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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	NMR spectra were acquired using Bruker 400 MHz NMR Spectrometer. Transmission electron microscope (TEM) measurements for nanoparticles were conducted on a JEM-F200 Multi-purpose Electron Microscope. Transmission electron microscope (TEM) measurements for cells were conducted on a Hitachi H-7500 Electron Microscope. DLS size and zeta potential data were acquired by Brookhaven NanoBrook 90Plus zeta and Malvern Instruments Zetasizer Nano-ZS. Fluorescence spectra were acquired by ThermoFisher LUMINA fluorescence spectrometer. ITC data were acquired by TA Nano-ITC LV instrument. FT-IR spectra were obtained and analysed on a ThermoFisher Scientific Nicolet is50 FT-IR Spectrometer. Platinum concentration was determined by ThermoFisher Scientific a ICP-MS. Confocal fluorescence images were acquired by Nikon A1 confocal laser scanning microscopy. Flow cytometry samples were analyzed using BD LSRFortessa X-20 flow cytometer. MTT data were acquired by BioTek Synergy H1 microplate reader. In vitro and in vivo fluorescence data were acquired by Bruker FX Pro and Caliper IVIS Lumina II. Western blot band were taken by Tanon™ 5200CE Chemi-Image System. Prothrombin time and activated partial thromboplastin time were determined by Automated Blood Coagulation Analyzer RAC-030. Leukocytes, erythrocytes, and thrombocytes were determined by Veterinary hematology analyzer.
Data analysis	NMR spectra were analyzed using MestReNova 12. Confocal fluorescence images and western blot band were analyzed using Image J (Version 1.8.0). Flow cytometry data were analyzed using FlowJo software package (version 10; BD, USA). NDP.view (Version 2.9) was used for the analysis of images from H&E staining. All statistical analyses were performed with Graphpad Prism 9.5 and Origin 2018.The figures were assembled in PowerPoint (version Office16). PowerPoint (version Office16) and Adobe Illustrator (version 2022) were used for scheme drawing.

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 data that support the findings of this study are available within the Article, Supplementary Information and Source Data file, or from the corresponding author upon request. Source data are provided with this paper.

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	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

Life sciences study design

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

Sample size	No statistical methods were used to predetermine sample sizes but our sample sizes are similar to those reported in previous publications (PMID: 36959501).
Data exclusions	No data was excluded from the analysis.
Replication	The number of replicates performed is indicated in each figure legend.
Randomization	For in vivo study of pharmacokinetic behaviours, mice were randomly allocated into experimental groups. For in vivo tumor studies, tumor-bearing mice having similar tumor sizes were randomly allocated into experimental groups.
Blinding	Investigators were not blinded to allocation during experiments and outcome assessment.

