nature portfolio

Corresponding author(s): Yajun Duan

Last updated by author(s): Jul 30, 2024

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	Schematic diagram of experimental designs were drawn with Adobe illustrator 2022. Other data were collected with GraphPad Prism software (9.0).
Data analysis	The following software was used for data analysis: GraphPad Prism (9.0), R software (V.3.0.1), ImageJ (v1.51), limma package (version 3.26.8), VennDiagram software (version 1.7.3).

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

Data supporting the findings of this manuscript are available from the corresponding authors upon reasonable request.
Three microarray datasets (GSE171269, GSE31953, and GSE145052) were obtained from the Gene Expression Omnibus database.

Approximately 100 mg of liver tissue was collected and flash-frozen in liquid nitrogen for subsequent RNA-seq analysis. The RNA-seq analysis was performed by Novogene Bioinformatics Technology Co., Ltd (Beijing, China). The raw RNA-seq data generated in this study have been deposited in the Gene Expression Omnibus (GEO) database under the accession number GSE236979.
The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD046104 and PXD046118.

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	Male mice were used for the experiments in this study because the prevalence of diabetes is much higher in males than in females, and the experiments and results are usually analyzed in males. This study included 10 (5 males, 5 females) patients aged 40-60 years with pancreatic occupations from June 2022 to December 2022 at the China-Japan Friendship Hospital (Beijing, China). The results showed that male and female patients did not present significant differences in Nogo-B protein, and all diabetic patients had significantly increased intestinal Nogo-B level.
Reporting on race, ethnicity, or other socially relevant groupings	The study didn't involve race, ethnicity, or other socially relevant groupings.
Population characteristics	This study included 12 patients aged 40-60 years with pancreatic occupations from June 2022 to December 2022 at the China-Japan Friendship Hospital (Beijing, China). All patients underwent their first surgery without prior radiotherapy or chemotherapy.s.
Recruitment	The 12 patients with pancreatic occupations were divided into two groups, one without T2DM and the other with T2DM. Patients with a history of other malignancies or other abnormal metabolic diseases (except T2DM) were excluded at the time of inclusion.
Ethics oversight	Each patient provided signed informed consent, and the study was approved by the Ethics Committee of China-Japan Friendship Hospital (No 2018-72-K52).

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	The sample size of our animal experiments was determined based on previous experiments and to minimize the use in accordance with animal care guidelines. Additional details regarding sample size can be found in the corresponding figure legends.
Data exclusions	No data were excluded from the analyses.
Replication	Each independent experiment was replicated at least 3 times.
Randomization	For in vitro experiments, all mice were assigned to different groups according to a randomized block experimental design. For in vitro experiments, cells were randomly allocated into different groups.
Blinding	The investigators were blinded to group allocation during data collection and analysis.

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used

Anti-Flag (Cat# M20008), anti-GFP (Cat# M20004), anti-GLP1 (Cat# T56696), and anti-HA (Cat# M20003), anti-INSR (Cat# T55803), anti-IRS1 (Cat# T55830), anti-pIRS1 (Cat# TA3272), anti-IRS2 (Cat# PA5455), anti-pIRS2 (Cat# TA8383), anti-AKT (Cat# T55561), anti-pAKT (Cat# T40067), anti-PERK (Cat# TP52759), anti-pPERK (Cat# TA4499), anti-IRE1 (Cat# TA7651), anti-pIRE1 (Cat# T55605), anti-ATF4 (Cat# T55873), anti-XBP1 (Cat# T56725) antibodies were purchased from Abmart.

Anti-cleaved caspase3 (Cat# 9664) antibody was purchased from Cell Signaling Technology.

Anti-Nogo (Cat# IMG-5346A) antibody was purchased from Novus.

Anti-GAPDH (Cat# HRP-60004), anti-pINSR (Cat# 31133-1-AP), anti-GCG (Cat# 15954-1-AP), anti-GRP94 (Cat# 14700-1-AP), anti-HSP90 (Cat# 13171-1-AP), anti-Rabbit IgG (Cat# 30000-0-AP), fluorescein (FITC)–conjugated Affinipure Goat anti-Mouse IgG(H+L) (Cat# SA00003-1), fluorescein (FITC)–conjugated Affinipure Goat anti-Rabbit IgG(H+L) (Cat# SA00003-2), Rhodamine (TRITC)–conjugated Goat anti-Mouse IgG(H+L), (Cat# SA00007-1), and Rhodamine (TRITC)–conjugated Goat anti-Rabbit IgG(H+L) (Cat# SA00007-2) antibodies were purchased from Proteintech.

Anti-insulin (Cat# sc-377071) and anti-PCSK1 (Cat# sc-100578) antibodies were purchased from Santa Cruz Biotechnology.

