

## 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 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                                                                                                                                                                                                                                                                                      |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement                                                                                                                                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly                                                                                                                                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>                                                               |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of all covariates tested                                                                                                                                                                                                                                |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons                                                                                                                                                   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. $F$ , $t$ , $r$ ) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted<br><i>Give <math>P</math> values as exact values whenever suitable.</i>                            |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings                                                                                                                                                                      |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes                                                                                                                                                |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> 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 | BD Accuri C6 flowcytometer, GE deltavision microscope                                                                                                                                                                                                          |
| Data analysis   | Graphpad Prism 6 (unpaired t-test, two-way ANOVA, Row means with SD or SEM, Nonlinear regression (curve fit) with inhibitor vs. response or one phase decay), FSC Express 4, Volocity 6.3.1, Image J, SAMtools, GSNAP, featureCounts, and R for data analysis. |

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 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

Transcriptome data shown in Supplementary Figure 3C are deposited in the DNA Data Bank of Japan (DDBJ) Sequencing Read Archive under the accession numbers DRA009832 and DRA010661. Other data that support the findings of this study are available from the corresponding author upon request.

## 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](https://www.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 methods were used to predetermine sample sizes. Sample sizes were determined based on previous experience (Nishimura et al. Nature Methods, 6, 917-912, 2009; Natsume et al. Cell Reports, 15, 210-218, 2016). In case of testing degradation in a clone, we used at least two independent clones to confirm the consistency. |
| Data exclusions | No data was excluded from the analysis.                                                                                                                                                                                                                                                                                                      |
| Replication     | All experiments were reliably reproduced. Each experiment was performed independently at least two times, but usually more than three times.                                                                                                                                                                                                 |
| Randomization   | No randomization was performed for cell analyses because of complication of the experiments. Mice were paired based on gender, age and weight.                                                                                                                                                                                               |
| Blinding        | Blinding was not performed in this study because of complication of the experiments.                                                                                                                                                                                                                                                         |

## 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                                           |
|-------------------------------------|-----------------------------------------------------------------|
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Antibodies                  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Eukaryotic cell lines       |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology          |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Animals and other organisms |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Human research participants            |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Clinical data                          |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Dual use research of concern           |

### Methods

| n/a                                 | Involved in the study                              |
|-------------------------------------|----------------------------------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> ChIP-seq                  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Flow cytometry |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> MRI-based neuroimaging    |

## Antibodies

|                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Antibodies used | For protein detection, the following commercially available antibodies were used. Primary antibodies: anti-mAID (MBL, #M214-3), anti-OsTIR1 (MBL, #PD048), anti-V5 (Invitrogen, #R960-25), anti-DHC1 (SantaCruz, #sc-9115), anti-SMC2 (Bethyl, #A300-058A-T), anti-CTCF (Bethyl, #A300-543-T), anti-POLR2A (Abcam, #ab817), anti-BRD4 (GeneTex, #GTX130586), anti-TOP2A (MBL, #M042-3S), anti-alpha-tubulin (MBL, #M175-3). Secondary antibodies: anti-rabbit IgG HRP (GE Healthcare, #NA934), anti-mouse IgG HRP (SantaCruz, #PI-2000), anti-rabbit IgG StarBright Blue 700 (Bio-Rad, #12004161), Alexa Fluor 647 anti-mouse IgG (ThermoFisher, #A-21236).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Validation      | All used primary antibodies were validated by the manufactures and previous publications. References can be found at the manufactures' web site.<br><a href="https://ruo.mbl.co.jp/bio/dtl/A/?pcd=PD048">https://ruo.mbl.co.jp/bio/dtl/A/?pcd=PD048</a><br><a href="https://www.scbt.com/p/dynein-hc-antibody-r-325?productCanUrl=dynein-hc-antibody-r-325&amp;_requestid=682743">https://www.scbt.com/p/dynein-hc-antibody-r-325?productCanUrl=dynein-hc-antibody-r-325&amp;_requestid=682743</a><br><a href="https://www.bethyl.com/product/A300-058A/SMC2+Antibody">https://www.bethyl.com/product/A300-058A/SMC2+Antibody</a><br><a href="https://www.bethyl.com/product/A300-543A/CTCF+Antibody">https://www.bethyl.com/product/A300-543A/CTCF+Antibody</a><br><a href="https://www.abcam.com/rna-polymerase-ii-ctd-repeat-ysptsp-antibody-8wg16-chip-grade-ab817.html">https://www.abcam.com/rna-polymerase-ii-ctd-repeat-ysptsp-antibody-8wg16-chip-grade-ab817.html</a><br><a href="https://www.genetex.com/Product/Detail/BRD4-antibody/GTX130586">https://www.genetex.com/Product/Detail/BRD4-antibody/GTX130586</a><br><a href="https://ruo.mbl.co.jp/bio/e/dtl/A/?pcd=M042-3">https://ruo.mbl.co.jp/bio/e/dtl/A/?pcd=M042-3</a><br><a href="https://ruo.mbl.co.jp/bio/e/dtl/A/?pcd=M175-3">https://ruo.mbl.co.jp/bio/e/dtl/A/?pcd=M175-3</a><br><a href="https://www.sigmaaldrich.com/catalog/product/sigma/t4026?lang=ja&amp;region=JP">https://www.sigmaaldrich.com/catalog/product/sigma/t4026?lang=ja&amp;region=JP</a><br><a href="https://www.bio-rad.com/en-jp/sku/12004165-hfab-rhodamine-anti-tubulin-primary-antibody-200-ul?ID=12004165">https://www.bio-rad.com/en-jp/sku/12004165-hfab-rhodamine-anti-tubulin-primary-antibody-200-ul?ID=12004165</a> |

