nature research

Corresponding author(s): Nicolas L. Fawzi and Jeetain Mittal

Last updated by author(s): Aug 11, 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 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 | |
|---|---|---|
| ☐ | ☒ | 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 | NMR data: Topspin 3.5; Simulation data: GROMACS 4.6.7 software package with PLUMED 2.4 |
| Data analysis | NMR data: NMRPipe v10, NMRFAM-Sparky 1.3; Simulation data: PLUMED v2.7.2 |

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

Chemical shift assignments can be accessed on the BMRB. NOESY data can be accessed at https://doi.org/10.6084/m9.figshare.16598861. Plasmids and constructs used in this study can be accessed on AddGene (https://www.addgene.org/Nicolas_Fawzi). All other data are available from the corresponding author.

# 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

# Life sciences study design

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

| | |
|---|---|
| Sample size | No sample size calculations were performed. Triplicate samples were used for all quantitative in vitro biochemical assays which is standard for these in vitro technical replicate experiments. All replication experiments showed consistent results. See figure legends for details. |
| Data exclusions | Data was not excluded. |
| Replication | Replication is specifically described in the legend for each figure panel. All quantified data were collected as specified with three replicates for in vitro biochemical assays or NMR accepted standards for uncertainty estimation based on quantification of spectral intensity and baseline uncertainty. As indicated, experiments were successfully replicated. Only the NMR chemical shift perturbations and NMR spin relaxation for MBP-RGG3 R10xK and R10xS were not replicated, though the consistent data obtained for each of these and MBP-RGG3 (WT) (previously replicated and WT replicated here by a different experimenter) in both NMR assays, providing justification for single experiments (as well as the impacts of COVID-19 pandemic on ability to generate additional data). |
| Randomization | Samples were numbered and logged but not randomized for in vitro assays. No co-variates are relevant for these in vitro assays. |
| Blinding | Blinding was not done for in vitro assays. Data were repeated with appropriate controls included each time. It was not practical to have blinding of in vitro assays, NMR experiments, or simulation experiments as these were performed and analyzed by single experimenters. |

# 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 |