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

The following antibodies were used for western blot:
Human NPC1L1 Polyclonal Antibody, Affinity, cat.no.: DF8449, Dilution: 1:1000;
Human NPC1L1 Polyclonal Antibody, Proteintech, cat.no.: 28085-1-AP, Dilution: 1:1000;
Mouse Tubulin Polyclonal Antibody, Proteintech, cat.no.: 11224-1-AP, Dilution: 1:10000;
Mouse GAPDH Monoclonal Antibody, Proteintech, cat.no.: 60004-1-Ig, clone number: 1E6D9, Dilution: 1:20000;
Mouse alpha-SMA Polyclonal Antibody, Affinity Biosciences, cat.no.: AF1032, Dilution: 1:1000;
Mouse E-cadherin Polyclonal Antibody, Proteintech, cat.no.: 20874-1-AP, Dilution: 1:2000;
Mouse N-cadherin Polyclonal Antibody, Proteintech, cat.no.: 22018-1-AP, Dilution: 1:2000;
Mouse TGF Beta 1 Recombinant Monoclonal Antibody, Proteintech, clone number: 230544B7, cat.no.: 81746-2-RR, Dilution: 1:1000;
Mouse Smad2+Smad3 Multiclonal Antibody, HUABIO, clone number: PSH21-36, cat.no.:HA724174, Dilution: 1:1000;
Mouse Smad2 (Phospho Ser250) Polyclonal Antibody, UpingBio, cat.no.:YP-rAb-01304, Dilution: 1:2000;
Mouse Smad3 (Phospho Ser423/Ser425) Polyclonal Antibody, UpingBio, cat.no.:YP-rAb-01471, Dilution: 1:2000;
Mouse β-Catenin Rabbit Polyclonal Antibody, Beyotime, cat.no.: AF0066, Dilution: 1:1000;
Mouse Fibronectin Polyclonal Antibody, Affinity Biosciences, cat.no.: AF5335, Dilution: 1:1000;
HRP-conjugated Affinipure Goat Anti-Mouse IgG Antibody, Proteintech, cat.no.: SA00001-1, Dilution: 1:5000;
HRP-conjugated Affinipure Goat Anti-Rabbit IgG Antibody, Proteintech, cat.no.: SA00001-2, Dilution: 1:5000;
The following antibodies were used for immunofluorescence:
Human NPC1L1 Polyclonal Antibody, Affinity Biosciences, cat.no.: DF8449, Dilution: 1:200;
Mouse Rab 11A Monoclonal Antibody, Santa Cruz Biotechnology, cat.no.: sc-166523, clone number: D-3, Dilution: 1:100;
Mouse alpha-SMA Polyclonal Antibody, Affinity Biosciences, cat.no.: AF1032, Dilution: 1:200;
Mouse PDI Polyclonal Antibody, Proteintech, cat.no.: 11245-1-AP, Dilution: 1:300;
Mouse GOLGA2/GM130 Polyclonal Antibody, Proteintech, cat.no.: 66662-1-Ig, Dilution: 1:300;
Mouse Anti-CD31 Monoclonal Antibody, Abcom, cat.no.: ab182981, clone number: EPR17259, Dilution: 1:1000;
Mouse CD34 Polyclonal Antibody,Boster, cat.no.: BA0532, Dilution: 1:250;
Human Collagen Type I Polyclonal Antibody, Proteintech, cat.no.: 14695-1-AP, Dilution: 1:200;
Mouse Fibronectin Polyclonal Antibody, Affinity Biosciences, cat.no.: AF5335, Dilution: 1:200;
Goat Anti-Rabbit IgG (H+L) Fluor594-conjugated, Affinity Biosciences, cat.no.: S0006 , Dilution: 1:200;
Goat Anti-Mouse IgG (H+L) Fluor594-conjugated, Affinity Biosciences, cat.no.: S0005 , Dilution: 1:200;
Goat Anti-Mouse IgG (H+L) Fluor647-conjugated, Affinity Biosciences, cat.no.: S0014, Dilution: 1:200;
Goat Anti-Rabbit IgG(H+L)(Elab Fluor® 647 conjugated), Elabscience, cat.no.: E-AB-1075, Dilution: 1:200;
Alexa Fluor®488 donkey anti-rabbit IgG(H+L), Thermo Fisher, cat.no.: A21206, Dilution: 1:200;
The following antibodies were used for flow cytometer:
PE/Cyanine7 Anti-Mouse CD31 antibody, clone number: 390, Elabscience, cat.no.:E-AB-F1180H, Dilution: 1:100;
PerCP/Cyanine5.5 Anti-Mouse CD45 antibody, clone number:30-F11, Elabscience, cat.no.:E-AB-F1136J, Dilution: 1:100;
PE Anti-Mouse CD206/MMR Antibody[C068C2], Elabscience, clone number: C068C2, cat.no.:E-AB-F1135D, Dilution: 1:100;
Mouse alpha-SMA Polyclonal Antibody, Affinity Biosciences, cat.no.: AF1032, Dilution: 1:50;
Goat Anti-Rabbit IgG(H+L)(Elab Fluor® 647 conjugated), Elabscience, cat.no.: E-AB-1075, Dilution: 1:50;

