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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, 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> 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 <u>statistics for biologists</u> contains articles on many of the points above.
Software and code
Policy information about <u>availability of computer code</u>
Data collection n/a
Data analysis The sequence chromatogram data were analyzed with Tracking of Indels by Decomposition (TIDE) version 2.0.1 (https://tide.deskgen.com/), and the sequencing data from HindIII-digested products were analyzed using CRISP-ID version 1.1 (http://crispid.gbiomed.kuleuven.be/).
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

The sequence information of constructed plasmids were described in Supplemental information and the plasmid DNA have deposited in Addgene (#131467, https:// www.addgene.org/Wataru_Fujii/). The data that support the findings are available on request from the corresponding author.

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 t	he document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>	
Life scier	nces study design	
All studies must dis	close on these points even when the disclosure is negative.	
Sample size	The sample size was determined based on previous publications (https://www.ncbi.nlm.nih.gov/pubmed/23997119 , https://www.ncbi.nlm.nih.gov/pubmed/29088065).	
Data exclusions	data were extruded from the analyses.	
Replication	Biological and technical replicates were performed.	
Randomization	Zygotes used for microinjections were randomly picked up from in vitro or naturally fertilized zygotes pools. Sequenced embryos were randomly chosen from the microinjection-derived GFP-positive blastocyst stage-reached embryos.	
Blinding	The experimenters were not blinded during the experiments or analysis.	
We require informatis system or method list Materials & ex n/a Involved in th Antibodies Eukaryotic Palaeontol Animals an Human res Clinical dat	ChIP-seq cell lines MRI-based neuroimaging d other organisms earch participants	
Antibodies		
Antibodies used	anti-Flag M2 monoclonal antibody (F1804, Sigma-Aldrich), anti-β-actin polyclonal antibody (GTX109639, GeneTex, Inc., CA, USA), horseradish peroxidase-conjugated anti-mouse IgG and anti-rabbit IgG (Jackson ImmunoResearch Laboratories, Inc., West Grove, PA, USA)	
Validation	Manufacturer's website; (anti-Flag M2) https://www.sigmaaldrich.com/catalog/product/sigma/f1804 , (anti-ACTB) http://www.genetex.com/beta-Actin-antibody-GTX109639.html , (anti-mouse lgG) https://www.jacksonimmuno.com/catalog/products/115-035-003 , (anti-Rabbit lgG) https://www.jacksonimmuno.com/catalog/products/111-035-144 Our previous applications; https://www.ncbi.nlm.nih.gov/pubmed/23997119 , https://www.ncbi.nlm.nih.gov/pubmed/29088065	
Eukaryotic c	ell lines	
Policy information	about <u>cell lines</u>	
Cell line source(s	HEK293 gifted from Dr K Chida of the University of Tokyo (https://www.ncbi.nlm.nih.gov/pubmed/21239526).	
Authentication	The cell line used was not authenticated.	
Mycoplasma con	tamination Not tested.	

Commonly misidentified lines (See <u>ICLAC</u> register)

Animals and other organisms

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

Laboratory animals

3-week-old female and >8-week-old male C57BL/6Ncr mice (Sankyo Labo Service Corporation, Tokyo), >8-week-old male DBA/2J mice (CLEA Japan, Tokyo), and 8-week-old female ICR mice (Sankyo Labo Service Corporation) were housed at $24 \pm 2^{\circ}$ C and $50 \pm 10\%$ humidity under a 12/12 h light/dark cycle with free access to water and diet.

Wild animals

This study did not involve wild animals.

Field-collected samples

This study did not involve samples collected from field.

Ethics oversight

All animal care and experimental procedures conformed to the Guidelines for Animal Experiments of The University of Tokyo, and were approved by the Animal Research Committee of The University of Tokyo (approval No. P18-093).

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