

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 Images of both live cell and Immunostaining were collected by Zeiss LSM980 or LSM710 microscope. ATP concentration was measured using ThermoFisher Varioskan LUX. RNA sequencing was used NovaSeq 6000 system. Young's modulus was measured using the Optics11 Life Chiaro Nanoindenter LC/MS-MS was used Agilent 1290 Infinity II/Agilent 6495A Triple Quadrupole LC/MS system

Data analysis GraphPad Prism 9.3.1
Excel 2016
Origin 2021b
DESeq2 3.16
Fiji ImageJ ver. 1.52p
IMARIS 9.9.1 (Oxford Instruments)
R (4.2.2)
CRAN 1.0.12
EnhancedVolcano 3.16
clusterProfiler 3.16
Agilent MassHunter Workstation 10.0.127
Agilent Qualitative Analysis 10.0
Huygens Professional software (Scientific Volume Imaging b.v.)
mixOmics packages
ropls packages

pheatmap package
tidyverse package

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 RNA-seq dataset generated and analyzed during the current study is available in the Gene Expression Omnibus database under accession number GSE270016. The rest of the data generated or analyzed during this study are all included in the published article and its supplementary information files. Source data are provided with this paper.

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](https://www.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 statistical methods were used to predetermine sample sizes, but our sample sizes are similar to those reported in previous publications. This has been stated in the Statistics and Reproducibility section of the study.
Data exclusions	All data collected for this study were included and analyzed, and no data were excluded.
Replication	All the experimental finding were reproduced as validated by at least three independent experiments.
Randomization	No randomization method was used to allocate animals experiments, as these were performed on already randomized animals in each condition.
Blinding	Data collection and analysis were not performed blinded to the conditions of the experiments

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

Methods

- 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

- n/a Involved in the study
- ChIP-seq
- Flow cytometry
- MRI-based neuroimaging

Antibodies

Antibodies used

rabbit anti-Ki-67 (#9129S, CST; 1:100),
 mouse anti-Oct3/4 (sc-5279, Santa Cruz Biotechnology; 1:50)
 rabbit anti-CDX2 (NB100-2136, Novus Biologicals; 1:100)
 rabbit anti-RFP (# 600-401-379, Rockland; 1:100)
 chicken anti-RFP (# 600-901-379, Rockland; 1:100)
 rabbit anti-Phospho-Histone H2A.X (Ser139) (#9718, CST; 1:100)
 human anti-Centromere Protein Antibody (ACA, #15-234, Antibodies Incorporated; 1:50)
 rabbit anti-N Cadherin antibody (ab18203, Abcam; 1:100)
 rabbit anti-Rec8 antibody (from Lampson Lab; homemade, non-commercial; 1:1000)

For secondary antibodies:

Alexa Fluor 488-labeled anti-mouse (Invitrogen, A28181, 1:500)
 Alexa Fluor 488-labeled anti-rabbit (Invitrogen, A-11036, 1:500)
 Alexa Fluor 568-labeled anti-mouse (Invitrogen, A28181, 1:500)
 Alexa Fluor 568-labeled anti-rabbit (Invitrogen, A-11036, 1:500)
 Alexa Fluor Plus 647-labeled anti-chicken (Invitrogen, A32933, 1:500)
 Alexa Fluor Plus 647-labeled anti-mouse (Invitrogen, A28181, 1:500)
 Alexa Fluor Plus 647-labeled anti-rabbit (Invitrogen, A27040, 1:500)
 Alexa Fluor Plus 647-labeled anti-human (Invitrogen, A48279, 1:500)

Validation

All primary antibodies utilized in this study were validated for compatibility with the species (mouse and human) and intended applications (western blots, immunofluorescence, and immunohistochemistry) either by the manufacturers or through previous publications, as documented in Citeab (<https://www.citeab.com>).

Clone name / Published Species / Applications / citations

anti-Ki-67 (<https://www.cellsignal.com/products/primary-antibodies/ki-67-d3b5-rabbit-mab/9129/>) / Human, Mouse, Rat / IF, Flow / cited 369 times.
 anti-Oct3/4 (<https://www.scbt.com/p/oct-3-4-antibody-c-10/>) / Human, Mouse, Rat / IHC, IP, WB, IF / cited 2514 times.
 anti-CDX2 (https://www.novusbio.com/products/cdx2-antibody_nb100-2136/) / Human, Mouse/ WB, IP, IF, IHC(P), FCM and ELISA / cited 12 times.
 anti-RFP (<https://www.rockland.com/categories/primary-antibodies/rfp-antibody-pre-adsorbed-600-401-379/>) / ELISA, IF, IHC, WB / cited 1187 times.
 anti-RFP (<https://www.rockland.com/categories/primary-antibodies/rfp-antibody-600-901-379/>) / ELISA, IF, IHC, WB / cited 62 times.
 anti-Phospho-Histone H2A.X (Ser139) (<https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h2a-x-ser139-20e3-rabbit-mab/9718/>) / Human, Mouse, Rat / WB, IP, IF, IHC(P), FCM / cited 2237 times.
 anti-Centromere Protein Antibody (<https://www.antibodiesinc.com/products/anti-centromere-protein-antibody-15-234/>) / Human, Mouse, Rat / WB, IP, IF, IHC, ICC / cited 254 times.
 anti-N Cadherin antibody (<https://www.abcam.com/products/primary-antibodies/n-cadherin-antibody-intercellular-junction-marker-ab18203.html>) / Human, Mouse, Rat / WB, IP, IF, IHC, ICC / cited 554 times.
 Rabbit anti-Rec8 antibody (from Lampson Lab) / Mouse / IF, WB/ Used in Chiang et al., Curr Biol. 2010, PubMed 20817534.

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

ICR mice
 MTS-mCherry-GFP1-10 mice (C57BL/6J background)
 mTmG mice (FVB background)
 B6C3HF2 mice
 Unless otherwise noted, all young mice were studied between 2-3 months old and all aged mice were studied at 14-17 months old.
 Surrogate mothers (B6C3HF2 mice) 3-6 months old.
 The mice were kept under standard conditions, with constant temperature (21-25°C) and humidity (30-70%), and a 12-hour light:12-hour dark cycle with light onset at 07:00.

Wild animals	No wild animals were used in the study.
Reporting on sex	Follicles and oocytes were obtained from female mice. Sperm for IVF was collected from male mice. Surrogate mothers were female mice.
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	The animal experiments conducted in this study were approved by the Institutional Animal Care and Use Committee at the National University of Singapore (protocol R20-0072) and were carried out in compliance with the relevant guidelines and regulations.

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