nature research

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Last updated by author(s): Dec 10, 2019

Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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	All microscopy images were acquired either with an Inverted Confocal Spinning Disk Roper/Nikon for fixed cells or a Super-resolution microscope OMX (Applied Precision Incorporation, DeltaVision) for live cells. Sequencing data was collected using the Illumina platform. Pyrosequencing data was collected using the PyroMark Q24 System from Qiagen. QPCR was performed on a ViiA 7 Real-Time PCR System from Thermo Fisher Scientific. Mass Spectrometry was performed on Thermo Scientific Orbitrap Fusion Tribrid MS from Thermo Fisher Scientific. Western blot (chemiluminescent) images were collected using a ChemiDoc MP from BioRad.
Data analysis	Trimgalore (v 0.4.4), STAR (2.5.3a), SNPsplit (v 0.3.2), picard (v2.18.2), DESeq2 (v1.18.1), R (3.4.1), featureCount (1.6.3), Fiji (2.0.0), dplyr (0.7.4), readr (1.1.1), tidyr (0.8.0), ggplot2 (2.2.1), macs2 (v 2-2.1.2.1), Subread (v1.28.1), HiC-Pro (v2.11.0)

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data generated in this study are available on GEO database under the number GSE131784.

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 size was not predetermined. For mouse experiments, we used a sample size commonly used and accepted for basic statistical inference while using an justifiable number of mice. For tissue culture based experiments, at least two independent clones were systematically assessed for each genotype. Typically, for the SPOC tethering experiment, 4 independent clones were characterized with very little variation being observed between them.
Data exclusions	No data were excluded from the analysis, with the exception of live imaging analysis, from which dying cells, as well as cells which moved outside from the field of view during movie acquisition were removed.
Replication	All attempts at replication were successful and noted in the relevant figure legend.
Randomization	Samples were not randomized, given that samples were grouped according to their respective genotypes.
Blinding	For most experiments, no blinding was performed as most measurements were derived from third party machines/softwares, and hence not affacted by subjective interpretation. For RNA FISH image analysis (counting of Xist RNA clouds and X-linked gene pinpoints), each experimental condition was blinded from the first author F. Dossin during counting.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used	Epitope, Antibody, reference, Application, Dilution HaloTag, Promega cat. #G9211, WB, 1/1000 V5, Sigma cat. #V8012, WB, 1/2500, Flag, Sigma cat. #F1804, WB and IF, 1/1000 and 1/200 GFP, Abcam cat. #ab290 LotGR3222604-1, Cut&Run and IF, 1/200 GFP, Roche cat. #11814460001, WB, 1/1000 H2Ak119ub1, Cell Signaling cat. #8240, IF, 1/500 Lamin B1, Abcam cat. #ab16048, WB, 1/3000 PCNA, DAKO cat. #M0879, WB, 1/3000 Ncor1, Abcam cat. #ab2482 LotGR320472-6, WB, 1/1000 Ncor2, Abcam cat. #ab5802 LotGR259451-18, WB, 1/1000 Mta1, Cell Signaling cat. #5647, WB, 1/1000 Wtap, Proteintech cat. #10200-1-AP, WB, 1/1000 Mettl3, Abcam cat. #ab195352, WB, 1/1000 Hdac3, SantaCruz cat. #sc-376957, WB, 1/1000 Rpb1, Abcam cat. #ab817, WB, 1/2000
Validation	The HaloTag antibody is validated for western blot in Fig. 1b, with specific signal disappearing upon auxin treatment, and reappearing upon removal of auxin from the culture medium. The V5 antibody is validated for Western blot in Extended Data Fig. 1a, with specific signal being observed only in cells expressing

V5-tagged Tir1.
The Flag antibody is validated for immunofluorescence in Fig. 3c, with specific nuclear signal being observed only in cells expressing Flag-tagged SPEN truncations.
The GFP antibody is validated for CUT&RUN by showing specific genomic signal for GFP-tagged SPEN, which disappears upon treatment of cells with auxin.
The H2AK119ub1 has been validated for immunofluorescence in Zylicz et al., 2019
The Lamin B1 antibody have been KO validated by abcam.
The PCNA antibody is cited 361 times according to CiteAb.
The Ncor1/Ncor2 antibodies are validated for western blot in Fig3. h, as showing increased signal upon immunoprecipitation of SPOC.
The Mta1 antibody has been cited 12 times previously according to CiteAb.
The Wtap antibody have been KO validated by ProteinTech.
The Mettl3 antibody have been KO validated by Abcam.
The Hdac3 antibody has been cited 9 times according to CiteAb.
The Rpb1 antibody has been cited 280 times previously according to CiteAb.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	All cell lines were derived from the TX1072 female mouse embryonic stem cell line (Schulz et al., 2014)
Authentication	None of the cell lines were authenticated
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	cells used are not in the ICLAC database

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	We used adult animals (from 6 weeks to 3 months for females, and 7 weeks to 1 year for males) for producing preimplantation embryos (first 4 days post mating). For Spen matings a published conditional allele was used (Yabe at al., 2007). For oocyte deletions published Rosa26:Zp3-Cre allele was used (DeVries et al., 2000). F1 hybrid Spen+/- males were obtained by crossing Spen+/+ CAST/EiJ females with Spen+/- C57BL/6J males. For Spen maternally deleted embryos, Spenflox/flox Zp3-Cre+ve C57BL/6J females were crossed with Spen+/- F1 hybrid males. For Spen control embryos, Spenflox/flox Zp3-Cre-ve C57BL/6J females were crossed with Spen+/- F1 hybrid males.
Wild animals	this study does not contain any wild animals
Field-collected samples	this study does not contain animals collected from the fields.
Ethics oversight	Animal care and use for this study were performed in accordance with the recommendations of the European community (2010/63/UE). All experimental protocols were approved by the ethics committee of Institut Curie CEEA-IC118 under the number APAFIS#8812-2017020611033784v2 given by national authority in compliance with the international guidelines.

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