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	No software was used for data collection
Data analysis	distiller-nf, bwa mem v0.7.17, pairtools v0.3.0, cooler v0.9.2, HiCRep v0.2.6, cooltools v0.5.1, CoolBox v0.3.9, Bowtie2 v2.4.2, deeptools v3.5.1, bioframe v0.4.1, bedtools v2.30.0, Peakachu v2.2, R v4.1.2, ggplot2 v3.4.2, Stripenn v1.1.65.18, Coolpup v1.1.0

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 generated in this study can be found at NCBI GEO under accession number GSE246346. ChIP-seq data was obtained from publicly available datasets. A list of publicly available datasets used in this study is provided in Supplementary Data 1. The custom codes are available on Zenodo at https://zenodo.org/records/15084044?preview=1&token=eyJhbGciOiJIUzUxMiJ9.eyJpZCI6IjZiNmE2NjViLWI0NjctNGEzNC1iMTUyLTk4NDE1NGU2N2RjZSIsImRhdGEiOnt9LCJyYW5kb20iOiI2NDdjYTY3ZWFmZ

DhjYWUzOGE0MTdjZGNmN2U3NWM2NyJ9.3x4QIIzi4fUTkg7H140lwMCcWXoPslkr0iSmHm39_fOdT9knZawpSQ2fah5_f7Np35oEKRgsQQ7JblMx1roC7g

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	Not applicable
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable
Population characteristics	Not applicable
Recruitment	Not applicable
Ethics oversight	Not applicable

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 experiments were performed on at least two biological replicates.
Data exclusions	No data were excluded
Replication	Experimental findings reported in this study were reproduced in biological (hTERT-RPE1 datasets, mESC datasets) and technical(mESC H3K27me3 datasets) replicates. Reproducibility was confirmed via HiCRep.
Randomization	Randomization was not relevant to this study
Blinding	Blinding was not relevant to this study

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-H3K27me3: Cell Signaling Technology #9733S; Anti-H3K4me3: Cell Signaling Technology #9751S
Validation	All antibodies used are validated by manufacturer.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Mouse embryonic stem cells (mESC, E14JU cell line with a 129/Ola background, male); Primary retinal epithelial hTERT-RPE1 cells were obtained from ATCC (#CRL-4000); Human HCT-116-RAD21-mAID-mClover cells were previously generated and validated by Dr. Masato Kanemaki.
Authentication	n/a
Mycoplasma contamination	The cells tested negative for Mycoplasma
Commonly misidentified lines (See ICLAC register)	n/a

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	ChIP-seq data was obtained from publicly available datasets. A list of publicly available datasets used in this study is provided in Supplementary Data 1.
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	Narrow histone modification peaks (e.g., H3K4me3) were identified using MACS2 with a false discovery rate (FDR) cutoff of 0.01, using the corresponding input as control and an effective human genome size of 3.0×10^9 bp. Broad peaks (e.g., H3K27me3) were called using MACS3 in broad mode with a broad FDR cutoff of 0.1, a fixed fragment size of 200 bp, and the corresponding input as control, also using an effective genome size of 3.0×10^9 bp.
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	MACS2 v2.1.0, MACS3 v3.0.0b2, Bowtie2 v2.4.2, deeptools v3.5.1, bedtools v2.31.0, Samtools v1.17