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 custom software was used in this study. Datasets in this study as described and cited in the figure legend section. Sequencing was performed using PE150 mode on Illumina NovaSeq 6000.Membranes for Western blot were scanned using a ChemiDoc MP (BioRad).
Data analysis	Immunofluorescence data were visualized by ImageJ v1.49 and GraphPad Prism. Sequencing data were analyzed as described in the Methods section. Softwares were also include below: Fastp v0.12.4 Trimmomatic v0.36 Bowtie2, v2.4.1 STAR v2.7.8 BED Tools v2.29.2 MACS2, v2.2.7 Salmon tool v0.60.0 IGV software v2.4.15 SEACR v1.3 Deep Tools v3.5.0 Sambamba v1.0.1 SAM tools v1.6

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 supporting the findings of this study are displayed in the main text and supplementary material.

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	Our study exclusively examined female because the disease is only relevant in females.
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

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical method was used to pre-determine sample size. Sample sizes for 3 to 4 biological replicates including all human ang mouse endometrial sample. MeRIP-seq, CUT&Tag and ATAC-seq in this study were used according to common practice in the field (Zheng, Zhan-Hong et al. 2023,PMID:36693099.Liu, Jun et al.2020,PMID:31949099).
Data exclusions	During MeRIP-seq and ATAC-seq data processing, multiple mapped reads and duplicate reads were removed from downstream analysis.
Replication	Immunofluorescence, western blot, and Immunoprecipitation were preformed 2 to 3 times, and similar observation was made for eachl replicate. One representative result was shown in the figures. Replication of sequencing data was confirmed by calculating correlation and reproducibility between replicates (2 to 3 biological replicates), as shown in each figure and figure legend.
Randomization	Experimental materials were not divided into random subgroups. Most comparisons were done between WT and cKO.
Blinding	The authors were not blinded to group allocation during sample collection or analysis, as the information on genotype of materials wasessential for the experiment design and analysis.

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

Rabbit anti-m6A, Cell Signaling Technology,Cat# 56593S; RRID:AB_2799515,1:3000 for Dot Blot.
Rabbit anti-m6A, Millipore,Cat# ABE572-I; RRID: AB_2892214, 0.5μg for RIP.
Mouse anti-m6A, Millipore,Cat# ABE1006, 5μg for RIP.
Rabbit anti-METTL3, Abcam, Cat# ab195352; RRID: AB_2721254, 1:1000 for WB, 1:500 for IF,4μg for IP.
Rabbit anti-METTL3, Abclonal, Cat# A8370; RRID: AB_2770344,1:1000 for IB.
Rabbit anti-METTL14, Novus, Cat# NBP1-81329; RRID: AB_11021780,1:500 for IF.
Rabbit anti-EED, ProteinTech, Cat# 16818-1-AP;RRID: AB_2262065, 1:1000 for WB, 1:500 for IF,4μg for IP.
Rabbit anti-EED, Abclonal, Cat# A5371; RRID: AB_2766181, 1:1000 for IB.
Rabbit anti-EZH2, ProteinTech, Cat# 21800-1-AP; RRID: AB_10858790, 1:1000 for WB,1:500 for IF,4μg for IP.
Rabbit anti-SUZ12 Abclonal, Cat# A7786;RRID: AB_2863561, 1:1000 for WB, 1:500 for IF, 4μg for IP.
Rabbit anti-HAND2, Abclonal, Cat# A7044; RRID: AB_2767599, 1:1000 for WB, 1:500 for IF.
Rabbit anti-MUC1, Abclonal, Cat# A19081; RRID: AB_2862573, 1:1000 for WB, 1:500 for IF.
Rabbit anti-LIF, ProteinTech, Cat#26757-1-AP; RRID: AB_2880624. 1:1000 for WB, 1:500 for IF.
Rabbit anti-HOXA10, ProteinTech, Cat# 26497-1-AP; RRID: AB_2880533, 1:1000 for WB, 1:500 for IF.
Rabbit anti-FOXA2, ProteinTech, Cat# 22474-1-AP; RRID: AB_2879110. 1:1000 for WB, 1:500 for IF.
Mouse anti-CK18, Abcam, Cat# ab668; RRID: AB_305647, 1:1000 for WB, 1:500 for IF.
Rabbit anti-YTHDC1, ProteinTech, Cat# 14392-1-AP;RRID: AB_2878052, 1:1000 for WB, 4μg for IP, 1:1000 for IB.
Rabbit anti-H3K27me3 ActiveMotif, Cat# 39155; RRID: AB_2561020, 1:1000 for WB, 1:1000 for IF, .5μg per CUT&Tag.
Rabbit anti-H3K27ac, Abcam, Cat# ab177178; RRID: AB_2828007, 1:1000 for WB, 1:1000 for IF, .5μg per CUT&Tag.
Rabbit anti-H3, ProteinTech Cat# 17168-1-AP; RRID: AB_2716755, 1:10000 for WB.
Rabbit anti-Lamin B1, ProteinTech, Cat# 12987-1-AP; RRID: AB_2136290, 1:10000 for WB.
Rabbit anti-GAPDH, ProteinTech Cat# 10494-1-AP; RRID: AB_2263076, 1:10000 for WB.
Mouse anti-GAPDH, ProteinTech, Cat# 60004-1-Ig; RRID: AB_2107436, 1:10000 for WB.
Mouse anti-β-Actin, ProteinTech, Cat# 66009-1-Ig; RRID: AB_2687938, 1:1000 for WB.
Rabbit anti-Ki67, Abcam, Cat# ab15580; RRID: AB_443209, 1:1000 for IF.
Rabbit anti-Bcl2, Abcam, Cat# ab182858; RRID: AB_2715467, 1:500 for IF.
Rabbit anti-Phospho-Bad, Cell Signaling Technology,Cat# 5284; RRID: AB_560884, 1:200 for IF.
Rabbit anti-Bim, Cell Signaling Technology, Cat# 2933; RRID: AB_1030947, 1:200 for IF.
Rabbit anti-Bak, Cell Signaling Technology, Cat# 12105; RRID: AB_2716685, 1:1000 for WB.
Rabbit anti-p21, ProteinTech, Cat# 10355-1-AP; RRID: AB_2077682,1:500 for IF.
Rabbit anti-p27, ProteinTech, Cat# 25614-1-AP; RRID: AB_2880161,1:500 for IF.
Rabbit anti-Caspase3, ProteinTech, Cat# 19677-1-AP; RRID: AB_10733244, 1:500 for IF.
Alexa Fluor 488 anti-Mouse ThermoFisher Cat# A21202; RRID: AB_141607, 1:500 for IF.
Alexa Fluor 555 anti-Rabbit, ThermoFisher, Cat# A31572; RRID: AB_162543 , 1:500 for IF.
HRP*Goat Anti RabbitIgG(H+L), ProteinTech, Cat# RGAR001; RRID: AB_3073505,1:10000 for WB.
HRP* Goat Anti Mouse IgG(H+L) ProteinTech, Cat# RGAM001; RRID: AB_3068333,1:10000 for WB.
IPKine™ HRP, Mouse Anti-Rabbit IgG LCS, Abbkine, Cat# A25022; RRID: AB_2893334, 1:10000 for WB.
Normal Rabbit IgG Control R&D Systems Cat# AB-105-C; RRID:AB_354266, 4μg for IP.

