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.

- □ □ 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. mean) and 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 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: qPCR data were acquired with LightCycler® 96 Real-Time PCR System (Roche). Cellcycle data were acquired with BD FACSAria III using BD FACSDiva v8.0.1. Phase contrast images were acquired with Olympus X83 using cellSens Dimension software. Cell viability assay was conducted with TECAN infinite F200PRO using i-control software. Visible light images were acquired with Axiozoom V16 microscope (Carl Zeiss AG) with a TrueChrome II digital camera (BioTools Inc.) and TCapture software (ver. 4.30.602) (Fuzhou Tucsen Photons Co., Ltd.). The phase behaviour of the solutions was analysed by DSC-60A plus (Shimadzu corporation) and TA-60WS software (Shimadzu corporation). Number of cells were counted by Countess II (Thermo Fisher Scientific Inc.). Drug solubility was confirmed by ECLIPSE Ts2 (Nikon Corporation).

Data analysis: Cellcycle data were analyzed with FlowJo v10. Immune blotting results were analyzed and quantified with with Fiji (ImageJ, version 1.8.0). All the statistical data were analyzed with Microsoft Excel and/or GraphPad Prism 7.

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

All data are available from the authors upon reasonable 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.

- [x] 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 | Data exclusions | Replication | Randomization | Blinding |
|-------------|----------------|-------------|---------------|---------|
| Sample size was determined based on previous experience and published literature. | No data were excluded from the study | Experiments were carried out with the number of replicates indicated in the manuscript. All attempts at replication were successful. | Randomization was not necessary for the experiments. | No blinding. |

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 |
|---------------------------------|---------|
| n/a                             | Involved in the study |
| - [ ] Antibodies                | [x] ChIP-seq |
| - [x] Eukaryotic cell lines     | [ ] Flow cytometry |
| - [ ] Palaeontology and archaeology | [x] MRI-based neuroimaging |
| - [x] Animals and other organisms | |
| - [x] Human research participants | |
| - [x] Clinical data             | |
| - [x] Dual use research of concern | |

Antibodies

- Antibodies used: Rabbit anti-phospho-Rb (Ser780) antibody (9307, Cell Signaling Technology)
  Mouse anti-beta-tublin antibody (T7816, Sigma-Aldrich Co., Llc.)

- Validation: Antibodies were used and stored according to the manufacturer’s instructions.

Eukaryotic cell lines

Policy information about cell lines

- Cell line source(s): Human normal fibroblast-1 (hNF-1, KF-4009) was purchased from Kurabo Industries Ltd. Human normal fibroblast-2 (hNF-2) and mouse normal fibroblast (mNF) are kind gifts from Prof. Erik Sahai. Mouse primary astrocytes were established from euthanized neonatal CS7816 mice MDA-MB-231 human breast cancer cells and WM266.4 human melanoma cells are kind gifts from Prof. Erik Sahai (The Francis-Crick Institute, UK). PC9 human lung cancer cells and Mardin-darby canine kidney cells are kind gifts from Prof. Seiji Yano (Cancer Research Institute of Kanazawa University) and Prof. Etsuko Kiyokawa (Kanazawa Medical University), respectively. Human IPS cell line 201B7 was bought from Riken BRC.

- Authentication: MDA-MB-231, WM266.4, PC9, MDCK, IPS cell lines were STR profiled and species verified before acquisition. Human normal fibroblasts (hNF-1 and hNF-2), mouse normal fibroblasts (mNF) and mouse primary astrocytes have been species verified and tested for the expected phenotype in vitro.

- Mycoplasma contamination: All cells were tested negative for mycoplasma contamination.

- 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 | Species, zebrafish: strain, AB* (wild type strain); sex and age, n/a |
|--------------------|---------------------------------------------------------------------|
| Wild animals       | n/a                                                                 |
| Field-collected samples | n/a                                                          |
| Ethics oversight  | n/a                                                                 |

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: Detailed protocols for cell culture and sample preparation are provided in Methods section.

Instrument: BD FACS Aria III

Software: BD FACSDiva v8.0.1 and FlowJo v10.

Cell population abundance: As shown in the figures.

Gating strategy: SSC-A/FSC-A gate was used to remove debris and dead cells, SSC-A/SSC-H and FSC-A/FSC-H were used to remove cell doublets. Cell cycle gates were set according to the DAPI and Alexa Fluor 647 intensity as shown in the figures.

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