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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 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	No software was used for data collection.
Data analysis	Raw data were processed and all curve fittings performed using GraphPad Prism 9. Phenix and Coot software was used to refine the crystal structure of VLCAD. DynamX 3.0 was used to process mass spectra data for HDX MS experiments. ImageJ v. 1.53 was used to perform densitometry analyses of western blots.

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 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 generated or analyzed for this study are included in this manuscript, its supplementary information, and source data file. The raw HDX MS data for VLCAD have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD029565 (http://proteomecentral.proteomexchange.org/cgi/GetDataset?ID=PXD029565). Structures corresponding to PDB IDs 3B96 (https://www.wwpdb.org/pdb?id=pdb_00003b96), 2UXW (https://www.wwpdb.org/pdb?id=pdb_00002uxw), and 7S7G (https://www.wwpdb.org/pdb?id=pdb_00007s7g) were used in this study.

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	All experiments were performed in at least biological duplicate using independent experimental preparations. The number of biological and technical replicates are indicated in the figure legends and were chosen to ensure reproducibility in accordance with standard operation procedures for the corresponding experiments. Sample size calculations were not performed for this study (N/A).
Data exclusions	No data were excluded during analysis.
Replication	All experiments were reproducibly performed in at least biological duplicate. Biological and associated technical replicates where applicable are detailed in each figure legend.
Randomization	No experimental grouping or randomization was used in this study.
Blinding	N/A for the biochemical and structural studies performed since proper tracking of samples was required and outcome measures were objective.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	VLCAD Antibody: Cat# PA5-29959, RRID: AB_2547433, Thermo Fisher Scientific
Validation	The antibody was validated by the manufacturer to interact with the species of protein used in this study (human) based on western blot in a variety of human cell lines (293T, A431, HeLa, and HepG2).