

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	MALDI-TOF spectrometry data was collected on a Shimadzu Benchtop Linear MALDI-8020 with Shimadzu MALDI Solutions (Version 2.6.0). HPLC data was collected using LabSolutions Realtime Analysis version 5.81 SP1 software on a Shimadzu system consisting of two LC-20AP pumps and an SPD-20AV photodiode array detector. MS data was collected using Bruker Daltonics Hystar version 3.2 SR4 software on a Bruker Daltonics microOTOF-QIII spectrometer by electron spray ionization time-of-flight (ESI-TOF-MS). NMR spectroscopy was collected using Bruker Topspin version 4.1.1 on a Bruker NMR 400 MHz instrument. Cell fluorescence microscopy was collected using BZ-X700 Viewer on a Keyence BZ-X710 all-in-one fluorescence microscope. Cell confocal microscopy images were collected using an Olympus Fluoview FV3000RS confocal laser scanning microscope. In vivo imaging was collected using Clairvivo OPT measurement/viewer (Version 2.6.0.0) on a Shimadzu Clairvivo OPT kinetics fluorescence imager. All software packages and code used are commercially or freely available.
Data analysis	MALDI-TOF spectrometry data was analyzed by Shimadzu MALDI Solutions (Version 2.6.0). HPLC data was analyzed on LabSolutions Postrun Analysis (version 5.81 SP1). MS data was analyzed on Bruker Daltonics Compass DataAnalysis version 4.2 (Build 383.1). NMR spectroscopy was analyzed using MestReNova (Version 14.21). Cell fluorescence microscopy was analyzed on a software BZ-X Analyzer (Version 1.4.0.1). TAMRA fluorescence intensity/per cell was analyzed on a free software ImageJ (Version 1.54). Cell confocal microscopy was analyzed on a software FV31S-SW (Version 2.4.1). In vivo imaging was analyzed on a Clairvivo OPT measurement/viewer (Version 2.6.0.0). MALDI-TOF-MS data in Figure 4b-c were plotted on a software Microsoft Excel (Version 16.87) according to the raw data. Graphs in Figures 5e, 6e, 7c-e, 8c-e and Kinetic data in Supplementary Figure 10 were plotted on a software Graphpad prism (Version 8.0.2) according to the raw data. All software packages and code used are commercially or freely available.

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 on synthetic compounds, cell-based experiments, and animals generated in this study are provided in the Supplementary Information/Source Data file and can also be obtained from the corresponding author upon request. The source data underlying Figures. 4b–c; 5–6; 7b–c, and 8, Supplementary Figures. 6–10, and 27–53 are provided as a Source Data file. 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

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used.

Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected.

Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Reporting on race, ethnicity, or other socially relevant groupings

Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).

Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)

Please provide details about how you controlled for confounding variables in your analyses.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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

In both in cellulo and in vivo experiments, we have followed widely accepted standards of scientific practice. We used 3 biological replicates (cell-based experiments) or 5 animals per group (animal-based experiments) to calculate the means and standard deviations.

Data exclusions

No data were excluded from the analysis, unless an obvious error/spillage/fault was encountered during the experiment.

Replication

All experiments were replicated at least three times (three independent cell or five independent animals). Exact number of samples and animals are shown in figures legend. Significance p values were determined by two-way ANOVA.

Randomization

For the animal experiment in Fig. 7, mice were randomly divided into three groups. For the animal experiment in Fig. 8, tumor-bearing mice were randomly divided into three groups.

Blinding

There was no blinding. For data collection, we have followed standard laboratory procedures of randomization. All samples for comparison

were collected and analyzed under the same conditions.

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

Eukaryotic cell lines

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

Cell line source(s)	HepG2 cell line (Human hepatocellular carcinoma cells) was obtained from RIKEN Cell Bank (RCB1648). SW620 cell line (human colon cancer cells) was obtained from American Type Culture Collection (ATCC) (CCL-227).
Authentication	HepG2 cell line obtained from RIKEN Cell Bank, where Quality Control includes STR analysis. SW620 cell line obtained from ATCC, where Quality Control includes STR analysis.
Mycoplasma contamination	HepG2 cell line obtained from RIKEN Cell Bank, where Quality Control includes tests for Mycoplasma infection and they were negative for mycoplasma contamination. SW620 cell line obtained from ATCC, where Quality Control includes tests for Mycoplasma infection and they were negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	HepG2 cell line obtained from RIKEN Cell Bank, where Quality Control includes tests for misidentification via Short Tandem Repeat polymorphism analysis and no commonly misidentified cell lines were used. SW620 cell line obtained from ATCC, where Quality Control includes implementing STR profiling as part of ATCC routine authentication procedures and no commonly misidentified cell lines were 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 or 10 week-old female nude mice BLAB/cA ₁ cl-nu/nu were housed in a facility with controlled temperature (24–26 °C), controlled humidity (30–60%), aeration, ad libitum access to food and water, and a regular 12-h light-dark cycle.
Wild animals	Study did not involved wild animals
Reporting on sex	Study did not involved sex.
Field-collected samples	Study did not involve samples collected from the field.
Ethics oversight	All animals experiments were carried out with approval by RIKEN's Animal Ethics Committee (W2019-2-049)

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

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.