## Eukaryotic cell lines

Policy information about [cell lines](#)

|                                                                   |                                                                                                                                                                                                                                          |
|-------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cell line source(s)                                               | HCT116 and HEK293 cell lines were originally obtained from ATCC.                                                                                                                                                                         |
| Authentication                                                    | The original HCT116 and HEK293 were authenticated by ATCC. Other HCT116 derivative cell lines were not authenticated. However, all HCT116 cell lines used in this study were frequently checked their morphology, growth, and karyotype. |
| Mycoplasma contamination                                          | The original HCT116 line was tested, but other resultant clones were not tested for mycoplasma contamination. However, we did not observe any phenotypes related to mycoplasma infection.                                                |
| Commonly misidentified lines (See <a href="#">ICLAC</a> register) | No commonly misidentified cell lines were used.                                                                                                                                                                                          |

## Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

|                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Laboratory animals      | To obtain hippocampal neurons (Figure 2), pregnant female C57BL/6J mice (10- or 11-week old) were obtained from Japan SLC. Nude mice used for xenograft assay in Figure 5 were Balb/c-nu female mice (7-week old) weighing 16 to 20 g and were obtained from Charles River Japan. To generate transgenic (TG) mice (Figure 6), female B6C3F1 (C57BL/6N X C3H/HeN) (4- or 5-week old) were obtained from CLEA Japan.                                                                                              |
| Wild animals            | None.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Field-collected samples | None.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Ethics oversight        | All protocols and procedures involving the care and use of animals were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of National Institute of Genetics and The University of Tokyo prior to conduct. Throughout the study, the care and use of animals were conducted in accordance with the guidelines and regulations set by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the Ministry of the Environment, and the Science Council of Japan. |

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

## Flow Cytometry

### Plots

Confirm that:

- ☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☒ All plots are contour plots with outliers or pseudocolor plots.
- ☒ A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

|                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sample preparation                                                                                                                                        | For detecting EGFP and Clover signals after ligand treatment, cells were trypsinized and fixed in 4% methanol-free paraformaldehyde phosphate buffer (FUJIFILM Wako Pure Chemical Corporation) at 4°C overnight. Fixed cells were washed and resuspended in PBS containing 1% BSA. For measuring the DNA signal after ligand treatment, cells were trypsinized and fixed in 70% EtOH. Fixed cells were washed, resuspended in PBS containing 1% BSA, 50 µg/ml of RNase A, and 40 µg/ml of propidium iodide, and incubated at 37°C for 30 min. 10,000 cells were analyzed from each sample. |
| Instrument                                                                                                                                                | BD Accuri C6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Software                                                                                                                                                  | FSC4 Express                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Cell population abundance                                                                                                                                 | No cell sorting was done in this study.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Gating strategy                                                                                                                                           | Cells were gated with SSC and FSC for analyses.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <input checked="" type="checkbox"/> Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |