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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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Cryo-EM data was carried out with SerialEM 3.7
Data analysis	Microscale Thermophoresis data analysis was done with MO Control software provided by (NanoTemper, Munich, Germany) Multi-angle light scattering (MALS) data analysis was carried out using ASTRA V Cryo-EM data analysis was done with MotionCor2, CTFFIND4, RELION 3.0, cisTEM 1.0.0., Gautomatch v0.56, Gctf v1.18, ROME 1.1.2 package, Coot-0.8.9.2, Chimera1.13.1, Pymol 2.3.1 Phyre2 server http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index Thermal Shift assay data was analyzed with Protein Thermal ShiftTM Software (Thermo Fisher Scientific) Adobe Photoshop software for image processing Statistical analysis were performed using MS Excel and GraphPad Prism 7 All references are given in the Material and Methods section

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 upon request. 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

The cryo-EM map has been deposited in the Electron Microscopy Data Bank under the accession number EMD-0476. The atomic coordinates have been deposited in the Protein Data Bank under the accession number 6NPY.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-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 predetermine sample sizes.
Data exclusions	No data were excluded.
Replication	All experiments were confirmed with multiple biological replicates as detailed in Methods or Figure Legends
Randomization	No randomization was performed.
Blinding	No blinding is used.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All data can be obtained from the corresponding author upon reasonable request.

Antibodies

Antibodies used	anti-human NLRP3 antibody (Adipogen, Cat no: AG-20B-0014-C100), anti-mouse caspase-1 antibody (Adipogen, Cat. no: AG-20B-0042-C100), anti-FLAG F1804-Sigma, Anti-NEK7 antibody [EPR4900] Abcam, anti-ASC Cell Signaling Technology, Cat. no: 67824S, Goat anti-rabbit (H+L) Alexa Fluor 647 HRP conjugated, Thermo Fischer Scientific, Cat. no: A- 21245, Anti-β-actin (mouse monoclonal, Santa Cruz Biotechnology, Cat. no: 47778)

Validation	All the commercial antibodies were verified by the manufacturers according to immunoblots and/or images on their websites.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	NLRP3 KO iBMDM was a kind gift by Kate Fitzgerald and NEK7 KO iBMDM by Gabreil Nunez HEK293T (ATCC) https://www.atcc.org/en/Products/All/CRL-3216.aspx SF9 cells from Thermo Fischer Scientific https://www.thermofisher.com/order/catalog/product/11496015 BL21(DE3) from Agilent https://www.agilent.com/en/product/protein-expression/competent-cells-for-routine-protein-expression/general-protein-expression/bl21(de3)-competent-cells-232943
Authentication	Cell lines were verified by manufacturer's website and Identity of these cell lines were frequently checked by their morphological features HEK293T (ATCC) https://www.atcc.org/en/Products/All/CRL-3216.aspx SF9 cells from Thermo Fischer Scientific https://www.thermofisher.com/order/catalog/product/11496015 BL21(DE3) from Agilent https://www.agilent.com/en/product/protein-expression/competent-cells-for-routine-protein-expression/general-protein-expression/bl21(de3)-competent-cells-232943
Mycoplasma contamination	All cell lines were tested to be mycoplasma-negative by PCR.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines are used in this study.