Validation

Rabbit anti-m6A, Cell Signaling Technology,Cat# 56593S;(https://www.cellsignal.cn/products/primary-antibodies/n6-methyladenosine-m6a-d9d9w-rabbit-mab/56593)
Rabbit anti-m6A, Millipore,Cat# ABE572-I; (https://www.sigmaaldrich.cn/CN/zh/product/mm/abe572i)
Mouse anti-m6A, Millipore,Cat# MABE1006, (https://www.sigmaaldrich.cn/CN/zh/product/mm/mabe1006)
Rabbit anti-METTL3, Abcam, Cat# ab195352; (https://www.abcam.cn/products/primary-antibodies/mettl3-antibody-epr18810-ab195352.html)
Rabbit anti-METTL3, Abclonal, Cat# A8370; (https://abclonal.com.cn/catalog/A8370)
Rabbit anti-METTL14, Novus, Cat# NBP1-81329; (https://www.novusbio.com/products/mettl14-antibody_nbp1-81392)
Rabbit anti-EED, ProteinTech, Cat# 16818-1-AP; (https://www.ptgcn.com/products/EED-Antibody-16818-1-AP.htm)
Rabbit anti-EED, Abclonal, Cat# A5371; (https://abclonal.com.cn/catalog/A5371)
Rabbit anti-EZH2, ProteinTech, Cat# 21800-1-AP; (https://www.ptgcn.com/products/EZH2-Antibody-21800-1-AP.htm)
Rabbit anti-SUZ12 Abclonal, Cat# A7786; (https://abclonal.com.cn/catalog/A7786)
Rabbit anti-HAND2, Abclonal, Cat# A7044; (https://abclonal.com.cn/catalog/A7044)
Rabbit anti-MUC1, Abclonal, Cat# A19081; (https://abclonal.com.cn/catalog/A19081)
Rabbit anti-LIF, ProteinTech, Cat#26757-1-AP; (https://www.ptgcn.com/products/LIF-Antibody-26757-1-AP.htm)
Rabbit anti-HOXA10, ProteinTech, Cat# 26497-1-AP; (https://www.ptgcn.com/products/HOXA10-Antibody-26497-1-AP.htm)
Rabbit anti-FOXA2, ProteinTech, Cat# 22474-1-AP; (https://www.ptgcn.com/products/FOXA2-Antibody-22474-1-AP.htm)
Mouse anti-CK18, Abcam, Cat# ab668; (https://www.abcam.cn/products/primary-antibodies/cytokeratin-18-antibody-c-04-

ab668.html)

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Bewo cells and ISHIKAWA cells were from Wuhan Pricella Biotechnology Co., Ltd.
Authentication	All the cells were authenticated by Pricella Biotechnology following the international guidelines.
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No misidentified cell lines were used in this study.

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	C57/BL6, male and female, 4-8 weeks, from Animal Center, Nanjing Medical University.Mettl3 flox/flox and Pr-Cre mice were gifted by Prof. Jilong Liu, College of Veterinary Medicine, South China Agricultural University.All mice were housed in a Specific Pathogen Free (SPF) facility with individually ventilated cages. The room has controlled temperature (20-22°C), humidity (30%-70%) and light (12 hour light-dark cycle). Mice were provided ad libitum access to a regular rodent chow diet. All animals maintenance and experimental procedures used in current study were carried out according to guidelines of Institutional.
Wild animals	No wild animals were used in the study.
Reporting on sex	All the samples in this study were female mice.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All animal maintenance and experimental procedures used in this study were conducted in accordance with the guidelines of the Nanjing Medical University Institutional Animal Care and Use Committee (IACUC).

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A