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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, seeAuthors & Referees and theEditorial Policy Checklist.

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n/a	Confirmed
	\mathbf{x} 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
x	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 <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
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Our web collection on <u>st<mark>atistics for biologists</mark> contains articles on many of the points above</u>.

Software and code

Policy information about availability of computer code

Data collection Data was collected using standard Illumina software for the HiSeq 1500 and 2500 platforms. WGBS: HCS v2.2.68 and RTA v1.18.66.3

MEA v1.0, Trimmomatic v0.32, Bismark v0.16.3, Bowtie2 v2.2.3, STAR v2.4.0i, Cufflinks v2.1.1, Bedtools v2.22.1, Bedops v2.4.26, Samtools v1.1, Picard-tools v1.92, VisRseq v0.9.12 & v0.9.37, ChromHMM v1.12, Morpheus, DESeq2 v1.26.0, HOMER findMotifs.pl

v4.11.1, MEME suite v5.1.1, Stringtie v1.3.5.

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

Data analysis

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. 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

Sequencing datasets generated in this study have been deposited in GEO under the accession number GSE141877 [https://www.ncbi.nlm.nih.gov/geo/ query/acc.cgi?acc=GSE141877]. See Supplementary Table 2 for the full list of data analyzed for this study.

Field-specific reporting

Life sciences study design

All studies must dis	sclose on these points even when the disclosure is negative.			
Sample size	No statistical method was used to pre-determine sample size. Practical considerations limited the number of samples that we could analyze			
Data exclusions	High-thoughput sequencing data: PCR duplicate reads or reads aligning to multiple genomic regions were excluded from analysis. This is standard practice for high-throughput sequencing datasets.			
Replication	All datasets were generated in biological duplicates and high correlation was observed. Similarly, replicate datasets from publicly available data were confirmed for high correlation and combined for analysis and visualization. In addition, high reproducibility between publicly available dataset and relevant datasets generated in this study was observed.			
Randomization	The experiments were not randomized. This study does not involve randomized samples.			
Blinding	The investigators were not blinded to group allocation during sample collection or analysis. None of the analyses applied were based on subjective observations.			

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		Methods	
n/a	Involved in the study	n/a Involved in the study	
	✗ Antibodies	ChIP-seq	
X	Eukaryotic cell lines	Flow cytometry	
×	Palaeontology	MRI-based neuroimaging	
	🗷 Animals and other organisms	·	
×	Human research participants		
X	Clinical data		
	•		

Antibodies

Antibodies used

DNMT3A immunofluorescence: IMGENEX #IMG-268 (0.5 µg/ml)
ICM immunodissection: anti-mouse IgG (Cedarlane, catalogue #CLA3340, 1:100 dilution) and guinea pig complement (Rockland, catalogue #C200-0005, 1:50 dilution)

Validation

As previously described: Hirasawa 2008, Genes & Development; Solter & Knowles 1975 PNAS

Animals and other organisms

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

Laboratory animals

All animal experiments were performed under the ethical guidelines of Kyushu University and Tokyo University of Agriculture.

All mice were at least 10-week-old at the time of each experiment. All mice were maintained at 22°C ambient temperature, 55% humidity and 12 hour/12 hour dark/light cycle.

Dnmt3a matKO F1 hybrid embryos: Dnmt3a KO oocytes were generated using Dnmt3a2lox and Zp3-cre C57BL/6J mice as described previously (Hirasawa 2008, Genes & Development). Superovulation was induced using PMSG/hCG (7.5 U) and MII oocytes were collected from oviducts. Dnmt3a2lox;Zp3-cre MII oocytes were artificially inseminated with DBA/2J spermatozoa. DNMT3A immunofluorescence: wild-type C57BL/6J females were mated with JF1 males and IF was performed on one-cell

zygotes, as described previously (Hisarawa 2008, Genes & Development).

 $Diploid\ and rogen ones\ were\ prepared\ from\ B6D2F1/Jcl\ oocytes\ and\ C57BL/6NJcl\ spermatozoa.$

Wild animals Study did not involve wild animals.

Field-collected samples Study did not involve samples collected from the field.

Ethics oversight All animal experiments were performed under the ethical guidelines of Kyushu University and Tokyo University of Agriculture.

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