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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	Bio-Rad image lab ChemiDoc XRS+ system for western blot. Zeiss-LSM880 confocal microscopy for immunofluorescence data collection. BD FACS Aria-TM and Agilent NovoCyte Quanteon for flow cytometry analysis. Applied Biosystems OptiFlex™ with white LED light Thermofisher for RT-qPCR. RNA-Seq, ATAC-Seq, ChIP-Seq and HiC data were collected by Illumina NovaSeq. The electronic imaging data were collected using Philips CM100 Transmission Electron Microscope with Olympus SIS Tengra CCD Camera (2.3k x 2.3k pixel).
Data analysis	GraphPad Prism 9 were used for statistical analyses. FlowJo 10.6 was used for FACS data analysis. ImageJ software was used for quantitative analysis in SA-β-gal staining and immunofluorescence staining assays. The details of bioinformatic analysis were described in the methods part, associated softwares include: Trim Galore v 0.6.7 Bowtie2 v2.2.5 STAR_v2.5.4b SAMtools v 1.9 BEDTools v2.29.1 macs2 v2.1.2 ngsplot deepTools v3.1.1 HTSeq-count v0.9.1 edgeR v3.246.3 HiC-Pro v2.11.1 Juicebox v1.11.08 CscoreTool

TopDom v0.0.2
diffHiC v1.22.0
GENOVA v0.9
HICExplorer v3.5.3
cLoops2 v0.93
ggplot2
DAVID 6.8

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 high-throughput sequencing data,including RNA-Seq, ATAC-Seq, ChIP-Seq and HiC-Seq data , were deposited to a public data repository (GEO, accession number GSE193694).

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	Skin tissues were collected from a 3-year-old male MAD patient and a 5-year-old male HGPS patient.
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable.
Population characteristics	Not applicable.
Recruitment	MAD and HGPS patient were recruited during annual physical examination.
Ethics oversight	Informed consent were given by the precipitants or their guardians and under the guidance of ethical regulations in Dongguan Eighth People's Hospital, Dongguan, China.We have also obtained informed consent from all participants or their guardians for the publication of information, including clinical information, that may identify them.

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	No sample-size calculation was performed, and the sample-size was determined based on the availability of the patients.
Data exclusions	No data was excluded from the analysis.
Replication	Two biological replicates of MSCs were performed for ChIP-seq, ATAC-seq, RNA-seq and HiC, and for the functional experiment section, at least three times were performed. The number of replicates are indicated in figure legends.
Randomization	Not applicable.
Blinding	Blinding is not relevant to this study because no clinical data were involved or reported.

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

Antibody Species Vendor Catalog Number WB dilution IF dilution ChIP
HP1 alpha Rb abcam ab109028 1 3000 1 250 N/A
FOXO3a Ms Santa Cruz sc-166212 1 1500 N/A N/A
HADC2 Rb abcam ab12169 1 2000 N/A N/A
Lamin A/C Ms Santa Cruz sc-376248 N/A 1 100 1 100
LMNB2 Rb Beyotime AF0219 1 2000 1 200 N/A
Lamin B1 Rb Beyotime AF1408 1 1500 1 50 N/A
Lamin B1 Rb Proteintech 12987-1-AP 1/2000 1 50 N/A
Lamin A/C Rb Santa Cruz sc-20681 1 3000 N/A N/A
Lamin A/C Rb Proteintech 10298-1-AP 1 500 - 1 1000 1 50 - 1 100 N/A
Nanog Ms Santa Cruz sc-374001 N/A 1 50 N/A
Oct-3/4 Ms Santa Cruz sc-5279 N/A 1 50 N/A
SSEA-4 Ms Santa Cruz sc-21704 N/A 1 50 N/A
TRA-1-60 Ms Santa Cruz sc-21705 N/A 1 50 N/A
γH2A.X (Ser139) Ms Millipore 05-636 N/A 1?100 N/A
53BP1 Rb Santa Cruz sc-22760 N/A 1 50 N/A
Lamin B1 Rb CST 13435S N/A N/A 1 100
H3K9me3 Rb abcam ab176916 N/A 1 500 1 200
H3K27me3 Rb abcam ab6002 N/A 1 500 1 200
H3K27Ac Rb Active motif 39034 N/A N/A 1 200
CTCF Rb Active motif 61311 N/A N/A 1 200
H3K4me3 Rb abcam ab8580 N/A 1 200 N/A
H4K20me3 Rb abcam ab177190 N/A 1 200 N/A
Ku70 Rb abcam ab92450 1 2000 N/A N/A
WRN Rb abcam ab124673 1 1500 N/A N/A
Emerin Rb abcam ab156871 1 1500 1 200 N/A
TRF2 Rb abcam ab108997 N/A 1 200 N/A
LAP2 Rb abcam ab223768 1 1000 1 100 N/A
β-Actin Ms Sigma A5316 1?5000 N/A N/A
Ki67 Rb Millipore AB9260 N/A 1 200 N/A
eNOS Rb Proteintech 27120-1-AP N/A 1 50 N/A
VWF Rb Proteintech 27186-1-AP N/A 1 50 N/A
Nestin Ms Novus Biologicals NB300-266AF488 N/A 1 50 N/A
SOX2 Ms Novus Biologicals IC2018R N/A 1 50 N/A
PAX6 Ms Novus Biologicals NBP2-47915AF594 N/A 1 50 N/A
Calponin Rb Proteintech 13938-1-AP N/A 1 50 N/A
smooth muscle actin Rb Proteintech 14395-1-AP N/A 1 50 N/A
TAGLN/Transgelin Rb abcam ab14106 N/A 1 100 N/A

