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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 *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	EPU 2.2.0.65REL was used for cryo-EM data collection. X-ray diffraction data was collected by the program Blu-Ice 5.0. SAXS data was collected using the program Albula (Dectris, Baden-Dättwil, Switzerland).
Data analysis	cryo-EM data was processed by using CryoSparc V2.8.0 to V2.11.0, X-ray data was processed by using HKL-3000, and the structure was solved and refined by using Phenix 1.14-3260. The structures were adjusted by using Coot 0.8.9.1 EL or WinCoot 0.8.2. The structures were analyzed or portrayed by using the qtPISA program in the CCP4i2 program suit 7.0.060, MUSTANG 3.2.3, UCSF Chimera 1.16-42360, UCSF ChimeraX 1.6.dev202303040240, and PyMOL 1.8.2.1. The bands on the SDS-PAGE were analyzed by ImageJ 1.50i. The SAXS data was processed and analyzed by BioXTAS RAW 2.2.2 and the ATSAS program suite 2.7, 2.8.1, and 3.2.1. MALS data analysis was carried out using the program ASTRA ver. 6.0.5.3. Bar charts were made by Excel version 16.54.

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

The atomic coordinates and reflection files for the crystal structures generated in this study have been deposited in the Worldwide Protein Data Bank (wwPDB) under accession codes 8YM4 [http://doi.org/10.2210/pdb8YM4/pdb] (The SeMet derivative of the CFH7G-C8FGLG complex), 8YM5 [http://doi.org/10.2210/pdb8YM5/pdb] (Native CFH7G-C8FGLG complex), and 8YM6 [http://doi.org/10.2210/pdb8YM6/pdb] (Native CF-C8FGLG complex). The cryo-EM structures and the corresponding atomic coordinates generated in this study have been deposited in the Electron Microscopy Data Bank (EMDB) and wwPDB, respectively, under accession codes EMD-39424 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39424] and 8YNI [http://doi.org/10.2210/pdb8YNI/pdb] (The 5:3:3 CF-C8FuL_FGLG_CADA-FAFuL_F25G DED Complex C), EMD-39425 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39425] and 8YNK [http://doi.org/10.2210/pdb8YNKpdb] (The 5:3 CF-C8FGLG Complex D), EMD-39426 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39426] and 8YNL [http://doi.org/10.2210/pdb8YNLpdb] (The 6:3 CF-C8FGLG Complex E), EMD-39427 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39427] and 8YNM [http://doi.org/10.2210/pdb8YNMpdb] (The 8:3 CF-C8FGLG Complex F), and EMD-39428 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39428] and 8YNN [http://doi.org/10.2210/pdb8YNNpdb] (The 4:3 CF-C8FGLG Complex G). The cryo-EM structure used in this study are available in the EMDB under accession codes EMD-39126 [https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-39126] (The triple-FADD-Casp-8-cFLIP DED Complex B)56. The atomic coordinates for the cryo-EM structure used in this study are available in the wwPDB under accession codes 8YBX [http://doi.org/10.2210/pdb8YBX/pdb] (The triple-FADD-Casp-8-cFLIP DED complex B)56, and 8YD8 [http://doi.org/10.2210/pdb8YD8/pdb] (Native single-FADD-Casp-8-cFLIP DED complex)56. The atomic coordinates for the NMR structure used in this study are available in the wwPDB under accession codes 2GF5 [http://doi.org/10.2210/pdb2GF5/pdb] (Full-length FADD)63. The SDS-PAGE data, western blot data, representative micrographs, and other source data generated in this study are provided in the Supplementary Information or in a Source Data file. Source data are provided with this paper. Source data are provided as a Source Data file.

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	not applicable (This data didn't involve human participants or human data.)
Reporting on race, ethnicity, or other socially relevant groupings	not applicable (This data didn't involve human participants or human data.)
Population characteristics	not applicable (This data didn't involve human participants or human data.)
Recruitment	not applicable (This data didn't involve human participants or human data.)
Ethics oversight	not applicable (This data didn't involve human participants or human data.)

