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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 *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 *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	Xcalibur v2.2 was used for mass spectrometry data collection. Image Lab v5.2.1 was used for fluorescence gel scanning. CLARIOstar v5.4 was used for absorbance (Pierce BCA Protein Assay) data collection. Li-COR Odyssey v3.0.30 was used for IRDye secondary antibodies imaging.
Data analysis	RAWconverter (v1.1.0.22) was used to convert raw mass spectrometry files to .ms2 and .mzXML files. Integrated Proteomics Pipeline (IP2) v6.0.02, DTASelect 2.0 (embedded in IP2) and in-house software CIMAGE (Weerapana, E. et al. 2010) were used to analyze all mass spectrometry data, including SILAC-, ReDiMe- and TMT-based experiments. RStudio (v1.1.456, R version 3.5.1) was used to compile proteomics data. Image Lab v5.2.1 was used for relative quantization of fluorescence gel scanning. Image Studio Lite v5.2.5 was used to process western blot images. GraphPad Prism v7.03 was used to perform statistical tests and to generate all graphs and plots. AutoDock v4.2.6 and AutoDockTools were used for molecular modeling.

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

All data associated with this study are available in the published article and its supplementary information. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD015104. All other raw data are available upon request.

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	No statistical methods were used to pre-determine the sample size. Sample size (N ≥ 2) was chosen according to literature showing similar methods of analysis.
Data exclusions	No data was excluded
Replication	All experiments were performed at least twice independently at different time points. Similar results were obtained after data analysis in all attempts. Therefore all attempts at replication were successful.
Randomization	Cell lines used in experiments were grown under identical conditions, and therefore randomization was not used. Human blood was acquired from de-identified healthy patient donors. No experimental human groups were designated in this study, therefore randomization was not used.
Blinding	Cell lines used in experiments were grown under identical conditions, human blood was acquired from de-identified healthy patient donors (female and male, age 30-65), and therefore blinding was not used.

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

Antibodies

Antibodies used	Primary: Mouse anti-FLAG® clone M2 (Sigma Aldrich, SKU F1804-1MG, 1:10000 dilution). Secondary: IRDye® 800CW Goat anti-Mouse secondary antibody (LICOR, 925-32210, 1:10000 dilution).
Validation	Mouse anti-FLAG® clone M2 (Sigma Aldrich, SKU F1804-1MG): validated for western blotting by manufacturer using extracts from CHO cells with spiked FLAG-BAP protein.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293T (ATCC)
Authentication	All cell lines used in this study were authenticated by the vendors
Mycoplasma contamination	All cell lines used in this study were tested negative for mycoplasma
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study

Human research participants

Policy information about studies involving human research participants

Population characteristics	Healthy donors were recruited through Scripps Research's Normal Blood Donor Services (NBDS), which has the following requirements: Be between 30 and 65 years of age. Weigh at least 110 pounds (50 kg). Have a Body Mass Index (BMI) between 19 – 39. Have blood pressure between 90-180 mm Hg systolic and 50-100 mm Hg diastolic. Not have had major surgery within the past six months. Have had an adequate hemoglobin on initial screening test. Have negative screening for HIV and Hepatitis B, C, at initial screening, and annually thereafter. Is not on daily aspirin or daily anti-inflammatory medications. No auto-immune diseases.
Recruitment	Healthy donors were recruited through Scripps Research's Normal Blood Donor Services (NBDS) after informed consent. All donors are initially screened for infectious diseases prior to being recruited, and screened on a yearly basis after the initial screen to remain active in the program. Human blood is acquired on a as needed basis. No self-selection of donors is involved.
Ethics oversight	The Scripps Research Institute Institutional Review Board.

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