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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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n/a	Confirmed
	$oxed{oxed}$ 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.
\boxtimes	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)
\boxtimes	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>
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes	\square Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
,	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection Commercial software was used to collect data. No custom software was used.

Data analysis Leica MM AF v1.7 and ImageJ64 v1.51 was used for confocal image processing. CorelDRAW v20.0.0.412 was used for western blot image processing. FlowJo v10.0 was used to analyse flow cytometry data. GraphPad Prism v7.0 was used to analyze the data.

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 <u>data availability statement</u>. 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 <u>policy</u>

All relevant data supporting the findings of this study are available within the paper and its Supplementary Information files. Additional data are available from the corresponding authors upon request.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

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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 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.

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 b	pelow that is the best fit for your research.	. If you	are not sure, read the appropriate sections before making your selection.	
X Life sciences	Behavioural & social sciences		Ecological, evolutionary & environmental sciences	

For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size

Sample size was determined based on preliminary experiments and previous published research studies to achieve statistical power.

Sample size is indicated in the figure legends for each experiment. A minimum sample size of n=3 was uesd. For analysing the therapeutic effects in vivo, complying with animal ethical guidelines, 5 mice from each group were housed based on preliminary data or previous reports.

Data exclusions

No data were excluded from the analyses.

Replication

Experiments were replicated independently for at least three times with similar results.

Randomization

For all in vitro experiments, cultured cells were randomly assigned to experimental groups. For the animal study, mice were randomly allocated to each group before treatment.

Blinding

The investigator was blinded to the group allocation during data collection and analysis.

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.

iviateriais & experimental systems	Methods		
n/a Involved in the study	n/a Involved in the study		
Antibodies	ChIP-seq		
Eukaryotic cell lines	Flow cytometry		
Palaeontology and archaeology	MRI-based neuroimaging		
Animals and other organisms			
Clinical data			
Dual use research of concern			

Antibodies

Antibodies used

- 1. Mouse anti-phospho-Histone H2A.X (Ser 139) (Cell Signaling, 80312S, WB 1:1000).
- 2. Rabbit anti-PARP-1 (Cell Signaling, 9532S, WB 1:1000).
- 3. Mouse anti-p53 (Cell Signalling, 2524S, WB 1:1000).
- 4. Rabbit anti-Bax (Cell Signalling, 5023S, WB 1:1000).
- 5. Rabbit anti-Bcl-2 (Cell Signalling, 4223S, WB 1:1000).
- 6. Rabbit anti-GAPDH (Cell Signaling, 5174S, WB 1:1000)
- 7. Rabbit anti-Cyclin B1 (Cell Signaling, 12231S, WB 1:1000)
- 8. Rabbit anti- Cyclin E1 (Cell Signaling, 20808S, WB 1:1000)
- 9. Rabbit anti-Vimentin (Cell Signaling, 5741S, WB 1:1000)
- 10. Rabbit anti-Snail (Cell Signaling, 3879S, WB 1:1000)
- 11. Rabbit anti-AIF (Cell Signaling, 5318S, WB 1:1000, IP 1:50)