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	No sample size calculations were made to predetermine the sample size. Biochemical experiments were repeated at least twice to confirm the repeatability of their results. For cryo-EM data processing, all available particles are subject to 2D and 3D classification by the CryoSparc program in order to find similar particles. Only particles of the same kind of complex are qualified and picked by the CryoSparc program for 3D reconstruction. As shown in Supplementary Fig. 5 and Supplementary Table 3, 2,228 movies were collected to produce approximately 246,000 particles. Approximately 120,000 particles were used to reconstruct the final 3D volume of Complexes C to G to a resolution ranging from 3.55 to 3.97 angstroms, based on the FSC threshold of 0.143. The production of the atomic coordinates, shown in Supplementary Fig. 5d, indicates that the sample sizes are sufficient, as supported by the validation reports in wwPDB. For X-ray structure, since only the same kind of the protein complex could form a protein crystal, a small crystal of 0.001 cubic millimeter that could produce X-ray diffraction spots would contains at least 1,000,000,000,000 same protein complex, which could confirm the repeatability of the structural results. In this study, our crystals are bigger than 0.001 cubic millimeter. In the case of the binary CFH7G-C8FGLG complex, we collected 143,410 reflections, with a redundancy of 3.75, completeness of 98.6, and average I/sigma of 21.46. The resultant crystal structure of the binary CFH7G-C8FGLG complex has a resolution of 2.09 angstrom. The X-ray Data collection, phasing and refinement statistics in Supplementary Table 1 indicate that the sample sizes are sufficient, which is supported by the validation report in wwPDB.

Data exclusions	For cryo-EM data, according to standard practices, movies with image drift, ice contamination, or poor CTF estimation were excluded. In addition, bad particles with no secondary structural features in 2D classification were excluded. For X-ray data, according to standard practices, poor diffraction images and bad reflections would be excluded.
Replication	Cryo-EM or EM experiments were performed independently at least three times with similar results or with similar resultant structures of different resolutions. The reproducibility could also be evaluated and verified by statistical analyses (Supplementary Table 3) and the validation report. Furthermore, the 3D volume of Complex C, for example, was reconstructed by approximately 24,000 particles to a resolution of 3.66 angstrom, indicating that approximately 24,000 particles consistently have the same structure at a resolution of 3.66 angstrom. X-ray diffraction experiments were data was performed independently at least three times with similar crystal parameters or with similar resultant X-ray structures of different resolutions. The reproducibility could also be evaluated and verified by statistical analyses (Supplementary Table 1) and the validation report. In addition, the reproducibility could be verified by the same structures produced by the native complex and its SeMet derivative. Furthermore, since each single crystal used in the X-ray diffraction experiment contains at least a billion protein molecules, the generation of the structure of the binary complex at a resolution of 2.09 angstrom, for example, indicates the a least a billion protein molecules in the crystal have the same structure at a resolution of 2.09 angstrom. Other biochemical experiments were repeated at least twice with similar results.
Randomization	No randomization was involved in biochemical experiments if the samples are from the same strain, same tube, or the same flask. However, in the cryo-EM data processing, particles in the refinement step were randomly split into two halves automatically by the CryoSparc software and cross correlation coefficients between the two half sets are calculated. In addition, for the refinement of X-ray structure, Phenix would randomly pick 5% of reflections to calculate R-free.
Blinding	Blinding is not applicable to our experiments, such as cryo-EM and X-ray diffraction, because the measurements are objective and easily measurable. Therefore, the parameters for the experiments in this study did not require subjective assessments of the treatment. E. coli for experiments are derived from the same batch. Investigators were blinded to group allocation.

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	Cell lysate-based experiments: FLIP (D5J1E) (Cell Signaling, #56343, 1:2000); Caspase 8(D35G2) (Cell Signaling, #4790, 1:4000); Caspase-3 Antibody (Cell Signaling, #9662, 1:4000); Cleaved Caspase-3 (Asp175) (5A1E) (Cell Signaling, #9664, 1:2000); Human FADD (Cell Signaling, #2782, 1:2000); PARP (46D11) (Cell Signaling, #9532,1:2000); RIP (Cell Signaling, #4926, 1:2000); Phospho-RIP (Ser166) (D1L3S) (Cell Signaling, #65746, 1:2000); GAPDH (14C10) (HRP Conjugate) (Cell Signaling, #3683, 1:4000); Goat Anti-Rabbit IgG H&L (HRP) (Abcam, #ab6721, 1:10000)
Validation	Primary antibodies were validated by the manufacturers as shown on the corresponding websites. All the antibody are available from the commercial sources listed above. All the RRID are listed below: Caspase 8 (D35G2) (Cell Signaling, #4790)RRID:AB_10545768; Cleaved Caspase-3 (Asp175) (5A1E) (Cell Signaling, #9664)RRID:AB_2070042; PARP (Cell Signaling, #9532)RRID:AB_659884; FADD (human specific) (Cell Signaling, #2782)RRID:AB_2100484; FLIP (D5J1E) (Cell Signaling, #56343)RRID:AB_2799508; Caspase-3 Antibody (Cell Signaling, #9662)RRID:AB_331439; RIP (Cell Signaling, #4926)RRID:AB_2224503; Phospho-RIP (Ser166) (D1L3S) (Cell Signaling, #65746)RRID:AB_2799693; GAPDH (14C10) (HRP Conjugate) (Cell Signaling, #3683)RRID:AB_1642205; Goat Anti-Rabbit IgG H&L (HRP) (Abcam, #ab6721)RRID:AB_955447

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a