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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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	GeneSys Pxi6 V1.5.6.0 was used for WB. Microbeta2 V2.0.0.87 was used for scintillation counting and photon emission detection. Fluostar Optima V1.20-0 was used for fluorescence detection. BD FACSCalibur was used for Flow Cytometry. Agilent LC/MSD chemstation VB.04.03 was used for LC/MS. Bruker Topspin V1.3 was used for NMR.
Data analysis	Microsoft Excel V2011, Graphpad Prism V4.03 and FlowJo V7.5.5 were used to analyze the data in this study.

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 upon request. 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 datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	Three biological (independent) replicates were used for experiments except mouse study. For the mouse study, at least 5 mice were used for each group. Based on Student T test, for comparison between two groups, a sample size of 5 is efficient to calculate the statistical significance.
Data exclusions	No data were excluded from the analyses.
Replication	In the Figure legend, we stated how many number of replications were performed. All attempts at replication were successful.
Randomization	Mice of equal average baseline body weight were randomly allocated to the experiments.
Blinding	For mice studies, investigators were blinded to group allocation during samples collection and data analysis.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	The following antibodies were used for western blot: Ent1 (Santa Cruz, sc377283, mouse, 1:500), FKBP12 (abcam, ab92459, rabbit, 1:1000), FKBP51 (abcam, ab126715, rabbit, 1:1000), GAPDH (Santa cruz, sc20357, goat, 1:3000).
Validation	Anti-ENT1 is a mouse monoclonal IgG2a and recommended for detection of ENT1 of mouse, rat and human origin by Western Blotting. Anti-Ent1 has 3 product citations on the Santa Cruz's website; Anti-FKBP12 has validation statement on the abcam's website. Anti-FKBP12 is a rabbit monoclonal antibody and suitable for WB and ICC; Anti-FKBP51 has validation statement on the abcam's website. Anti-FKBP51 is a rabbit monoclonal antibody and suitable for WB, IP, IHC-P, Flow Cyt and ICC/IF; Anti-FKBP51 has been reference in 1 publication; Anti-GAPDH is a goat polyclonal IgG and recommended for detection of GAPDH of mouse, rat, human, equine, canine, bovine, porcine, abian and feline by WB, IP, IF, IHC(P) and ELISA; Anti-GAPDH has 153 product citations on the Santa Cruz's website.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Human umbilical vein endothelial cells (HUVEC) were purchased from Lonza (Cat#: C2519A). Jurkat T and HEK293T cells were purchased from ATCC. Human red blood cells were obtained from Fisher Scientific (Cat#: 50-643-497). Swine kidney tubular epithelial cell line PK15 (from ATCC), its derivatives PK15-ENT1 and PK15-ENT2 were provided by Dr. Chung-Ming Tse (Johns Hopkins University School of Medicine). Sf9 cells, a clonal isolate of Spodoptera frugiperda Sf21 insect cells, were purchased from ATCC.
Authentication	None of the cell lines used were authenticated.

Mycoplasma contamination	All cell lines were tested negative for mycoplasma.
Commonly misidentified lines (See ICLAC 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	8-10 week old C57BL/6J male mice were used.
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.

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	Sample preparation described in Extended Data. Briefly, Human umbilical vein endothelial cells (HUVEC) were seeded at 5 x 10^5 cells / 15 cm dish, allowed to recover overnight and subsequently treated with drugs or vehicle control for 24 h. Media was then collected and set aside. Cells were washed with PBS, trypsinized, combined with set aside media, pelleted at 500 x g and then washed with 10 mL PBS followed by another 500 x g spin. The pellet was resuspended in 0.5 mL PBS and added dropwise using a Pastuer pipet to 2 mL 75% ethanol in a 5 mL polystyrene tube being slowly agitated by a vortex. The cells were stored at 4°C until staining. To do so, cells were pelleted at 500 x g, resuspended in 5 mL PBS, rested 60 seconds, pelleted again and washed in 5 mL PBS. The cell pellet was then resuspended in 0.5 mL staining solution (0.1% Triton-X-100, 0.2 mg/mL DNase free RNase A, and 0.02 mg/mL propidium iodide). Cells were allowed to stain for 30 min – 1 h prior for analysis. Propidium iodide incorporation was measured using a FACSCalibur. The percentage of cells in each cell cycle stage was determined with FlowJo (v7.5.5) using a Watson analysis.
Instrument	BD FACSCalibur
Software	FlowJo v7.5.5
Cell population abundance	N/A. Flow Cytometry used for cell cycle analysis
Gating strategy	Cells were identified using FSC-A vs SSC-A and doublets were excluded using FSC-A/FSC-H.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.