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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	No software was used to collect data.
Data analysis	Graphpad Prism 7.0 was used for statistical tests. Image Studio Lite was used to visualize Western blots that were developed using an Odyssey scanner (Licor). Mass spectrometry data was analyzed with XCalibur QuanBrowser 2.2.

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data generated that support the findings of this study are available from the corresponding author upon reasonable request. Individual data points for figures that cannot be presented with a dot plot overlay (Figures 1f, 1g, 2c, 2e, 4b, 4d, 4i and Supplementary Figures 1g, 2f, 2g, 2h, 3b, 4a, 4c, 4d, 4f, 4g, 4i, 4j) have been

provided in Supplementary Table 1. Metabolomics data for Supplementary Figures 2h and 4j have also been deposited at https://doi.org/10.6084/m9.figshare.6169409.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	Experiments were performed using sample sizes based on standard protocols in the field. No statistical test was performed to predetermine sample size.
Data exclusions	No data was excluded.
Replication	All attempts to replicate the experiments performed here were successful.
Randomization	Allocation of groups was random.
Blinding	The investigator was not blinded to group allocation, although results were qualitatively verified by blinded investigators. For the metformin xenograft experiment, quantitation of tumor volumes was done by a blinded investigator as discussed in methods.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	No restrictions on materials.

Antibodies

Antibodies used	Primary antibodies: FLAG (Cell Signaling, 2368, 1:1000), Vinculin (Abcam, ab18058, 1:10,000), ASNS (Sigma, HPA029318, 1:250), HIF1alpha (BD Transduction Laboratories, 610958, 1:250). Secondary antibodies: IR680LT dye conjugated anti-rabbit IgG (Licor Biosciences, 925-68021, 1:10,000), IR800 dye conjugated anti-mouse IgG (Licor Biosciences, 925-32210, 1:10,000), HRP-linked Anti-mouse IgG (Cell Signaling, 7076S, 1:10,000).
Validation	Antibodies were validated by the suppliers and by the appearance of a band at the predicted size and using biologically relevant conditions (hypoxia increasing HIF1alpha). Otherwise the antibodies were not validated before use, but are standard antibodies in the field.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	All cell lines were obtained from ATCC, aside from AL1376 cells which were derived from a pancreatic tumour from the KP-/-C (KrasG12D/+; Trp53fl/fl; Pdx1-cre) mouse model of pancreatic adenocarcinoma.
Authentication	The identity of 143B, 468, 786-o, A172, AsPC-1, HCT116, HeLa, HT1080, and TT cells were authenticated by satellite tandem repeat testing and referenced to ATCC values. AL1376 cells were generated in house.
Mycoplasma contamination	Mycoalert testing was done to test for mycoplasma contamination, as described in methods.
Commonly misidentified lines (See ICLAC register)	None of our cell lines are listed in ICLAC as commonly misidentified cell lines.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	6-8 week old male nu/nu mice were purchased from Charles river (088) and used for xenograft studies.
Wild animals	Study did not involve wild animals.
Field-collected samples	Study did not involve samples collected from the field.