nature research

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| Last updated by author(s): | Aug 13, 2021 |

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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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| 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> 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 |
| \square Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated |
| Our web collection on <u>statistics for biologists</u> contains articles on many of the points above. |
| Software and code |
| Policy information about availability of computer code |

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.

Cary Eclipse: Scan (v1.2(147)), Kinetics (v1.2(146)), Thermal (v1.2(146)); SX20 Stopped Flow: Pro-Data SX (v2.5.1852.0)

Data analysis and plotting: Excel (v2101), KaleidaGraph (v4.0), OriginPro (v9.0.0); Kinetic fitting: MATLAB (vR2019a); Docking, MD or DFT:

Amber2020, Avogadro (v1.2.0), MOE2019 (v2019.0102), UCSF Chimera (v1.11; ViewDock tool, file type: Dock 4, 5 or 6); Molecular structure

Data

Data collection

Data analysis

Policy information about availability of data

 $All \ manuscripts \ must \ include \ a \ \underline{data \ availability \ statement}. \ This \ statement \ should \ provide \ the \ following \ information, \ where \ applicable:$

- Accession codes, unique identifiers, or web links for publicly available datasets

images and log D calculations: MarvinSketch (v18.9.0)

- A list of figures that have associated raw data
- A description of any restrictions on data availability

The fluorescent signature of all substrates (Fig. 3) and the effect of inhibitors on the fluorescent signature of the substrate amifostine (Fig. 4) are provided on figshare (DOI: 10.6084/m9.figshare.16798174).

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| 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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u> | | | | | |
| | | | | | |

Life sciences study design

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

We employed triplicate measurements as this is typically the standard employed when performing enzymatic studies. Sample size

Data exclusions No data were excluded

Blinding

Data collection

Data exclusions

Non-participation

Randomization

Timing

Replication Fluorescent nanoantenna experiments on the hydrolysis of pNPP were performed dozens of times on different days and under different conditions. For other substrates, inhibitors and antibodies, all experiments were replicated at least three times.

This is not relevant to our study. All our attempts to replicate experiments led to similar results. Randomization

> Fitting of the data was performed by a different person than the one who collected the data, and was without detailed knowledge of the properties of the substrate or inhibitor employed.

Behavioural & social sciences study design

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

Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, Study description quantitative experimental, mixed-methods case study).

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic Research sample information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to Sampling strategy predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a

rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.

Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample

If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.

Ecological, evolutionary & environmental sciences study design

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

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, Study description hierarchical), nature and number of experimental units and replicates.

Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Research sample

Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and

| | any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source. | | | |
|----------------------------|--|--|--|--|
| Sampling strategy | Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. | | | |
| Data collection | Describe the data collection procedure, including who recorded the data and how. | | | |
| Timing and spatial scale | Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken | | | |
| Data exclusions | If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established. | | | |
| Reproducibility | Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful. | | | |
| Randomization | Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why. | | | |
| Blinding | Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study. | | | |
| Did the study involve fiel | d work? Yes No tion and transport | | | |
| Field conditions | Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall). | | | |
| Location | State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth). | | | |
| Access & import/export | Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information). | | | |
| Disturbance | Describe any disturbance caused by the study and how it was minimized. | | | |
| Reporting fo | r specific materials, systems and methods | | | |
| ' | authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, evant 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 & experime | ental systems Methods | | | |
| n/a Involved in the study | n/a Involved in the study | | | |

| Ma | terials & experimental systems | Methods | | |
|-------------|--------------------------------|-------------|------------------------|--|
| n/a | Involved in the study | n/a | Involved in the study | |
| | Antibodies | \boxtimes | ChIP-seq | |
| \boxtimes | Eukaryotic cell lines | \boxtimes | Flow cytometry | |
| \boxtimes | Palaeontology and archaeology | \boxtimes | MRI-based neuroimaging | |
| \boxtimes | Animals and other organisms | | | |
| \boxtimes | Human research participants | | | |
| \boxtimes | Clinical data | | | |
| \boxtimes | Dual use research of concern | | | |
| | | | | |

Antibodies

Antibodies used

Goat IgG, Rockland Immunochemicals, lot # 32090, catalogue # 005-0102-0010.

VIROTROL SARS-CoV-2, Bio-Rad, Reactive for SARS-CoV-2 total IgG/IgM and IgG antibodies, human plasma based, lot # 390300, catalogue # 200300A

VIROCLEAR SARS-CoV-2, Bio-Rad, Non-reactive for SARS-CoV-2 total IgG/IgM and IgG antibodies, human plasma based, lot # 390600, catalogue # 200500.

