nature portfolio

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Last updated by author(s): Jul 31, 2022

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	TA NANO-ITC SV microcalorimeter, Andor Revolution-XD high-speed rotary disctype fluorescence confocal microscope, PerkinElmer microplate reader Victor X3, Tanon 5200Multi Chemiluminescent Imaging System, AB SCIEX QTRAP 6500+ LC-MS/MS System, Agilent 1260 infinity II for HPLC with a C18 reversed-phase column and a UV detector, LightCycler 96 thermocycler, Biotek Epoch Microplate Reader
Data analysis	Microsoft Excel 2019, Prism Graphpad 7.0, Primer premier 5.0, Tanon gel analysis 2.30, NanoAnalyze_3.4, AlphaFold2, POCASA v1.1, AutoDock4, AutoDock Vina v1.1.2, PyMOL v2.5.2, LigPlot+ v2.2.4, Perkinlmer 2030 Workstation 4.0, clustalX v1.81, MEGA 7.0.26, Cluspro 2.0, ImageJ v1.52a

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 data that support the findings of this study are available within the article and its Supplementary Information and Supplementary Data, and are also available from the corresponding author upon request. The source data underlying Figs. 1, 2b, d, 3, 4a-f, i-k and 5a, h, k-m and Supplementary Figs. 1, 3-5, 7-11, 13, 16, 17, 19, 22 and 24 are provided as a Source Data file.

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 calculation was performed. We used 3-5 biological replicates for in vitro experiments as that is standard practice for most biochemical or microbiological assays. Mouse virulence assays and in vivo competition assays were conducted twice with at least 4 mice (n ≥ 4) in each infection group, and the combined data for the two experiments were used for statistical analysis, according to the method by Jiang et al. (Nat. Commun. 2021, 12:879).
Data exclusions	No data were excluded from the analyses.
Replication	Mouse virulence assays and in vivo competition assays were performed in two independent experiments, with 4–5 mice/group/experiment. All other experiments were performed for at least 3 times. All the attempts at replication were successful.
Randomization	All animals used were age, sex and vendor matched. Animals were randomly allocated to each group.
Blinding	Investigators were not blinded during data collection or analysis since there was not 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
☒	☐ 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	Purified His6-SipB, His6-SipC and His6-SopB were used to raise rabbit specific antibodies and the respective antibodies were affinity purified using Protein A Sepharose (GE Healthcare). Rabbit anti-ICDH is a kindly gift from Dr. ZQ. Luo in Purdue University and was described in: Xu, L. et al. Inhibition of host vacuolar H+-ATPase activity by a Legionella pneumophila effector. PLoS Pathog. 6, e1000822 (2010). Commercial antibodies used are listed as below: Mouse anti-His (Abways, Shanghai, China, cat# AB0002), 1:5,000; Mouse anti-HA (Abways, Shanghai, China, cat# AB0004), 1:5,000; Goat anti-Mouse horseradish peroxidase-conjugated secondary antibodies (DIYIBIO, China, cat# DY60203), 1:10,000; Goat anti-Rabbit horseradish peroxidase-conjugated secondary antibodies (DIYIBIO, China, cat# DY60202), 1:10,000.
Validation	The homemade antibodies have been validated by our lab using appropriate positive and negative controls. The antibodies obtained commercially have been validated by the manufacturers. Antibody, catalogue number, manufacturer information for commercial antibodies: -Mouse anti-His (Abways, Shanghai, China, cat# AB0002): http://www.abways.com/showproduct.asp?cid=AB0002 -Mouse anti-HA (Abways, Shanghai, China, cat# AB0004): http://www.abways.com/showproduct.asp?cid=AB0004 -Goat anti-Mouse horseradish peroxidase-conjugated secondary antibodies (DIYIBIO, China, cat# DY60203): http://www.diyibio.com/goods.php?id=815 -Goat anti-Rabbit horseradish peroxidase-conjugated secondary antibodies (DIYIBIO, China, cat# DY60202):http://www.diyibio.com/goods.php?id=770

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Human colonic epithelial Caco-2 cells were obtained from the Procell Life Science & Technology Co., Ltd. (cat# CL-0050, Wuhan, China).
Authentication	Cell lines were authenticated by short tandem repeats (STR) DNA profiling analysis in the Procell Life Science & Technology Co., Ltd. (Wuhan, China).
Mycoplasma contamination	The cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used in this study.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Six-week-old female BALB/c mice were used in this study.
Wild animals	No wild animals were used in the study.
Field-collected samples	No field-collected samples were used in the study.
Ethics oversight	All mouse experimental procedures were performed in accordance with the Regulations for the Administration of Affairs Concerning Experimental Animals Approved by the State Council of the People's Republic of China. The protocol was approved by the Animal Welfare and Research Ethics Committee of Northwest A&F University (protocol number: NWAFUSM2018001).

Note that full information on the approval of the study protocol must also be provided in the manuscript.