nature portfolio

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Last updated by author(s): Jun 23, 2024

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	We have not used any coding in this work. All statistical analysis were done using GraphPad Prism software or Microsoft Excel. Flow Cytometry data was collected using FACSDiva software, all immunofluorescence images were captured and processed by Zen software.
Data analysis	We have not used any coding in this work. All statistical analysis were done using GraphPad Prism software or Microsoft Excel. Flow Cytometry data was collected using FlowJo software, all immunofluorescence images were analyzed using Fiji 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

The full list of peptides identified by untargeted proteomics analysis of HT1080 p53KO cells in five different conditions (untreated, treated with DMSO for 24h, treated with MEL23 for 24h, transfected with siRNA control for 24h, transfected with siRNA against Mdm2 #1 for 24h, and transfected with siRNA against Mdm2 #2

for 24h), for which data is shown in Fig. 4A and Supplementary Fig. 4, was deposited at in the ProteomeXchange Consortium (http://proteomecentral.proteomexchange.org) via the jPOST partner repository (http://jpostdb.org) with the dataset identifier PXD033789. Files containing full analysis with fold changes and statistical parameters for the proteomics analysis can be found as an Excel file in the supplemental material.
All statistical analysis performed and exact p values as well as uncropped and unprocessed scans of all blots in Figures can be found in the Source Data file.

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	Our study does not have any data collected from human subjects.
Reporting on race, ethnicity, or other socially relevant groupings	Our study does not have any data collected from human subjects.
Population characteristics	Our study does not have any data collected from human subjects.
Recruitment	Our study does not have any data collected from human subjects.
Ethics oversight	Our study does not have any data collected from human subjects.

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	All experiments using human cancer cell lines were performed with minimum sample size of 3 independent biological replicates, while in vivo experiments had a minimum sample size of 4 mice per condition.
Data exclusions	There was no data exclusion in the analysis performed in this work.
Replication	All experiments that are included in this work were replicated at least 3 times to ensure reproducibility of the measurements.
Randomization	For in vivo experiments, once mice were received and before injections they were randomly distributed in different cages for different experimental groups. We used equal ratio of males and females in each experimental group.
Blinding	For in vivo experiments, after the lungs were collected, imaging acquisition and quantification of lung metastasis were done in a blind manner.

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

Primary and secondary antibodies used for immunoblotting were at 1:1,000 and 1:2,000 dilution, respectively. Antibodies anti-Mdm2 (cat.#86934), anti-N-cadherin (cat.#13116S), anti-tensin-2 (cat.#11990), anti-talin-1 (cat.#4021), anti-vinculin (cat.#4650), anti-paxilin (cat.#12065), anti-alpha-actinin (cat.#6487), anti-focal adhesion kinase (FAK) (cat.#3285) , anti-integrin beta1 (cat#9699), anti-cofilin-1 (cat.#5175T) and anti-p-cofilin-1 (Ser3) (cat.#3313T) were purchased from Cell Signaling Technology. Anti-β-actin (A2066 and A2228), anti-fibronectin (cat.#F3648), anti-mouse peroxidase (cat.#A4416) and anti-rabbit peroxidase (cat.#A6154) were purchased from Sigma-Aldrich. Anti-E-cadherin (cat.#sc-8426) and anti-RhoA (cat.#sc-418) were purchased from Santa Cruz Biotechnology. Anti-p-FAK(Tyr397) (cat.#05-1140) was purchased from Millipore. Anti-laminin (cat.#AHP2491) was purchased from Bio-Rad. Anti-α-tubulin (cat.#AA4.3) was purchased from DSHB. Anti-sprouty4 (cat.#A04343-2), anti-integrin alpha-3 (cat#A02902) and anti-integrin alpha-2 (cat#A01933-2) were purchased from Boster Biological Technology. Anti-vinculin AlexaFluor647 (cat.#ab196579) and anti-Ki67 (cat.#ab16667) were purchased from Abcam. Phalloidin AlexaFluor Plus 555 (cat.#A30106) was purchased from Thermo Fisher Scientific. Goat anti-rabbit IgG (H+L) biotinylated secondary antibody (cat.# BA-1000-1.5) was purchased from Vector Laboratories. FITC anti-CD51/61 (cat.#304403), PE anti-CD49e (cat.#328009), APC/Cyanine7 anti-human CD18 (cat.# 302133), APC anti-CD29 (cat.# 303007) and FITC anti-CD49b (cat.# 359305) were purchased from BioLegend. Anti-p53 DO-I and 1801 were purified from hybridomas produced in-house. Anti-MdmX mAb 8C6 was produced in Dr. Jiandong Chen's lab and kindly gifted to our group.

Validation

All commercial antibodies used in this work have been validated by the manufacturer. The anti-p53 DO-I and 1801 as well as the anti-MdmX antibodies have been previously validated in published articles, for instance doi: 10.1128/MCB.22.21.7562-7571.2002; 10.1038/sj.emboj.7601032; 10.1186/s12943-017-0626-7; 10.1128/mcb.25.15.6509-6520.2005.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

HT1080 cells were obtained from Dr. Brent Stockwell's lab which purchased the cell line from American Type Culture Collection(ATCC), the cells were then subjected to deletion of p53 using CRISPR technology. H1299 cells were obtained from ATCC.

Authentication

ATCC attests the authenticity of the cell lines.

Mycoplasma contamination

All cells lines were tested for mycoplasma contamination (Lookout Mycoplasma PCR detection kit, Sigma-Aldrich, cat#MP0035) and used only if showing a negative result.

Commonly misidentified lines
(See ICLAC register)

No cell lines used in this work are found in the ILAC register of misidentified lines.

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: mouse. Strain: athymic nude mice (Ncr background). All animal studies were approved by Institutional Animal Care and Use Committee at Columbia University, and all experiments were conducted in compliance with the NIH guidelines for animal research. To establish the lung metastasis model, an equal number of 5-week-old male and female athymic nude mice were purchased (NCr-Foxn1nu, n=19, Taconic). Mice were housed under controlled environmental conditions (22–24 °C, 45–60% humidity) in a 12-h dark–light cycle with ad libitum access to food and tap water. Mice were 7-weeks old in the beginning of the experiments.

Wild animals

No wild animals were involved in this study.

Reporting on sex

We used an equal number of males and females in every experimental group.

Field-collected samples

The study did not involved field-collected samples.

Ethics oversight

All animal studies were approved by the Columbia University Institutional Animal Care and Use Committee (IACUC).

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

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	Cells were detached from 6-well plates, washed and resuspended in PBS. Samples were subjected to flow cytometry analysis of cell size in solution by forward scatter.
Instrument	BD FACS Celesta, model #:660344.
Software	BD FACSDiva software was used to collect the data. FlowJo V10 software was used for data analysis.
Cell population abundance	The sample analyzed is a cell line with no subpopulations. Samples were not gated.
Gating strategy	The whole population was analyzed, there was no gating of samples.

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