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 | Biolayer interferometry: OctetRED96 DataAcquisition software 9<br>ThT assays: Omega software 5.70 R2<br>Fluorescence microscopy: AcquireSR Acquisition control software and SoftWoRx 7.0.0<br>SEC: Unicorn 7.3<br>Protein design: PyRosetta4 2021, Rosetta (various builds between 2020-2022)<br>NMR: topspin3.2 and topspin3.5 |
| Data analysis | Fluorescent Tht data processing and fitting: AmyloFit 2.0, Graphpad 9.5.0, Mars 4.01 R2<br>MDS: OneM 1.8.911-11359<br>Xray data processing, refinement and model building: XDS(VERSION Jan 10, 2022 BUILT=20220220), REFMAC 5.8.0267, Aimless 0.7.4, COOT 0.8.9, PDB-REDO server, Phaser 2.8.3, Phenix v1.20.1, CCP4-7.0.076<br>Biolayer interferometry: OctetRED96 data analysis software 9.1<br>SEC: Unicorn 7.3<br>Fluorescence microscopy: ImageJ2 (v_2.1.0. & v_2.3.0)<br>NMR: nmrPipe 11.0, CARA 1.9.1.7 |

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

Data is contained within the manuscript and in open access repositories or can be made available upon request. The crystal structure is available in the ProteinDataBank (8FG6). Supporting files and data are available through Zenodo doi: 10.5281/zenodo.10391229

## Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

| | |
|---|---|
| Reporting on sex and gender | n/a |
| Population characteristics | n/a |
| Recruitment | n/a |
| Ethics oversight | n/a |

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 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 | Three independent replicates were performed. This is standard practice in the field. No significant variation was observed to suggest more replicates were required |
| Data exclusions | No data were excluded |
| Replication | Unless stated otherwise, all experimental results were reproduced at least two times with two different preparations of protein reagents. Many of the BLI binding experiments were performed three or more times with three to five protein preparations that were purified independently. |
| Randomization | Randomization was not used because no samples were assigned to a treatment group in this study. |
| Blinding | There was no blinding in this study. All assays where performed in vitro and blinding has no effect on the quantitative measurements that were perfomed |

# 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 |
| ☒ | ☐ 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 and Sex and Gender in Research

| | |
|---|---|
| Cell line source(s) | HeLa cells (ATCC CCL-2), SHSY-5Y human neuroblastoma cells (ATCC CRL-2266) |
| Authentication | SHSY-5Y cells were authenticated at CRUK services using NGS based cell line authentication assay; HeLa cells were authenticated by commercial vendor through STR profiling. |
| Mycoplasma contamination | Cell lines tested negative for mycoplasma contamination. |
| Commonly misidentified lines (See ICLAC register) | No commonly misidentified cell lines were used. |