

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
<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 SerialEM 3.7, Schrodinger, Dowser, Dabble 2.7.6, AmberTools18

Data analysis GraphPad Prism 8.0, Modeller 9.23, Phenix 1.17.1, Coot 0.8.9.1, MolProbity 4.5, EMRinger, Chimera 1.14, ChimeraX 0.92, PyMOL 2.3.2, CTFFIND 4, cryoSPARC 2, Relion 3.0, cisTEM 1.0.0, MotionCor2, PropKa, OPM server, VMD 1.9.3

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 generated or analyzed during this study are included in this published article and its Supplementary Information. Crystallographic coordinates and structure factors for the Fab45D8 complex have been deposited in the Protein Data Bank under accession code 6W4V. Coordinates for Fab45D8-FPN complex have been deposited in the Protein Data Bank under accession code 6W4S and the maps have been deposited in the Electron Microscopy Data Bank under accession code 21539. Coordinates for the FPN-Co2+-hepcidin-Fab45D8 complex have been deposited in the Protein Data Bank under accession code 6WBV and the maps have been deposited in the Electron Microscopy Data Bank under accession code 21599.

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](https://www.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 prior sample size calculation was performed. For biochemical experiments, we used a sample size of >3 to control for biological variance typical in biochemical assays.
Data exclusions	Single outlier datapoints in the fluorescence polarization experiments were excluded if they were >50% different than other replicates. These did not change the overall fit Kd values significantly. This exclusion criteria was pre-established.
Replication	Biochemical assays were replicated with n>3. The structural biology approaches represent ensemble averages, and the individual experiments were not repeated. Data processing approaches were replicated and assessed with well-established approaches as outlined in the Methods section.
Randomization	Randomization was not relevant to the experiments in our study as the assays don't have unknown covariates.
Blinding	Blinding was not relevant to the experiments in our study since no subjective allocation was involved.

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		Methods	
n/a	Involved in the study	n/a	Involved in the study
☐	☒ Antibodies	☒	☐ ChIP-seq
☐	☒ Eukaryotic cell lines	☒	☐ Flow cytometry
☒	☐ Palaeontology	☒	☐ MRI-based neuroimaging
☒	☐ Animals and other organisms		
☒	☐ Human research participants		
☒	☐ Clinical data		

Antibodies

Antibodies used	Fab45D8 was expressed in Expi293 cells and purified to homogeneity using recombinant DNA
Validation	Validation was primarily by size exclusion chromatography to directly assess binding of purified antibody to purified ferroportin.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Sf9 insect cells (Expression Systems) and Expi293 cells (ThermoFisher)
Authentication	None of the cell lines were authenticated.
Mycoplasma contamination	Cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study.