Validation

Antibody validations were performed by antibody supplier (see links below).

anti-Flag (Cat# M20008), https://www.ab-mart.com.cn/page.aspx?node=%2059%20&id=%20968

anti-GFP (Cat# M20004), https://www.ab-mart.com.cn/page.aspx?node=%2059%20&id=%20971

anti-GLP1 (Cat# T56696), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%202364

anti-HA (Cat# M20003), https://www.ab-mart.com.cn/page.aspx?node=%2059%20&id=%20963

anti-INSR (Cat# T55803), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%202041

anti-IRS1 (Cat# T55830), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%202067

anti-pIRS1 (Cat# TA3272), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2018193

anti-IRS2 (Cat# PA5455), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2052742

anti-pIRS2 (Cat# TA8383), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2022789

anti-AKT (Cat# T55561), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%201801

anti-pAKT (Cat# T40067), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%201224

anti-PERK (Cat# TP52759), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2048763

anti-pPERK (Cat# TA4499), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2019544

anti-IRE1 (Cat# TA7651), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%2019136

anti-pIRE1 (Cat# T55605), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%201845

anti-ATF4 (Cat# T55873), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%202110

anti-XBP1 (Cat# T56725), https://www.ab-mart.com.cn/page.aspx?node=%2077%20&id=%202393

anti-cleaved caspase3 (Cat# 9664), https://www.cellsignal.cn/products/primary-antibodies/cleaved-caspase-3-asp175-5a1e-rabbit-mab/9664?_requestid=577454

anti-Nogo (Cat# IMG-5346A), https://www.novusbio.com/products/nogo-antibody_nb100-56681

anti-GAPDH (Cat# HRP-60004), https://www.ptglab.com/products/GAPDH-Antibody-HRP-60004.htm

anti-pINSR (Cat# 31133-1-AP), https://www.ptgcn.com/products/Phospho-INSR-Tyr1150-1151-Antibody-31133-1-AP.htm

anti-GCG (Cat# 15954-1-AP), https://www.ptglab.com/products/GCG-Antibody-15954-1-AP.htm

anti-GRP94 (Cat# 14700-1-AP), https://www.ptglab.com/products/HSP90B1-Antibody-14700-1-AP.htm

anti-HSP90 (Cat# 13171-1-AP), https://www.ptglab.com/products/HSP90-Antibody-13171-1-AP.htm

anti-Rabbit IgG (Cat# 30000-0-AP), https://www.ptglab.com/products/IgG-control-Antibody-30000-0-AP.htm

Fluorescein (FITC)–conjugated Affinipure Goat anti-Mouse IgG(H+L) (Cat# SA00003-1), https://www.ptglab.com/products/Fluorescein-FITC-conjugated-Affinipure-Goat-Anti-Mouse-IgG-H-L-secondary-antibody.htm

Fluorescein (FITC)–conjugated Affinipure Goat anti-Rabbit IgG(H+L) (Cat# SA00003-2), https://www.ptglab.com/products/Fluorescein-FITC-conjugated-Affinipure-Goat-Anti-Rabbit-IgG-H-L-secondary-antibody.htm

Rhodamine (TRITC)–conjugated Goat anti-Mouse IgG(H+L), (Cat# SA00007-1), https://www.ptglab.com/products/Rhodamine-TRITC-conjugated-Goat-Anti-Mouse-IgG-H-L-secondary-antibody.htm

Rhodamine (TRITC)–conjugated Goat anti-Rabbit IgG(H+L) (Cat# SA00007-2), https://www.ptglab.com/products/Rhodamine-TRITC-conjugated-Goat-Anti-Rabbit-IgG-H-L-secondary-antibody.htm

Anti-insulin (Cat# sc-377071), https://www.scbt.com/p/insulin-b-antibody-c-12?requestFrom=search

anti-PCSK1 (Cat# sc-100578), https://www.scbt.com/p/pcsk1-antibody-j-18?requestFrom=search

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK293T cells (Cat# CRL-3216, ATCC) and STC-1 cells (Cat# CRL-3254, ATCC)
Authentication	Cell lines were authenticated by genomic DNA profiling assays (STR) performed by Biofavor Biotech.
Mycoplasma contamination	Cell lines were tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None

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	The db/db mice, db/m mice, Nogo global deficient (Nogo-/-) mice, and Nogo conditional knockout (Nogof/f) mice were obtained from GemPharmatech Co., Ltd. (Nanjing, China). The Villin-Cre (VillinCre) mice were acquired from Shanghai Model Organisms
Wild animals	No wild animals were used in the study
Reporting on sex	This study wad performed on male mice. Because the incidence of diabetes is higher in males than in females, and hormonal changes in female mice can affect the results of the experiment.
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	All animal procedures conformed to the guide for the Care and Use of Laboratory Animal published by the US National Instituted of Health and was approved by the Brigham and Women's Hospital Standing Committee on Animals (protocol #2016N000442)

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A