nature portfolio

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Last updated by author(s): 20 May 2026

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	Gen5 (v2.01.14) for microplate luminescence, fluorescence, and absorbance data acquisition; Roche LightCycler® 96 software for qPCR and RT-qPCR data acquisition; Image Lab (Bio-Rad) for gel image documentation; and FLoid™ Cell Imaging Station (Life Technologies) for fluorescence microscopy image acquisition.
Data analysis	GraphPad Prism (v10.6.0), Roche LightCycler® 96 software, and Image Lab (Bio-Rad). Microsoft Excel (v16.89.1) was used for data organization and simple calculations.

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

All data supporting the findings of this study are available within the Article, Supplementary Information, Source Data file and Supplementary Data 1. Source data are provided with this paper. Oligonucleotide, primer, ASO, splint and ssDNA sensor sequences used in this study are provided in Supplementary Data 1.

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	This study did not involve human participants
Reporting on race, ethnicity, or other socially relevant groupings	This study did not involve human participants
Population characteristics	This study did not involve human participants
Recruitment	This study did not involve human participants
Ethics oversight	This study did not involve human participants

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 predetermine sample size. Sample sizes were chosen on the basis of standard practice for transient cell-based reporter, qPCR, fluorescence and flow-cytometry assays, and to assess reproducibility across independent biological replicates. Most quantitative experiments were performed with n = 3 independent biological replicates, unless otherwise indicated in the figure legends, with selected supportive assays performed with n = 4 or n = 5 biological replicates. These sample sizes were sufficient to assess reproducibility and detect consistent differences between experimental and control conditions in the assays performed.
Data exclusions	No data were excluded from the analyses
Replication	Experiments were independently repeated at least two times on different days, with consistent results. Minor variations in fold change were observed in some experiments, likely reflecting expected variability in transient transfection assays and reagent batches. However, the overall trends and conclusions were reproducible across independent repeats.
Randomization	Randomization was not performed because this study consisted of controlled experiments in cultured cells. Experimental and control samples were processed in parallel under identical conditions.
Blinding	Blinding was not applicable because this study consisted of controlled experiments in cultured cells, and data acquisition relied on automated measurements and predefined analysis workflows rather than subjective assessment by the investigators.

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

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK293T (CRL-3216), HeLa (CCL-2), HCT116 (CCL-247), U2OS (HTB-96), and Hepa1-6 (CRL-1830) cell lines were acquired from ATCC.
Authentication	The cell lines used in this study were obtained from commercial sources and were not further authenticated.
Mycoplasma contamination	Cell lines were not tested for mycoplasma
Commonly misidentified lines (See ICLAC register)	None

Plants

Seed stocks	Not relevant to this study
Novel plant genotypes	Not relevant to this study
Authentication	Not relevant to this study

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	As described in the Methods, cells were harvested 48 h post-transfection, washed with PBS, dissociated with TrypLE Express, resuspended in PBS + 2% FBS, filtered through flow tubes with cell strainers, and used for flow cytometry and sorting. For single-cell sorting experiments, GFP$^+$ single cells were deposited directly into 96-well plates containing complete growth medium.
Instrument	Symphony A1 and BD FACSAria™ cell sorter, BD Biosciences
Software	BD FACSDiva™ software was used for data collection, and FlowJo v10 software was used for flow cytometry analysis
Cell population abundance	Two fluorescently labeled cell lines (BFP or mCherry) were used to enable unambiguous lineage identification during and after sorting. Post-sort abundance was assessed by experiment. For bulk enrichment, events were gated on SONAR-activated GFP$^+$ cells, and lineage composition (as a proxy for purity) was quantified by flow cytometry as the fraction of BFP$^+$ versus mCherry$^+$ cells within the GFP$^+$ gate. For single-cell sorting, individual GFP$^+$ singlets were deposited into 96-well plates; after clonal outgrowth, lineage identity per well was assigned by plate-reader fluorescence (BFP/mCherry).
Gating strategy	The gating strategy is provided in the Supplementary Information. FSC-A/SSC-A was used to select cells, SSC-H/SSC-A and FSC-H/FSC-A to select singlets, then GFP$^+$ cells were gated relative to negative controls; BFP$^+$/mCherry$^+$ boundaries were set using the respective single-line controls and analyzed within the GFP$^+$ gate

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