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

| Sta | atistics | | | | |
|--|--|---|--|--|--|
| For | all statistical and | alyses, 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 | | | | |
| | 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. | | | | |
| So | ftware and | d code | | | |
| Poli | cy information a | about <u>availability of computer code</u> | | | |
| Da | ata collection | n/a | | | |
| Da | ata analysis | n/a | | | |
| 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. | | | | | |
| Da | ta | | | | |
| Poli | cy information a | about <u>availability of data</u> | | | |
| | All manuscripts must include a <u>data availability statement</u> . 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 <u>policy</u> | | | | |
| All o | data generated or | analysed during this study are included in this published article (and its supplementary information files). | | | |

| Field-spe | ecific reporting | | |
|-------------------------|---|---|--|
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| | | | |
| Life scier | nces study desig | n | |
| All studies must dis | sclose on these points even when t | he disclosure is negative. | |
| Sample size | Because this study includes diverse analyses, all details are provided in the methods section. | | |
| Data exclusions | No exclusions. All data are included in the article and its supplementary information. | | |
| Replication | Binding constants were measured by 3 independent methods. They are competitive inhibition enzyme kinetics, isothermal titration calorimetry (ITC), and sedimentation velocity analytical ultracentrifugation (SV-AUC). These three methods produced values within the experimental errors reported. The reproducibility of enzyme kinetics was tested at least 2-3 times with freshly prepared enzyme and stock solutions of the substrate and inhibitor. Once this was determined to provide consistent reaction rates within an error limit of 5%, the final experiment for the data displayed in the manuscript was carried out in duplicate and 2-4 reads per well for each time point. The mean of the data points was used for fitting. The same stock solutions of enzyme and inhibitor were used for SV-AUC and ITC to determine the binding constant of the inhibitor to the enzyme. | | |
| Randomization n/a | | | |
| Blinding | n/a | | |
| We require informati | ion from authors about some types of n | aterials, systems and methods naterials, experimental systems and methods used in many studies. Here, indicate whether each material, not sure if a list item applies to your research, read the appropriate section before selecting a response. | |
| Materials & ex | perimental systems | Methods | |
| n/a Involved in th | | n/a Involved in the study | |
| Antibodies | S | ∑ ChIP-seq | |
| Eukaryotic | c cell lines | Flow cytometry | |
| Palaeonto | ology and archaeology | MRI-based neuroimaging | |
| Animals ar | nd other organisms | | |

Human resea

Human research participants

Dual use research of concern