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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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ | 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ | 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	EPU 3.7 (ThermoFisher Scientific), Refeyn AcquireMP 2024 R1 (Refeyn), Unicorn 7 (Cytiva), ChromLab Software 6 (Bio-Rad), VICTOR3 (PerkinElmer), SerialEM 4
Data analysis	cryoSPARC 4.5 (Structura Biotechnology Inc.), AlphaFold 2, Coot 0.9, PyMOL 3.1 (Schrödinger), Refeyn DiscoverMP 2024 R1 (Refeyn), Jalview 2.11, ChimeraX 1.9, R 4.5, MATLAB 24.1 (MathWorks), PHENIX 1.21.2 (refinement & validation), 3DFSC

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](#)

Coordinates and maps are available for ITIH4 (PDB: 9TXI, EMDB: EMD-56397), ITIH4:Fab (PDB: 9TXJ, EMDB: EMD-56398) ITIH4N:Fab (PDB: 9TXK, EMDB: EMD-56399) and MASP-1cf:(ITIH4N:Fab)2 (PDB: 9TXL, EMDB Composite: EMD-56404, EMDB Consensus: EMD-56400, EMDB ITIH4N#1 Focus: EMD-56401, EMDB ITIH4N#2 Focus: EMD-6402). The map of the PKK:(ITIH4N:Fab)2 complex is available as EMDB entry EMD-56403. Circular dichroism data is available in the Source Data File provided

with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	One person donating blood was female
Reporting on race, ethnicity, or other socially relevant groupings	One person donating blood was caucasian
Population characteristics	As only one person donated blood, this is not relevant
Recruitment	Adult lab members giving written consent and not receiving compensation voluntarily donated blood for the preparation of serum. The use of serum for the research presented here complies with Danish ethical regulations according to the Central Denmark Region Committees on Health Research Ethics (case 1-10-72-214-13) and does not require ethical approval from the Aarhus University Research Ethics Committee
Ethics oversight	The research presented here complies with Danish ethical regulations according to the Central Denmark Region Committees on Health Research Ethics and the Aarhus University Research Ethics Committee.

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	Each EM structure determinations and CD measurements were done once. ELISAs were performed twice. Chromatographies were done at least twice.
Data exclusions	No data were excluded except during classification in EM data processing.
Replication	All replications were succesful
Randomization	not applicable
Blinding	not applicable

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
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	12A12, 5F5, and biotinylated anti-ITI4 monoclonal antibodies used are in-house developed and published as described in references
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mentioned in Materials and Methods. The biotinylated anti-C4 antibody is in-house biotinylated version of a commercial antibody (Q0369, Agilent) as also described under materials and methods.

Validation

See above

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

Commercially available HEK293F cell line for protein expression (Gibco™, catalogue number R79007)

Authentication

No authentication of the commercial cell line was conducted

Mycoplasma contamination

No testing

Commonly misidentified lines
(See [ICLAC](#) register)

Not applicable

Plants

Seed stocks

not applicable

Novel plant genotypes

not applicable

Authentication

not applicable