nature portfolio

Corresponding author(s):	Rafael Brüschweiler, Lei Bruschweiler-Li
Last updated by author(s):	Mar 3, 2023

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

\sim				
<.	tat	ŀις	:11	\sim

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
\boxtimes	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
\boxtimes	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.
X	A description of all covariates tested
\boxtimes	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)
\boxtimes	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 <i>Give P values as exact values whenever suitable.</i>
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X	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 <i>d</i> , Pearson's <i>r</i>), 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

Data collection

NMR spectrometer Bruker Avance III data acquisition: TopSpin version 3.6.2

Data analysis

NMR resonance assignments: NMRViewJ, version 9.2.0-b20 NMR data processing: nmrPipe, version 11.0 Rev 2022.193.18.59 64-bit

NMR dynamics analysis: ChemEx, version 2021.4.0.dev6 Protein ensemble visualization: PyMol, version 2.4.0 Secondary structure propensities: SSP software version 1.0

Chemical shift prediction: POTENCI, version $1.0\,$

Chemical shift prediction: Talos-N, version 4.12 Rev 2015.147.15.40

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 NMR assignments were deposited in the Biological Magnetic Resonance Data Bank (BMRB, (https://bmrb.io/) with accession codes: 52021 (WT K-Ras.GTP), 52023 (G12D K-Ras.GTP), 52024 (G12C K-Ras.GTP). All relaxation dispersion, CEST, and NASR results can be accessed at doi:10.5061/dryad.j6q573nm0.

Human research participants

Policy information about <u>studies involving human research participants and Sex and Gender in Research.</u>

Reporting on sex and gender	This project does not involve human subjects.
Population characteristics	This project does not involve human subjects.
Recruitment	This project does not involve human subjects.
Ethics oversight	No ethics oversight and approval were needed for this study.

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

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 be	fore making your selection.
🔀 Life sciences 👚 Behavioural & social sciences 📄 Ecological, evolutionary & environmental scien	ces

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

No statistical methods were used to determine sample size.

Life sciences study design

Sample size

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

Data exclusions	The only data points that were left out were due to NMR spectral overlap or poor sensitivity as described in the main text.
Replication	NMR experiments were performed once with technical replicates for error analysis as described in the figure captions.
Randomization	No randomized sample selection was applied and each sample received identical treatment.
Blinding	Blinding was not relevant for this study as the work was done with protein samples of known compositions and they were treated identically for all experiments and analysis

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.

portfolio reporting summar	ומנטות	Du+1 FD -
rtfolio reporti		5
olio reporti	Ξ	7
reporti		<u>)</u>
_ <u>-</u> 2.	5	2.

Materials & experimental systems		Methods		
n/a	Involved in the study	n/a	Involved in the study	
\boxtimes	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	Clinical data			
\boxtimes	Dual use research of concern			