

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** Mass spectrometry was performed with AB QTRAP 5500 (Applied Biosystems SCIEX); Thermo Scientific (Bremen, Germany) Q-Exactive HF-X hybrid quadrupole orbitrap high resolution mass spectrometer (HRMS), Seahorse XFe96 Analyzer (Seahorse BioScience), SpectraMax iD3 Multimode Plate Detection Platform (Molecular Devices, LLC) for absorbance, luminescence and fluorescence assay, Perkin-Elmer Enspire Multimode plate reader, Celigo image cytometer-4 Channel (Nexcelom Bioscience, UK), Primovert ZEISS microscope, LUNA-II™ Automated Cell Counter, Zeiss LSM 780 Laser Scanning Microscope, NanoZoomer 2.0-HT, slide scanner Zeiss Axioscan.Z1, BioRad CFX384 Touch Real-Time PCR Detection System, Benchmark Bead-Blaster Homogenizer (product code: D2400-R) from Marshall scientific, TraceFinder 5.1 (ThermoScientific). Images of mice for Figure 2f were obtained from Servier Medical Art (<https://smart.servier.com>) under a Creative Commons Attribution 3.0 Unported License (<https://creativecommons.org/licenses/by/3.0/>). The mice in the images in Figures 6a, 6h were obtained from Biorender (<https://biorender.com/>). The image in Figure 4a was assembled in Powerpoint, Microsoft 365®.
- Data analysis** Graph Pad Prism™ 8.4.3, Wave software (Agilent Technologies, Version 2.6.1 for Windows), TraceFinder 5.1 (ThermoFisher Scientific), MultiQuant 2.2.2 (Agilent Technologies, CA, version 2.1.1742.0), Adobe Fireworks 8®, Microsoft Excel 365®, Microsoft Powerpoint 365®, Celigo 5.1.0, ImageJ Java 1.8.0_172, ZEN 3.3.890000 (Blue ed) software, SoftMax Pro7 (version 7.1.0), MetaboAnalyst5.0 (www.metaboanalyst.ca), NDP.view 2 software (U12388-0), Bio-Rad CFX Manager version 3.1.1517.0823.

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](#)

Source data are provided with this paper. The data supporting our findings are available in the article, the supplementary files, or from the corresponding authors (B.D.M., I. B-S., or G.H.) upon request.

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	To ensure an adequate power of the statistical testing, we perform special analyses prior to running the experiments, to calculate how large an n is required. The null hypothesis (H0) = no difference between the untreated versus treated, while the alternative hypothesis (H1) = outcome where there is a difference. The power calculation is: power = P (reject Ho H1 is true) = P (accept H1 H1 is true). We estimate that the probability to obtain a difference between the groups is ~95% and that there is only 5% H0 is true. $n = \log\beta/\log p$, where β is the probability of committing a Type II error (0.05) and p is the proportion of the animals in the group that are not affected by the treatments. To obtain at least 50% of mice altered by the treatment in one group, we will need: $n = \log(0.05)/\log(0.5) = 4.32$. Five animals were included in each experiment.
Data exclusions	Data were not excluded.
Replication	Each experiment in the figures was independently repeated successfully more than two-three times and similar results were obtained. Two biologically complementary in vivo metastasis experiments were performed.
Randomization	The assignment of the experimental conditions of the mice was randomized. The running of samples for mass spectrometry was also randomized. Microscopic images were taken randomly. Randomization was not included for experiments involving Western blot, pPCR, proliferation or migration assays. Imbalance of covariates is not relevant to these experiments. Appropriate statistical analysis was consistently performed to ensure significance or non-significance of the data with or without randomization.
Blinding	The in vivo experiment was blinded, as one person prepared and assigned numbers to mice and samples, and the other person performed injection without prior knowledge of the sample identity. Investigators were not blinded for in vitro experiments, such as western blotting, qPCRs, proliferation, or cell migration assays, but all the data was collected and analyzed without bias. The in vitro experiments showed results that could not be influenced by conscious or unconscious selection of statistical tests and reporting.

