

## 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

- |                                     |                                     |  |
|-------------------------------------|-------------------------------------|--|
| <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 checked="" type="checkbox"/> | <input 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	Data were collected on an Odyssey (for western blotting, LI-COR), a Typhoon FLA 9500 (for autoradiography, GE Healthcare) and a LSRII Fortessa (for flow cytometry, BD Biosciences).
Data analysis	We used an ImageJ (for image quantification, NIH, ver 1.51), a FlowJo (for flow cytometry, BD Biosciences, ver 10.2) and a Snappene (for sequence analysis, GSL Biotech, ver 4.2).

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 authors declare that the data supporting the findings of this study are available within the paper. The source data underlying Figs. 1C, 1D, 2B, 2C, 2D, 2E, 3B, 4B, 4D and Supplementary Figs. 1A, 1B, 2C, 3B, 3D, 5 are provided as a Source Data file. Other data that support the findings of this study are available from the corresponding author 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.

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      Sample sizes were chosen based on similar published studies elsewhere. All analyzes were performed at least three independent times and each repeat yielded highly similar results.

Data exclusions      Experiments were excluded from analysis when either the positive or negative control failed.

Replication      All the results were reproduced at least three times for each experiment.

Randomization      Randomization was not required because we performed all the experiments using specified cell lines.

Blinding      Blinding was not performed because there is no way to introduce bias into the experiments in this study.

## 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

Animals and other organisms

Human research participants

Clinical data

### Methods

n/a      Involved in the study

ChIP-seq

Flow cytometry

MRI-based neuroimaging

## Antibodies

Antibodies used      Anti-Flag (1:1,000; Sigma #F1804), anti-actin (1:1,000; Sigma #A2066), and anti-16E7 (1:1,000; Santa Cruz #sc-51951).

Validation      Anti-Flag; the manufacturer validated that this antibody detects only the band(s) of Flag-tagged protein on a Western blot from an E. coli, plant or mammalian crude cell lysate.  
Anti-actin; the manufacturer validated that this antibody recognizes the 42 kDa actin band using immunoblotting with human or animal tissue extracts.  
Anti-16E7; the manufacturer validated that this antibody recognizes HPV16 E7 protein expressed in the HPV16-positive Caski cell line on a Western blot.

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)      HEK293T (ATCC) and Rpn11-Flag MEFs (Shigeo Murata, the University of Tokyo)

Authentication      Not authenticated.

Mycoplasma contamination      All cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines (See [ICLAC](#) register)      No commonly misidentified cell lines were used in the 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        | Yeast cells were cultured to early log phase before harvesting for analysis.  |
| Instrument                | LSRII Fortessa (BD Biosciences)   |
| Software                  | FlowJo v.10.2 (FlowJo LLC)  |
| Cell population abundance | The abundance of the desired cell population in post-gating was generally > 95% of the total cells.   |
| Gating strategy           | Living singlet yeast cells were determined by their sizes (FSC/SSC) and RFP-positive cells were gated for measurement of YFP over RFP fluorescence ratio of the final population. |
- Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.