nature portfolio

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Last updated by author(s): Aug 2, 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	Liquid chromatography-mass spectrometry data were collected using Analyst v1.6 software (Sciex).
Data analysis	For liquid chromatography-mass spectrometry data, peak integration was performed with the MultiQuantTM software v3.0.3. Lipid species signals were corrected for isotopic contributions with Python Molmass v2019.1.1. Unpaired T-test p-values and FDR corrected p-values (using the Benjamini/Hochberg procedure) were calculated in Python StatsModels v0.10.1. Pathway enrichment analysis of the lipidomics data was conducted using the Lipid Ontology (LION) enrichment analysis web application.

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

All data, including patient information and tumoral temperature data, lipidomics data, survival and expression data of patients with pancreatic cancer and the genes used for the ferroptosis signature, are available in the main text or the supplementary materials. Source data are provided with this paper. The bulk RNA-seq data

generated in this study have been deposited at the NCBI Gene Expression Omnibus (GEO) under accession number GSE249302.

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	This study does not consider categorization variables based on sex. However, neither sex was overly representative in this study with 4/11 male and 7/11 female participants. Moreover, in vitro experiments were performed in male and female cell lines.
Reporting on race, ethnicity, or other socially relevant groupings	This study does not consider categorization variables based on race, ethnicity, or other socially relevant groupings.
Population characteristics	No covariate-relevant population characteristics were analyzed.
Recruitment	Candidates for surgical resection of PDAC were invited for the study. Patients were selected from the pool of patients that would undergo surgery in UZ Leuven for the purpose of PDAC resection.
Ethics oversight	Ethics Committee Research UZ/KU Leuven

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	There was no sample-size calculation for tissue culture experiments. All tissue culture experiments included at least three independent biological replicates, which allowed the detection of significant differences. For animal studies, required sample-size was estimated by balanced one-way analysis of variance power calculation based on parameters derived from prior experience with the model.
Data exclusions	No data were excluded from the analyses.
Replication	All tissue culture experiments were replicated with a minimum of three independent biological replicates (3 replicates on different days). Key experiments were replicated in an independent pair of incubators.
Randomization	Animals were randomly assigned to cohorts.
Blinding	Animals were numbered which allowed experiments to be conducted in a blinded manner.

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-phospho-p38 MAPK (1/1000 dilution) (Cell Signaling, #4511) anti-p38 MAPK (1/1000 dilution) (Cell Signaling, #8690)
Validation	Validation data on vendor's website for anti-phospho-p38 MAPK: https://www.cellsignal.com/products/primary-antibodies/phospho-p38-mapk-thr180-tyr182-d3f9-xp-rabbit-mab/4511 Validation data on vendor's website for anti-p38 MAPK: https://www.cellsignal.com/products/primary-antibodies/p38-mapk-d13e1-xp-rabbit-mab/8690

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	PANC-1 (ATCC, isolated from a male patient) BxPC3 (ATCC, isolated from a female patient) HPAC (ATCC, isolated from a female patient) FC1245 cells were originally isolated from KPC mice
Authentication	Cell lines used were not authenticated.
Mycoplasma contamination	Cell cultures were periodically tested for mycoplasma contamination using the MycoAlert Mycoplasma Detection Kit (Lonza) and confirmed to be mycoplasma free.
Commonly misidentified lines (See ICLAC register)	There were no commonly misidentified cell lines used.

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 NMRInu/nu mice and 6-8 week old female C57BL/6J mice were used in this study.
Wild animals	This study did not involve wild animals.
Reporting on sex	This study did not consider sex.
Field-collected samples	This study did not involve samples collected from the field.
Ethics oversight	Animal Ethics Committee KU Leuven

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