Behavioural & social sciences study design

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

Study description	N/A
Research sample	N/A
Sampling strategy	N/A
Data collection	N/A
Timing	N/A
Data exclusions	N/A
Non-participation	N/A

Randomization

N/A

Ecological, evolutionary & environmental sciences study design

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

Study description

N/A

Research sample

N/A

Sampling strategy

N/A

Data collection

N/A

Timing and spatial scale

N/A

Data exclusions

N/A

Reproducibility

N/A

Randomization

N/A

Blinding

N/A

Did the study involve field work? Yes No

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 | Involvement | Included |
|-------------------------------------|-------------------------------------|-------------------------------|
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | Antibodies |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | Eukaryotic cell lines |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Palaeontology and archaeology |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | Animals and other organisms |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Human research participants |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Clinical data |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Dual use research of concern |

Methods

- | n/a | Involvement | Included |
|-------------------------------------|--------------------------|------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | ChIP-seq |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Flow cytometry |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | MRI-based neuroimaging |

Antibodies

Antibodies used

The following antibodies have been used in this study:

Alexa Fluor® 488, Cat. #8878, Cell Signaling Technology, 1:200, IF

Anti-S100, Cat. #Z0311, polyclonal, LOT:00060051, Dako, 1:500, IF

GART, Cat. #13659-1-AP, Proteintech, 1:1000, WB

p-S6 Kinase -T389, Cat. #9234, Lot:12, Cell Signaling Technology, 1:1000, WB

S6 Kinase, CST #2708, Lot:8, Cell Signaling Technology, 1:1000, WB

DHODH, Cat. #14877-1-AP, Proteintech, 1:1000, WB

APRT, Cat. #ab196558, Abcam, 1:1000, WB

HPRT, Cat. #sc-393901, Santa Cruz, 1:1000, WB

PKM1, Cat. #SAB4200094, LOT:117M4754V, Sigma, 1:1000, WB

PKM2, Cat. #4053S, LOT:6, Cell Signaling, 1:1000, WB

PHGDH, Cat. #14719-1-AP, Proteintech, 1:1000, WB

PSAT1, Cat. #10501-1-AP, Proteintech, 1:1000, WB

MTHFD1L, Cat. #16113-1-AP, Proteintech, 1:1000, WB

β -actin, Cat. #A5316, Sigma, 1:5000, WB

HRP-conjugated anti-mouse, Cat. #7076, Cell Signaling Technology, secondary antibody, 1:5000, WB

Anti-rabbit, Cat. #7074, Cell Signaling Technology, secondary antibody, 1:5000, WB

Validation

All antibodies were obtained from commercial vendors and the validity can be retrieved from the manufacturer's website.

We further made sure to identify the correct molecular weight for each of the antibodies.

Alexa Fluor® 488 (Cat. #8878, Cell signaling technology). This antibody can stain the cytoskeleton through the binding of phalloidin to F-actin. <https://www.cellsignal.com/products/buffers-dyes/alexa-fluor-488-phalloidin/8878?Ns=product.sortId%7C0&N=102284+4294956287&fromPage=plp>

Anti-S100 (Cat. #Z0311, Dako). [https://www.agilent.com/en/product/immunohistochemistry/antibodies-controls/primary-antibodies/s100-\(dakoomnis\)-76198](https://www.agilent.com/en/product/immunohistochemistry/antibodies-controls/primary-antibodies/s100-(dakoomnis)-76198)

GART (Cat. #13659-1-AP, Proteintech). <https://www.ptglab.com/products/GART-Antibody-13659-1-AP.html>

p-S6 Kinase -T389 (Cat. #9234, Cell Signaling Technology). <https://www.cellsignal.com/products/primary-antibodies/phospho-p70-s6-kinase-thr389-108d2-rabbit-mab/9234>

S6 Kinase (CST #2708, Cell Signaling Technology). <https://www.cellsignal.com/products/primary-antibodies/p70-s6-kinase-49d7-rabbit-mab/2708>

DHODH (Cat. #14877-1-AP, Proteintech). <https://www.ptglab.com/products/DHODH-Antibody-14877-1-AP.html>

APRT (Cat. #ab196558, Abcam). <https://www.abcam.com/aprt-antibody-ab196558.html>

HPRT (Cat. #sc-393901, Santa Cruz). <https://www.scbt.com/p/hprt-antibody-b-11?requestFrom=search>

PKM1 (Cat. #SAB4200094, Sigma). https://www.sigmaaldrich.com/US/en/product/sigma/sab4300663?gclid=Cj0KCQiAmpyRBhC-ARIsABs2EAqLC76TPAWEqHTEYF8tdP07cMCbh5g2qXu5LXlw94h6dRdTPV6ZoP8aAtGtEALw_wcB