Validation

- 1. Mouse anti-phospho-Histone H2A.X (Cell Signaling, 80312S, WB:1:1000) has been validated to be used for WB/IF and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/phospho-histone-h2a-x-ser139-d7t2v-mouse-mab/80312).
- 2. Rabbit anti-PARP-1 (Cell Signaling, 9532S, WB:1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/parp-46d11-rabbit-mab/9532?site-search-type=Products&N=4294956287&Ntt=9532s&fromPage=plp&requestid=119722).
- 3. Mouse anti-p53 (Cell Signalling, 2524S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/p53-1c12-mouse-mab/2524?site-searchtype=Products&N=4294956287&Ntt=2524s&fromPage=plp&_requestid=5179150)
- 4. Rabbit anti- Bax (Cell Signalling, 5023S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/bax-d2e11-rabbit-mab/5023?site-searchtype=Products&N=4294956287&Ntt=5023s&fromPage=plp&_requestid=5325536)
- 5. Rabbit anti-Bcl-2 (Cell Signalling, 4223S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/bcl-2-d55g8-rabbit-mab-human-specific/4223?site-search-type=Products&N=4294956287&Ntt=4223s&fromPage=plp& requestid=5326072)
- 6. Rabbit anti-GAPDH (Cell Signaling, 5174S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/gapdh-d16h11-xp-rabbit-mab/5174?site-searchtype=Products&N=4294956287&Ntt=5174s&fromPage=plp&_requestid=1149467)
- 7. Rabbit anti-Cyclin B1 (Cell Signaling, 12231S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/cyclin-b1-d5c10-xp-rabbit-mab/12231?site-searchtype=Products&N=4294956287&Ntt=12231s&fromPage=plp&_requestid=1149681)
- 8. Rabbit anti- Cyclin E1 (Cell Signaling, 20808S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/cyclin-e1-d7t3u-rabbit-mab/20808?site-search-type=Products&N=4294956287&Ntt=20808s&fromPage=plp&_requestid=1150398)
- 9. Rabbit anti-Vimentin (Cell Signaling, 5741S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/vimentin-d21h3-xp-rabbit-mab/5741?site-search-type=Products&N=4294956287&Ntt=5741s&fromPage=plp&_requestid=1150903)
- 10. Rabbit anti-Snail (Cell Signaling, 3879S, WB 1:1000) has been validated to be used for WB and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/snail-c15d3-rabbit-mab/3879?site-searchtype=Products&N=4294956287&Ntt=3879s&fromPage=plp&_requestid=1151296)
- 11. Rabbit anti-AIF (Cell Signaling, 5318S, WB 1:1000, IP 1:50) has been validated to be used for WB and IP and mentioned species reactivity with human. (https://www.cellsignal.cn/products/primary-antibodies/aif-d39d2-xp-rabbit-mab/5318?site-search-type=Products&N=4294956287&Ntt=5318s&fromPage=plp&_requestid=1152186)

Eukaryotic cell lines

Policy information about <u>cell lines and Sex and Gender in Research</u>

Cell line source(s) HeLa, MDA-MB-231, 4T1 cell lines were used and purchased from ATCC.

Authentication No further authentication was done after the cells were obtained from the vendors.

Mycoplasma contamination All cell lines were tested for mycoplasma contamination. No mycoplasma contamination was found.

Commonly misidentified lines (See <u>ICLAC</u> register)

No commonly misidentified cell lines were used.

Animals and other research organisms

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research, and <u>Sex and Gender in Research</u>

Laboratory animals

BALB/c nude mice (female, 6 weeks old) were purchased were obtained from Guangzhou Medical Laboratory Animal Center (China) and maintained under SPF conditions with an ambient temperature of 24±2°C, air humidity of 40-70% and a 12h dark/12h light

Wild animals

C57BL/6J mice (female, 6 weeks old) were purchased were obtained from Guangzhou Medical Laboratory Animal Center (China) and

maintained under SPF conditions with an ambient temperature of 24±2°C, air humidity of 40-70% and a 12h dark/12h light cycle.

Reporting on sex The study did not apply to only one sex.

Field-collected samples The study did not involve samples collected from the field.

Ethics oversight All animal experiment protocols were approved by the Institutional Animal Care and Use Committee of Shenzhen Institutes of Advanced Technologies, Chinese Academy of Sciences.

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

Flow Cytometry

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Confirm	that:

Plots

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	The sample preparation method was described in the Protocol.			
Instrument	Beckman Coulter			
Software	CytExpert v2.4 software was used to collect data. FlowJo v10.0 was used to analyse data.			
Cell population abundance	At least 10,000 cells were counted per condition.			
Gating strategy	In this study, initial cell populations were first gated on FSC-H/SSC-H. Singlet cells were usually gated using FSC-H and FSC-A.			
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Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.