nature portfolio

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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	Western Blot imaging: Azure 300 and 400 (Azure Biosystems); Flow cytometry: LSRForetessa Becton Dickinson & Company (BD); Cell sorting: FACSAria 3 Laser (BD); qPCR: QuantStudio 6 Pro Real-Time PCR System (Applied Biosystems); Single-cell RNA sequencing: NovaSeq (illumina)
Data analysis	Flow cytometry data:FlowJo v10.10 (BD); Statistical data: Prism 8 or 9 software (GraphPad) or SAS version 9.4 (SAS Institute Inc); Western blotting quantification: Image J; Single-cell RNA sequencing: 10X Genomics Chromium system (illumina), R package Seurat (version 4), Seurat 4.1.1. Data analyses and significances of the results for Single-cell RNA sequencing are shown in details in figure legends or method; Bulk tumor RNA sequencing : GSEA using MSigDB Hallmark (NES scores).

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

Data availability

The raw and processed single-cell/bulk RNA sequence data have been deposited and are available through the Gene Expression Omnibus (GEO) database under accession code GSE253094. The publicly released data used in this study are available in the GEO database under accession code GSE129392.

To review GEO accession GSE253094: Go to https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE253094 Enter token izgnimeijdcvhwr into the box.

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

Life sciences study design

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

Sample size	The 'n' numbers presented in our study represent individual biological replicates, and these sample sizes are always indicated either in the figure legends or the Methods section.
Data exclusions	In our analyses, no data were excluded, except for the following exceptions: In the TCGA analysis, samples without survival data were excluded. For onset and growth rate calculations, mice not developing tumors were excluded. Mice with severely ulcerated tumours and deep tumours were excluded for growth rate calculations due to inaccuracy of size measurements.
Replication	Experiments were performed at least three times independently and successfully reproduced. Reproducibility of the experiments and significances of the results are shown in details in figure legends or the Methods section.
Randomization	Randomization was not applicable to this study.
Blinding	Histological studies were blinded to pathologist (A.H.G).

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[ ]	[x] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used	Information regarding the antibodies used in the experiments, including the target antigen, fluorophore, clone, vendor, catalog number, and working dilutions, is listed in the Supplemental Table 4.
Validation	The antibodies we utilized are all commercially available. Staining patterns observed in our experiments were consistent with the manufacturer's product information. The validation data can be found on the manufacturer's website; using the information provided in the Key Resource Table listing the antibodies used, one can easily locate the necessary details for validation data.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The sources of all cell lines are described in the Methods section.
Authentication	Human cell line authentication is described in the Methods section.
Mycoplasma contamination	No contamination was found in the samples we randomly tested.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified 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	Species: Mus musculus, 2 strains on mixed C57BL/6, FVB, and 129 backgrounds. Mice used in this study ranged in ages less than 4 months old.
Wild animals	This study did not involve wild animals.
Reporting on sex	Male and female animals were used in this study and distributed equally. Animals were sexed at 17-21 days old by visual inspection. Sex-based analysis was performed (Supplementary Figure 1c)
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	Animal studies were performed in accordance with a protocol approved by the University of Utah Institutional Animal Care and Use Committee.

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 ICMJEguidelines for publication of clinical research and a completedCONSORT checklist must be included with all submissions.

Clinical trial registration	*Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.*
Study protocol	*Note where the full trial protocol can be accessed OR if not available, explain why.*
Data collection	*Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.*
Outcomes	*Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.*

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, mosiacism, off-target gene editing) were examined.*

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	See details in the Methods section.
Instrument	LSRForetessa Becton Dickinson & Company (BD)
Software	FlowJo v10.10 (BD)
Cell population abundance	The number of cells analyzed per sample ranged from 10,000 to 100,000.
Gating strategy	Please refer to Supplementary Figures 3A and 7 and Gating Strategy for Flow Cytometry (supplemental information).

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.