PKM2 (Cat. #4053S, Cell Signaling). <https://www.cellsignal.com/products/primary-antibodies/pkm2-d78a4-xp-rabbit-mab/4053>

PHGDH (Cat. #14719-1-AP, Proteintech). <https://www.ptglab.com/products/PHGDH-Antibody-14719-1-AP.html>

PSAT1 (Cat. #10501-1-AP, Proteintech). <https://www.ptglab.com/products/PSAT1-Antibody-10501-1-AP.html>

MTHFD1L (Cat. #16113-1-AP, Proteintech). <https://www.ptglab.com/products/MTHFD1L-Antibody-16113-1-AP.html>

β -actin (Cat. #A5316, Sigma). https://www.sigmaaldrich.com/US/en/product/sigma/a5316?gclid=Cj0KCQiAmpyRBhC-ARIsABs2EAqL7v2fSBrs90R0Mt7zAAXkzULtD8SvAXo-C_hVKyKnnHpRbpb0-TIaAk77EALw_wcB

HRP-conjugated anti-mouse (Cat. #7076, Cell Signaling Technology). <https://www.cellsignal.com/products/secondary-antibodies/anti-mouse-igg-hrp-linked-antibody/7076>

Anti-rabbit, Cat. #7074, Cell Signaling Technology). <https://www.cellsignal.com/products/secondary-antibodies/anti-rabbit-igg-hrp-linked-antibody/7074>

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)

HeLa, SK-MEL-28, A375, B16, CAL-51, A549, CCL-1, CCL-1.4 and LNCaP were from ATCC.

Authentication

Common cancer cells were authenticated via ATCC via short-tandem repeat profiling.

Mycoplasma contamination

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

Palaeontology and Archaeology

Specimen provenance

Specimen deposition

Dating methods

Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight

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

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

Wild animals

Field-collected samples

Ethics oversight

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

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics

Recruitment

Ethics oversight

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration

Study protocol

Data collection

Outcomes

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
<input checked="" type="checkbox"/>	<input type="checkbox"/> Public health
<input checked="" type="checkbox"/>	<input type="checkbox"/> National security
<input checked="" type="checkbox"/>	<input type="checkbox"/> Crops and/or livestock
<input checked="" type="checkbox"/>	<input type="checkbox"/> Ecosystems
<input checked="" type="checkbox"/>	<input type="checkbox"/> Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
<input checked="" type="checkbox"/>	<input type="checkbox"/> Demonstrate how to render a vaccine ineffective
<input checked="" type="checkbox"/>	<input type="checkbox"/> Confer resistance to therapeutically useful antibiotics or antiviral agents
<input checked="" type="checkbox"/>	<input type="checkbox"/> Enhance the virulence of a pathogen or render a nonpathogen virulent
<input checked="" type="checkbox"/>	<input type="checkbox"/> Increase transmissibility of a pathogen
<input checked="" type="checkbox"/>	<input type="checkbox"/> Alter the host range of a pathogen
<input checked="" type="checkbox"/>	<input type="checkbox"/> Enable evasion of diagnostic/detection modalities
<input checked="" type="checkbox"/>	<input type="checkbox"/> Enable the weaponization of a biological agent or toxin
<input checked="" type="checkbox"/>	<input type="checkbox"/> Any other potentially harmful combination of experiments and agents

ChIP-seq

Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links <i>May remain private before publication.</i>	N/A
Files in database submission	N/A
Genome browser session (e.g. UCSC)	N/A

Methodology

Replicates	N/A
Sequencing depth	N/A
Antibodies	N/A
Peak calling parameters	N/A
Data quality	N/A
Software	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
- Instrument
- Software
- Cell population abundance
- Gating strategy
- Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

- Design type
- Design specifications
- Behavioral performance measures

Acquisition

- Imaging type(s)
- Field strength
- Sequence & imaging parameters
- Area of acquisition
- Diffusion MRI Used Not used

Preprocessing

- Preprocessing software
- Normalization
- Normalization template
- Noise and artifact removal
- Volume censoring

Statistical modeling & inference

- Model type and settings
- Effect(s) tested
- Specify type of analysis: Whole brain ROI-based Both

Statistic type for inference
(See [Eklund et al. 2016](#))

N/A

Correction

N/A

Models & analysis

- | | |
|-------------------------------------|---|
| n/a | Involvement in the study |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Functional and/or effective connectivity |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Graph analysis |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Multivariate modeling or predictive analysis |