Validation

All antibodies were verified by the supplier and each lot has been quality tested. The detailed information was listed as below:
Human NPC1L1 Polyclonal Antibody; (DF8449); Rabbit; suitable for western blot (WB), Immunocytochemistry (ICC), Immunofluorescence (IF); Reacts with human;
Human NPC1L1 Polyclonal Antibody; (28085-1-AP); Rabbit; suitable for WB, Immunohistochemistry (IHC); Enzyme-Linked Immunosorbent Assay (ELISA); Reacts with human;
Mouse E-cadherin Polyclonal Antibody; (20874-1-AP); Rabbit; suitable for WB, IHC, IF/ICC, Immunofluorescence Paraffin (IF-P), immunofluorescence Frozen (IF-Fro), Immunoprecipitayion (IP), Co-immunoprecipitation (CoIP), ELISA; Reacts with human, mouse, and rat;
Mouse N-cadherin Polyclonal Antibody; (2018-1-AP); Rabbit; suitable for WB, IHC, IF/ICC, IF-P, IF-Fro, IP, CoIP, ELISA; Reacts with human, mouse, and rat;
Mouse TGF Beta 1 Recombinant Monoclonal Antibody; (81746-2-RR); Rabbit; suitable for WB, IHC, IF/ICC, IF-P, FC (Intra), ELISA; Reacts with human, mouse, and rat;
Mouse Smad2+Smad3 Multiclonal Antibody; (PSH21-36); Rabbit; suitable for WB, FC, IF-Cell; Reacts with human, mouse, and rat;
Mouse Smad2 (Phospho Ser250) Polyclonal Antibody; (YP-rAb-101304); Rabbit; suitable for WB, ELISA, IHC; Reacts with human, mouse, and rat;

Mouse Smad3 (Phospho Ser423/Ser425) Polyclonal Antibody; (YP-rAb-01471); Rabbit; suitable for WB, ELISA, IHC; Reacts with human, mouse, and rat;
Mouse β-Catenin Rabbit Polyclonal Antibody; (AF0066); Rabbit; suitable for WB, FC, IHC; Reacts with human, mouse, and rat;
Mouse Tubulin Polyclonal Antibody; (11224-1-AP); Rabbit; suitable for WB, IHC, IF/ICC, IF-P, IF-Fro, FC (Intra), IP, CoIP, ELISA; ; Reacts with human, mouse, and rat;
Mouse GAPDH Monoclonal Antibody; (60004-1-Ig); Mouse; suitable for WB, IHC, IF/ICC, FC (Intra), IP, ELISA; Reacts with human, mouse, rat, pig, zebrafish, and yeast;
Mouse alpha-SMA Polyclonal Antibody; (AF1032); Rabbit; suitable for WB, IHC, IF/ICC; Reacts with Human, Mouse, Rat, and Bovine;
Mouse Rab 11A Monoclonal Antibody; (sc-166523); Mouse; suitable for WB, IP, ELISA, IF; Reacts with mouse, rat, human and hamster;
Mouse Anti-CD31 Monoclonal Antibody; (ab182981); Rabbit; suitable for Multiplex immunohistochemical (mIHC); Immunohistochemistry-Paraffin (IHC-P); Reacts with Mouse, Rat, and Human;
Human Collagen Type I Polyclonal Antibody; (14695-1-AP); Rabbit; suitable for WB, IHC, FC (Intra), IP, ELISA; Reacts with human, mouse, rat, pig, rabbit, canine, chicken, bovine, toad, and duck;
Mouse Fibronectin Polyclonal Antibody; (AF5335); Rabbit; suitable for WB, IHC, IF/ICC; Reacts with Human, Mouse, and Rat;
Mouse PDI Polyclonal Antibody; (11245-1-AP); Rabbit; suitable for WB, IHC, IF/ICC, FC (Intra), IP, ELISA; Reacts with human, mouse, rat, zebrafish;
Mouse GOLGA2/GM130 Polyclonal Antibody; (66662-1-Ig); Mouse; suitable for WB, IHC, IF/ICC(, FC(Intra), ELISA; Reacts with human, mouse, rat;
Goat Anti-Rabbit IgG (H+L) Fluor594-conjugated; (S0006); Goat; suitable for WB, IF/ICC, FACS; Reacts with Rabbit;
Goat Anti-Mouse IgG (H+L) Fluor594-conjugated; (S0005); Goat; suitable for WB, IHC, IF/ICC, FACS; Reacts with Mouse;
Goat Anti-Mouse IgG (H+L) Fluor647-conjugated; (S0014); Goat; suitable for WB, IF/ICC, FACS; Reacts with Mouse;
Goat Anti-Rabbit IgG(H+L)(Elab Fluor® 647 conjugated); (E-AB-1075); Goat; suitable for IF; Reacts with Rabbit;
Alexa Fluor®488 donkey anti-rabbit lgG(H+L); (A21206); Donkey; suitable for IHC-P, ELISA, ICC/IF, IHC-Fr, Flow Cyt; Reacts with Rabbit;
PE/Cyanine7 Anti-Mouse CD31 antibody; (E-AB-F1180H); Rat; suitable for FCM; Reacts with Mouse;
PerCP/Cyanine5.5 Anti-Mouse CD45 antibody; (E-AB-F1136J); Rat; suitable for FCM; Reacts with Mouse;
PE Anti-Mouse CD206/MMR Antibody[C068C2]; (E-AB-F1135D); Rat; suitable for FCM, ICFCM; Reacts with Mouse;

