nature portfolio

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# 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<br>*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<br>*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 | Colony counting and selection of representative colonies for images was performed with a stereomicroscope (Stemi 305 Series, Carl Zeiss, Jena, Germany) at 8-40-fold magnification. Photographs were taken using either the Labscope Software (Version 3.0.1, Carl Zeiss, Jena, Germany), an Axio Lab A1 microscope equipped with an AxioCam ERc 5s (Carl Zeiss) or with a Samsung Galaxy A71 smartphone camera (Samsung, Seoul, South Korea). |
| Data analysis | OriginPro 2021 and MS-Excel were used for regression analyses, statistical procedures, and interpolations. |

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 colony counting raw data of clonogenic survival experiments in this article (i.e. S-C value pairs of all biological replicates) are provided in Source Data Figure 5 and Source Data Figure 9. The authors declare that some of the clonogenic survival data displayed in Figure 5 and Figure 9 of this manuscript were taken from Brix et al. 17 as specified in the corresponding figure legends. All other data supporting the findings of this study are available within the article and its supplementary information files. Additional information can be provided by 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

# Life sciences study design

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

| | |
|---|---|
| Sample size | No statistic method was used to predetermine sample size. The sample sizes in our experiments were determined based on experience and commonly accepted standards in the field. |
| Data exclusions | Data points at low densities were excluded if all biological replicates of an experiment yielded zero colonies in order to allow logarithmic transformation and regression. Culture dishes with exceedinly high numbers of colonies were not considered for counting. |
| Replication | All experiments were performed in three to four independent biological replicates. Information on data replication is provided in the respective Figure Legends. |
| Randomization | Cell culture of varying density and passage number (passage 2-10 post thawing) were randomly used for experiments. |
| Blinding | No blinding of investigators was performed. |

# 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 |
| ☒ | ☐ Human research participants |
| ☒ | ☐ Clinical data |
| ☒ | ☐ Dual use research of concern |

## Methods

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

# Eukaryotic cell lines

Policy information about cell lines

| | |
|---|---|
| Cell line source(s) | All cell lines were obtained from ATCC (Manassas VA, USA), the DSMZ (Braunschweig, Germany), or CLS (Heidelberg, Germany), respectively. |
| Authentication | Authentication of the frozen stock aliquots was performed by STR profiling at the cell authentication service from the DSMZ. |
| Mycoplasma contamination | All cell lines were routinely tested negative for Mycoplasma contamination. |
| Commonly misidentified lines (See ICLAC register) | No commonly misidentified cell lines were used. |