Validation

All the antibodies involved are commercially available and their applications are described in related instructions, and/or have been used in many published research articles.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

Primary fibroblasts were isolated from a male MAD patient, male HGPS and normal female control fibroblasts were described before and the details were in methods part. iPSCs cell lines were reprogrammed from the primary fibroblasts. NSCs, MSCs, VECs and SMCs were differentiated from iPSCs.

Authentication

The generated iPSCs were confirmed by pluripotency markers and teratoma formation assays. NSCs, VECs, SMCs and MSCs were confirmed by specific antibodies and the details were described in methods part.

Mycoplasma contamination	All the cell lines were tested free-of mycoplasma.
Commonly misidentified lines (See ICLAC register)	Not applicable.

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	Female NSG (NOD.Cg-Prkdcscidll2rgtm1Wjl/SzJ) mice aged between 6 to 8 weeks were used for teratoma formation assay.
Wild animals	No wild animals were used in this study.
Reporting on sex	Female mice used
Field-collected samples	No field-collected samples were used.
Ethics oversight	All mice experimental protocols were approved by the Committee on the Use of Live Animals in Teaching and Research (CULATR) of The University of Hong Kong.

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

Plants

Seed stocks	Not applicable.
Novel plant genotypes	Not applicable.
Authentication	Not applicable.

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.*	All datasets are available in GEO under the accession number GSE193694(https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE193694)
Files in database submission	Too many files to list here. Please check the GEO link.
Genome browser session (e.g. UCSC)	For each ChIP-seq sample, tracks of bigwig format and called peaks were uploaded to GEO as supplementary files.

Methodology

Replicates	All ChIP-seq or other profiling experiment were performed on two biological replicates. The biological replicates were two independent differentiation experiments.
Sequencing depth	The ChIP-seq were paired-end 150bp. The 40kb ICE normalized contact metrices of each chromosome were used to analyze relative contact probability (RCP) in Hi-C.
Antibodies	Antibody Species Vendor Catalog Number ChIP dilution Lamin A/C Ms Santa Cruz sc-376248 1 100 Lamin B1 Rb CST 13435S 1 100 H3K9me3 Rb abcam ab176916 1 200 H3K27me3 Rb abcam ab6002 1 200 H3K27Ac Rb Active motif 39034 1 200 CTCF Rb Active motif 61311 1 200 All these ChIP-related antibodies have been used in multiple published research articles.
Peak calling parameters	Peaks of ATAC-seq data and ChIP-seq data were called with MACS2[105] (version 2.1.2, parameters: '-g mm -q 0.05 -m 5 50' for

Peak calling parameters	ATAC-seq, H3K27ac and CTCF, '-g mm -q 0.05 -m 5 50 --broad' for H3K27me3, H3K9me3, Lamin A/C and Lamin B1) using input as control.
Data quality	Sufficient sequence depth were achieved according to ENCODE standards, each replicate has about 30 million usable fragments. Number of called peaks were compared to published data and it's quite comparable.
Software	Softwares include Trim Galore, Bowtie2, Samtools, bedtools, MACS2, trimLinker, HiC-Pro, which were stated earlier.

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	When MSCs reached 80-90% confluence, cells were washed with 1x PBS, dissected to single cells, and finally resuspended in 1.2ml of 1x PBS containing 3% FBS. Cells were aliquoted equally to six different tubes and stained with fluorescent antibodies for 30 min protected from light. Cells were washed twice with 1x PBS and resuspended with 150µl 1x PBS containing 3% FBS and transferred to Flow Cytometry Tubes for BD FACSAria SORP analysis. Data were analyzed with FlowJo 10.6.
Instrument	BD FACS Aria and Agilent NovoCyte Quanteon for flow cytometry analysis.
Software	FlowJo 10.6 was used for FACS data analysis.
Cell population abundance	The purity of iPSCs-derived MSCs were indicated after normalized to negative controls, and the majority of the cells were CD44, CD73, CD90 and CD105 positive.
Gating strategy	Negative controls were used to indicate the non-specific binding.

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