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Mouse embryonic fibroblast cell line NIH-3T3, human breast cancer cell line MDA-MB-231, human hepatic stellate cell (LX-2), and mouse breast cancer cell line 4T1 were sourced from American Type Culture Collection (ATCC). Mouse pancreatic cancer cell line Panc-02 and Panc-02 tagged with luciferase were purchased from Xiamen Immocell Biotechnology Co., Ltd. Mouse cancer-associated fibroblast (MC-6071m) was purchased from Shanghai Yaji Biotechnology Co., Ltd. Mouse pancreatic islet endothelial cell line (MS1) was purchased from Baidi Biotech Co., Ltd. Mouse vascular endothelial cell line (C166) was purchased from Wuhan Procell Co., Ltd.
Authentication	Cell lines were used without any modification once received from respective suppliers and therefore were not authenticated.
Mycoplasma contamination	Cell lines were all tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in the study.

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	6-8-week-old female BALB/c mice, 6-8-week-old female BALB/c nude mice,and 6-8-week-old female C56BL/6J mice. The mice were all purchased from Center for Experimental Animals, Southern Medical University. All mice were housed in pathogen-free conditions and kept in a room with controlled temperature (~22 ºC) and humidity (45%-60%) under 12 h light/dark cycle.
Wild animals	The study did not involve wild animals.
Reporting on sex	BALB/c mice were used to construct breast cancer models based on similar experiments reported in previous publications (PMID: 36379207). Female nude BALB/c mice Female construct breast cancer models based on similar experiments reported in previous publications (PMID:34774889). C57BL/6 mice were used to construct pancreatic cancer models based on similar experiments reported in previous publications (PMID: 37981050 and PMID: 37814010).
Field-collected samples	The study did not involve samples collected from field.
Ethics oversight	All animal experiments were carried out under the guideline approved by the Institutional Animal Care and Use Committee (IACUC) of Southern Medical University (2021178, SMUL202512095).

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

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	For cell uptake experiments, sample preparation is described in Methods.
Instrument	The data were acquired using BD LSRFortessa X-20 flow cytometer.
Software	The data were analyzed by FlowJo V10 software.
Cell population abundance	No sorting was performed.
Gating strategy	Generally, cells were first gated on FSC/SSC to exclude debris. Surface antigen gating was performed on the live cell population.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.