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Corresponding author(s): Kristian Helin

☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

The sample size used in each experiment was not predetermined or formally justified for statistical power.

2. Data exclusions

Describe any data exclusions.

No data were excluded

3. Replication

Describe whether the experimental findings were reliably reproduced.

Experimental findings were reliably reproduced

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

No formal randomization techniques were used

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

The investigators were not blinded to group allocation during data collection and analysis

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒	A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	A statement indicating how many times each experiment was replicated
☐	☒	The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☒	☐	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☒	☐	The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒	A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒	Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	The software Easeq was used for analysis of ChIP-Seq data. Reference: Lerdrup, M., Johansen, J. V., Agrawal-Singh, S. & Hansen, K. An interactive environment for agile analysis and visualization of ChIP-sequencing data. Nat Struct Mol Biol 23, 349-357, doi:10.1038/nsmb.3180 (2016).

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	Unique materials are available from authors upon request.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Please see attached list of antibodies, species and suppliers. Antibodies produced in own lab are tested for specificity in WB using knockout cells as controls.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	E14 cell line obtained from ATCC (ES-E14TG2a)
b. Describe the method of cell line authentication used.	Cells were not authenticated
c. Report whether the cell lines were tested for mycoplasma contamination.	Cell lines were tested negative for mycoplasma
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	No commonly misidentified cell lines were used

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.	For blastocyst injection experiment: Morula were derived from C57BL/6N (4 weeks old). Aggregated morula transferred to CD1 females (8-13 weeks old)

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	No human research participants used

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ChIP-seq Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data deposition

1. For all ChIP-seq data:

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

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

2. Provide all necessary reviewer access links. *The entry may remain private before publication.*	Token for GEO accession GSE103685: qnmpwaeodnqjpyp
3. Provide a list of all files available in the database submission.	62 raw ChIP-Seq data files (fastq), 9 raw RNA-Seq data files (fastq), 9 RNA-Seq read count files (HTSeq-count), 1 BED file (Suz12 peaks)
4. If available, provide a link to an anonymized genome browser session (e.g. UCSC).	Not applicable

Methodological details

5. Describe the experimental replicates.	One replicate of each ChIP experiments was sequenced. Reproducibility in replicate ChIP experiments was verified by qPCR at several loci.
6. Describe the sequencing depth for each experiment.	Libraries were amplified using < 12 PCR cycles. All samples except one, have at least 15 million uniquely mapped reads. H3K27me3 ChIP in Ezh1/Ezh2 dKO cells have 7 million uniquely mapped reads.
7. Describe the antibodies used for the ChIP-seq experiments.	Please see attached list of antibodies, species and suppliers. Antibodies produced in own lab are tested for specificity in WB using knockout cells as controls. Knockout cells are included in ChIP-Seq experiments.
8. Describe the peak calling parameters.	Suz12 peak calling was done with Easeq's Adaptive Local Thresholding (Window size 200bp, merge peaks within 800 bp, FDR < 0.0001, log2-fold difference > 2) based on Suz12 ChIP-seq reads from WT mESCs (129B6F1) with reads from Suz12 KO cells (129B6F1) as negative control.
9. Describe the methods used to ensure data quality.	7480 peaks have FDR < 0.0001 and log2-fold difference > 2.
10. Describe the software used to collect and analyze the ChIP-seq data.	Raw data processed and aligned within Galaxy environment. Details provided in Methods. Data analysis was performed in Easeq.