

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	NIS Elements Imaging software for Immunofluorescence, live cell timelapse, and TIRF image capturing, Leica LAS-X Imaging software for live cell timelapse image capturing.
Data analysis	Image J version 1.54f for microscopic image analysis. QuPath was used for analysis of IHC. Incucyte software was using for cell quantification. Rstudio was used to analyze the CRISPR screen. Microsoft Excel (Excel 2016 microsoft office), GraphPad Prism v10 (GraphPad software)

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 source data, including western blots, are included with the manuscript. Raw data from the CRISPR KO screen can be found in Supplementary Table 5.

RNA-Seq data were deposited into the Gene Expression Omnibus database under accession number GSE305033 and GSE305002 and are available at the following URLs: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE305033> and <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE305002>

Publicly available datasets used in this study:

Bulk RNA-Seq data: GSE227100 and EGA dataset EGAD00001006456 (Fig 1a)

Nanostring data: GSE181597, GSE201600, and GSE319500 (Extended Data Fig. 1a)

scRNA-Seq data: GSE266577 (Fig. 1b and Extended Data Fig. 1b)

The Cancer Genome Atlas (TCGA) Serous Ovarian Cancer (Nature, 2011) project was downloaded from cbiportal.org.

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	All data reported from patients are from ovarian cancer patients and are therefore only female.
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	For Pitt cohort: Human samples were from ovarian cancer patients treated at the University of Pittsburgh. BMI and age were considered in the analysis. For TCGA data: Transcriptomic data downloaded from cBioportal (Nature, 2011). https://doi.org/10.1038/nature10166
Recruitment	For Pitt cohort: De-identified samples were collected under University of Pittsburgh IRB approved protocols (20050019, 19070449, and 19060197). For TCGA data: See Nature, 2011 https://doi.org/10.1038/nature10166
Ethics oversight	For Pitt cohort: The collection of patient samples was approved by the University of Pittsburgh IRB (protocols: 20050019, 19070449, and 19060197). Written, informed consent was obtained from ovarian cancer patients. For TCGA data: See Nature, 2011 https://doi.org/10.1038/nature10166

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](https://www.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 chosen on the basis of extensive experience with the assays we have performed. For metabolomics data, an n = 8 was chosen based on prior experience and variability in the data. For detachment assays, n = 3 was chosen based on prior experience. For imaging experiments, >100 cells or a maximum number in imaged fields were analyzed. The data in figures are representative of one independent experiment in each cell line.
Data exclusions	Outliers were removed using PRISM outlier analysis (ROUT method). For in vivo studies, mice without tumor development, measured by IVIS imaging seven days post-implantation or by endpoint omental weight compared to tumor free omentum, were excluded. Further outliers were determined using ROUT method in GraphPad PRISM.
Replication	Experiments were repeated in multiple cell lines with at least 2 replicates, and all experiments were reproducible.
Randomization	All in vivo experiments and tests were randomly assigned, but no randomization was performed for cell culture experiments.
Blinding	Immunofluorescence analysis was blinded when possible. Investigators were not blinded during the other experiments.

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 obtained from the indicated suppliers: Primary antibodies: rabbit anti-Lamin B1 (#ab16048, RRID AB_443298, WB 1:1000) from Abcam, rabbit anti-NDUFA5 (#16640-1-AP, RRID AB_2251270, WB 1:1000), rabbit anti-SREBF1 (#14088-1-AP, RRID AB_2255217, IF 1:100, ChIP 1 ug) from Proteintech, rabbit anti-SREBP1 (#ab28481, RRID AB_778069, IF 1:150) from Abcam, rabbit anti-HMGCR (#PA5-37367, RRID AB_2554032, WB 1:1000) from Invitrogen, rabbit anti-HMGCS1 (#17643-1-AP, RRID AB_2248359, WB 1:1000) from Proteintech, rabbit anti-MVK (#12228-1-AP, RRID AB_2147565, WB 1:1000) from Proteintech, rabbit anti-AMPKa (#2532, RRID AB_330331, WB 1:1000) from Cell Signaling Technology, rabbit anti-phosphoAMPKa (Thr172) (40H9) (#2535, WB 1:1000) from Cell Signaling Technology, and rabbit anti-DYDDDDK Tag (D6W5B) (#14793, RRID AB_2572291, WB 1:500, rat anti-BrdU (#ab6326, RRID: AB_305426, Clone BU1/75 (ICR1), IF 1:500) from Abcam

Validation

All antibodies used in this study were purchased from commercial vendors who had validated specificity in human cells/mouse tissues for the specific assays (Western Blot, Chromatin Immunoprecipitation and Immunofluorescence). NDUFA5 antibody was validated by knockdown studies.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

Human ovarian cancer Ovar8 cells were a gift from Dr. Benjamin Bitler (University of Colorado). KPCA.B cells were a kind gift from Dr. Robert Weinberg (Whitehead Institute of Biomedical Research, Cambridge, MA). YUMM5.2 cells were obtained from ATCC (ATCC, cat# CRL-3367, RRID: CVCL_JK43). Capan-1 cells were obtained from ATCC (ATCC cat# HTB-79). Normal diploid IMR90 human fibroblasts were obtained from ATCC (ATCC, cat# CCL-186). HEK293FT cells were obtained from Thermo Fisher (R70007).

Authentication

Ovar8 cells were STR fingerprinted. The other cell lines were not authenticated.

Mycoplasma contamination

All the cells were tested monthly for Mycoplasma and cells used in this study were mycoplasma negative.

Commonly misidentified lines
(See [ICLAC](#) register)

No commonly misidentified cell lines were used in this 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

Eight-week-old female mice were purchased from Jackson Laboratories (C57Bl6/J mice: cat#000664). All mice were maintained in a HEPA-filtered ventilated rack system either at the Animal Facility of the Assembly Building of The Hillman Cancer Center at the University of Pittsburgh School of Medicine or the Animal Facility of The Wistar Institute. Mice were housed up to 5 mice per cage and in a 12-hour light/dark cycle. All experiments with animals were performed in accordance with institutional guidelines approved by the Institutional Animal Care and Use Committee (IACUC) at either the University of Pittsburgh School of Medicine or the Wistar Institute.

Wild animals

No wild animals were used in the study.

Reporting on sex

Only female mice were used in this study.

Field-collected samples

No field collected samples were used in the study.

Ethics oversight

All experiments with animals were performed in accordance with institutional guidelines approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pittsburgh School of Medicine or The Wistar Institute.

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Plants

Seed stocks

No plants were used in the study.

Novel plant genotypes

No plants were used in the study.

Authentication

No plants were used in the study.