statistically predetermined but were in line with those used in other SAT transcriptome studies112,113. Men and women were divided into four groups according to their BMI, and the American Diabetes Association for prediabetes and diabetes criteria for fast glucose plasma (FGP) concentration and glycated hemoglobin (HbA1c) percentage 114. Inclusion criteria: NW (BMI 18.5–24.9 kg/m2), FPG 70–100 mg/dL and HbA1c < 5.7% (n=22), OW (BMI 25–34.9 kg/m2), FPG 70–100 mg/dL and HbA1c < 5.7%) (n=23), PD (BMI 25–34.9 kg/m2, FPG 110-125 mg/dL or OGTT ≥ 140 and < 200 mg/dL and HbA1c 5.7-6.4%) (n=21), and T2D subjects (BMI 25–34.9 kg/m2), FPG ≥ 126 mg/dL or OGTT ≥ 200 mg/dL, HbA1c ≥ 6.5%, with an initial diagnosis < 5 years and treated with metformin (n=20). Exclusion criteria: Individuals who suffered from a 3rd and/or 4th degree burns at any time of life, catecholamine-secreting tumors, hyperthyroidism, and/or use of rosiglitazone.
Recruitment	Some participants were recruited by a phone call from the hospital's research unit database, while others were recruited through advertisements on panels that displayed information about the study
Ethics oversight	This study was conducted in accordance with the principles of the Declaration of Helsinki. The research protocol was reviewed and approved by the Ethics Committees. All subjects were informed about the purpose and procedures of the study and signed an informed consent to participate

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	Sample sizes were not statistically predetermined but were in line with other subcutaneous adipose tissue transcriptome studies (33671464, 37190014)
Data exclusions	No data were excluded
Replication	Cell-culture experiments were performed with a least three technical replicates. Experiments in subcutaneous adipose biopsies were not replicated.
Randomization	All samples were equally considered in the experiments.
Blinding	No blinding was done in this study, except for personal data of each participant.

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	mouse anti-Bak (AT38E2) 1:200 (SCBT sc-517390), mouse anti-Bax (B-9) 1:200 (SCBT sc-7480), rabbit anti-TH 1:1000 (Pel Freez P40101), rabbit monoclonal anti-MAX 1:1000 (ab199489). Secondary antibodies were HRP-conjugated anti-rabbit IgG (Cell Signaling 7074, 1:10,000) or HRP-conjugated anti-mouse IgG (Cell Signaling I8765, 1:10,000).
Validation	All antibodies were validated by the manufacturer and in previous publications, as follows: sc-517390 (PMID 36329234, 22898870); sc-7480 (PMID 38047085, 37993441); P40101 (PMID 27841875, 27407143); ab199489 (PMID 36997534, 30679434).

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, mosiacism, off-target gene editing) were examined.*