Validation

Goat IgG, Rockland Immunochemicals: "Goat IgG whole molecule was prepared from normal serum by a multi-step process which includes delipidation, salt fractionation and ion exchange chromatography followed by extensive dialysis against the buffer stated above. Goat IgG whole molecule assayed by immunoelectrophoresis resulted in a single precipitin arc against anti-Goat IgG and anti-Goat Serum." Reference provided on website: Yamada, Y. et al. Efficient and high-speed transduction of an antibody into living cells using a multifunctional nanocarrier system to control intracellular trafficking. J. Pharm. Sci. 104, 2845-2854 (2015). https://rocklandinc.com/Product.aspx?id=45482

VIROTROL SARS-CoV-2 and VIROCLEAR SARS-CoV-2, Bio-Rad:

"These products are unassayed quality controls designed to produce results within a target range established by each laboratory. These products should be analyzed in the same manner as unknown specimens according to instructions supplied by the manufacturer of the test kit being used. Levels of reactivity and specific performance characteristics of these products will vary with different manufacturers' kits and assay procedures."

https://www.bio-rad.com/webroot/web/pdf/cdg/literature/Q-1676-CE.pdf

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

State the source of each cell line used.

Authentication

Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.

Mycoplasma contamination

Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.

Commonly misidentified lines (See ICLAC register)

Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

Palaeontology and Archaeology

Specimen provenance

Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).

Specimen deposition

Indicate where the specimens have been deposited to permit free access by other researchers.

Dating methods

If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.

Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals.

Wild animals

Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Human research participants

Policy information about studies involving human research participants

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

| Clinical data | |
|---|--|
| Policy information about <u>c</u> All manuscripts should comply | <u>inical studies</u> with the ICMJE <u>guidelines for publication of clinical research</u> and a completed <u>CONSORT checklist</u> must be included with all submissions. |
| Clinical trial registration | Provide the trial registration number from ClinicalTrials.gov or an equivalent agency. |
| Study protocol | Note where the full trial protocol can be accessed OR if not available, explain why. |
| Data collection | Describe the settings and locales of data collection, noting the time periods of recruitment and data collection. |
| Outcomes | Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures. |
| Dual use research | n of concern |
| Policy information about d | ual use research of concern |
| Hazards | |
| in the manuscript, pose and the manuscript, pose and the manuscript, pose and the manuscript of the manuscript, pose and manuscript of the manuscript, pose and manuscript of the manuscript | tock Int area In the sexperiments of concern: It o render a vaccine ineffective to therapeutically useful antibiotics or antiviral agents |
| Increase transmis. Alter the host range in the | ence of a pathogen or render a nonpathogen virulent sibility of a pathogen ge of a pathogen diagnostic/detection modalities nization of a biological agent or toxin ally harmful combination of experiments and agents |
| ChIP-seq | |
| Data deposition | |
| | w and final processed data have been deposited in a public database such as GEO. |
| , | e deposited or provided access to graph files (e.g. BED files) for the called peaks. |
| Data access links May remain private before publ | For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data. |

Methodology

(e.g. <u>UCSC</u>)

Files in database submission

Genome browser session

Replicates

Describe the experimental replicates, specifying number, type and replicate agreement.

Sequencing depth

Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and

enable peer review. Write "no longer applicable" for "Final submission" documents.

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to

Provide a list of all files available in the database submission.

| Sequencing depth | (whether they were paired- or single-end. |
|-------------------------|--|
| Antibodies | Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number. |
| Peak calling parameters | Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used. |
| Data quality | Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment. |
| Software | Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details. |

| Flow Cytometry | |
|---|--|
| Plots Confirm that: The axis labels state the marke | r and fluorochrome used (e.g. CD4-FITC). |
| The axis scales are clearly visib | le. 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 | Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used. |
| Instrument | dentify the instrument used for data collection, specifying make and model number. |
| | Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details. |
| | Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the amples and how it was determined. |
| | Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined. |
| Magnetic resonance im | figure exemplifying the gating strategy is provided in the Supplementary Information. Laging |
| Design type | Indicate task or resting state; event-related or block design. |
| Design specifications | Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials. |
| Behavioral performance measures | State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects). |
| Acquisition | |
| Imaging type(s) | Specify: functional, structural, diffusion, perfusion. |
| Field strength | Specify in Tesla |
| Sequence & imaging parameters | Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle. |
| Area of acquisition | State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined. |
| Diffusion MRI Used | Not used |

| Preprocessing | |
|----------------------------|---|
| Preprocessing software | Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.). |
| Normalization | If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization. |
| Normalization template | Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized. |
| Noise and artifact removal | Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration). |
| Volume censoring | Define your software and/or method and criteria for volume censoring, and state the extent of such censoring. |

Statistical modeling & inference

| Mod | del type and settings | Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation). | |
|--|---|--|--|
| Effe | ct(s) tested | Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used. | |
| Specify type of analysis: Whole brain ROI-based Both | | | |
| | istic type for inference <u>Eklund et al. 2016</u>) | Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods. | |
| Cor | rection | Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo). | |
| Иod | els & analysis | | |
| n/a | Involved in the study | | |

| Models & analysis | |
|--|---|
| n/a Involved in the study | |
| Functional and/or effective connectivity | Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information). |
| Graph analysis | Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.). |
| | |

Multivariate modeling and predictive analysis | Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.