nature research

Corresponding author(s): Alexei A. Aravin
Andrey Kulbachinskiy
Anton Kuzmenko

Last updated by author(s): Jul 19, 2020

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.

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	No third party software was used during data collection step.
Data analysis	All data generated during this study are included in the published article and the Extended Data and are available from GEO database with the accession number GSE148596. The code used for data analysis is available at the GitHub repository https://github.com/AntKuzmenko/CbAgo_DNAi.git

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 HTS libraries and corresponding processed files are available using the following GEO accession number GSE148596. Lists of plasmids, strains and oligonucleotides used in this study are available in Supplementary Tables 1 , 2 and 3.

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	Sample size calculations were not performed. All experiments were performed with sample sizes based on standard protocols in the field.
Data exclusions	No data were excluded from the analysis. Any filters that were applied during data preprocessing and cleaning steps are explained in the Methods section.
Replication	Measurements of phage infection efficiency and cell survival were performed in at least three biological replicates. Number of replicates for all HTS experiments are listed in the Supplementary Table 4.
Randomization	This statement is not relevant to this study.
Blinding	This statement is not relevant to 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 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

Antibodies

Antibodies used	1. 6x-His Tag antibodies (HIS.H8) (Invitrogen Cat #MA1-21315, lot: TA258903) 2. F(ab')2-Goat anti-Mouse IgG (H+L) Secondary Antibody, HRP (Invitrogen Cat #A24512, lot: 46-170-060115)
Validation	1. Validation statement was taken from the manufacturer's website (https://www.thermofisher.com/antibody/product/6x-His-Tag-Antibody-Monoclonal/MA1-21315): 6x-His Tag Antibody (MA1-21315) in WB Western blot analysis of His-tagged protein in E. coli lysates. Membranes containing total cell lysates from uninduced E. coli (-) or induced E. coli (+) treated with 1mM Isopropyl beta-D-1-thiogalactopyranoside (IPTG) to induce expression of His-tagged IQ domain (IQD) protein were blocked with 5% non-fat milk in PBS-T and probed with a 6X-His Epitope Tag Antibody (Product # MA1-21315) at a dilution of 1:1400 followed by a donkey anti-mouse IgG-HRP secondary antibody. Blots were developed with SuperSignal West Dura (Product # 34076). His-tagged Repressor of Gibberellin (RGA) was used as a positive control. Data courtesy of the Innovators Program. 2. Validation statement was taken from the manufacturer's website (https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Secondary-Antibody-Polyclonal/A24512): Mouse IgG (H+L) Secondary Antibody (A24512) in WB Western blot analysis was performed on whole cell extracts (30 µg lysate) of U-87 MG (Lane 1) and K562 (Lane 2). The blots were probed with Anti-SOD2 Mouse Monoclonal Antibody (Product # MA1-106, 2 µg/mL) and detected by chemiluminescence using F (ab')2-Goat anti-Mouse IgG (H+L) Secondary Antibody, HRP conjugate (Product # A24512) at dilutions 1:500 (Fig. 1), 1:10,000 (Fig. 2) and 1:20,000 (Fig. 3). A 22 kDa band corresponding to SOD2 was observed. Known quantity of protein samples were electrophoresed using Novex® NuPAGE®12 % Bis-Tris gel (Product # NP0342BOX), XCell SureLock™ Electrophoresis System (Product # EI0002) and Novex® Sharp Pre-Stained Protein Standard (Product # LC5800). Resolved proteins were then transferred onto a nitrocellulose membrane with iBlot® 2 Dry Blotting System (Product # IB21001). The membrane was probed with the relevant primary and

secondary antibody after blocking with 5 % skimmed milk. Chemiluminescent detection was performed using Pierce™ ECL Western Blotting Substrate (Product # 32106).