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	Illumina NovaSeq 6000 was used for RNA sequencing; ACEA NovoCyte flow cytometer was used for flow cytometry; BioComp Auto Gradient Fractionator was used for polysome profiling.
Data analysis	Cutadapt (v3.7) was used to trim the 3' adaptors and low-quality bases; HISAT2 (v2.1.0) was used to map reads to the human genome; NovoExpress (v1.6.2) was used for analysis of flow cytometry data; DNBC4tools (v2.1.0) was used to process raw single-cell RNA data; Seura R package (v5.0) and DoubletFinder (v2.0.4) were used to perform single-cell downstream analysis; Graph Pad Prism 9 was used to perform data analysis and statistics.

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 datasets produced in this study are available in the following databases: Ribo-seq, and RNA-Seq data: Gene Expression Omnibus GSE310281 (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE310281).

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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	Sample sizes were determined from pilot data and variance estimates in prior studies, balancing statistical power with ethical/resource considerations. All key experiments used more than 3 independent biological replicates. Animal group sizes conformed to institutional ethics approvals. For sequencing experiments, sample numbers and read depths follow community standards and produced consistent effect sizes across replicates.
Data exclusions	No data were excluded from this study.
Replication	All key experiments were independently repeated at least three times with similar results, and representative data are shown in the figures.
Randomization	For cell culture experiments, all wells in each biological replicate were derived from the same batch of cells and randomly assigned to each treatment. In the mouse experiments, mice of the same sex were randomly assigned to cages to ensure uniformity.
Blinding	Investigators were blinded to allocation during experiments and outcome assessment.

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

anti-GAPDH (1:10000, AC002, Abclonal),
anti-beta-Actin (1:100000, AC026, Abclonal),
anti-alpha-tubulin (1:2000, A6830, Abclonal),
anti-Puromycin (1:1000, EQ0001, Kerafast),
anti-FLAG (1:1000, F1804, Sigma),
anti-RPL22L1 (1:1000, 40259, Cell Signaling),
anti-RPL22 (1:1000, 54055, Cell Signaling),
anti-gamma-H2AX (1:1000, 05-636, Upstate),
anti-DNA-PKcs (1:1000, 12311, Cell Signaling),
anti-Phospho-DNA-PKcs (1:1000, ab124918, Abcam),
anti-ATRX (1:1000, 10321, Cell Signaling),
anti-ATRX (1:1000, ab97508, Abcam).

Validation

anti-GAPDH (Human, Mouse, Rat; WB, IHC, IF, ChIP, ELISA), tested by the manufacturer;
anti-beta-Actin (Human, Mouse, Rat, Chicken, Zebrafish, Pig;WB, IF, FC, IP, IHC, ChIP), tested by the manufacturer;
anti-alpha-tubulin (Human, Mouse, Rat; WB, IF, IP), tested by the manufacturer;
anti-Puromycin (Species independent; WB, ELISA), tested by the manufacturer;
anti-FLAG (Species independent; WB, IP, IHC, IF), tested by the manufacturer;
anti-RPL22L1 (Human; WB), tested by the manufacturer;
anti-RPL22 (Human; WB), tested by the manufacturer;
anti-gamma-H2AX (Human;WB, IC, IF, ChIP), tested by the manufacturer;
anti-DNA-PKcs (Human; WB, IF, FC, IHC), tested by the manufacturer;
anti-Phospho-DNA-PKcs (Human; WB, IHC, IF, ELISA), tested by the manufacturer;
anti-ATRX (Human, Mouse, Rat, Mk; WB, IP, IHC), tested by the manufacturer;
anti-ATRX (Human, Mouse, Rat; WB, IF, IP, IHC), tested by the manufacturer.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

293T (ATCC, CRL-3216); HT29 (ATCC, HTB-38™); RKO(ATCC, CRL-2577).

Authentication

Cell lines were authenticated by DNA profiling assays (STR).

Mycoplasma contamination

Cell lines were confirmed negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell 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

Wild-type, BALB/c Nude, male, 6-8 weeks old. GemPharmatech.
Mice were maintained and bred in specific pathogen-free (SPF) conditions at the Animal Center of Zhejiang University, under a 12-hour light/dark cycle (lights on from 7:00 to 19:00), at an ambient temperature of 22 ± 2 °C and relative humidity of 50–60%, with food and water provided ad libitum.

Wild animals

No wild animals were used in this study.

Reporting on sex

Only male mice were used to ensure consistency and reduce variability associated with sex-specific hormonal influences.

Field-collected samples

No field-collected samples were used in this study.

Ethics oversight	All animal studies were performed in compliance with the Guide for the Care and Use of Laboratory Animals by the Medical Experimental Animal Care Commission of Zhejiang University. All animal studies used the protocol that has been approved by the Medical Experimental Animal Care Commission of Zhejiang University (ZJU20240214). According to the approved protocol, the maximal tumour size permitted was 15 mm in diameter. We confirm that this limit was not exceeded in any of the experiments described in this study.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	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	Cells were transfected with plasmids expressing GFP reporters. After 3 days, cells were collected, resuspended in 0.5 mL PBS, and analyzed by flow cytometry.
Instrument	Beckman Coulter, CytoFLEX LX flow cytometer
Software	NovoExpress (v1.6.2)
Cell population abundance	No sorting in this study.
Gating strategy	Initial gating of the cell population (FSC-A vs. FSC-H and PI-A vs. PI-H) was performed to exclude doublets and cell aggregates, ensuring that only single cells were included in the analysis. The same gating strategy was consistently applied across all samples analyzed simultaneously.

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