nature portfolio

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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	No software was used for data collection.
Data analysis	GraphPad Prism Software, v10.2.3 ImageStudio for western blots FIJI for immunofluorescence quantifications MacVector was used to analyze sanger sequencing results AlphaFold3, PROPKA, PDB2PQR, APBS, and ChimeraX were used to evaluate the electrostatic potential of GBP1 and the solvent-accessible molecular surface MUSCLE v3.8.31, SeaView v5.0.5, RAxML v8.2.12, and iTOL v7.1 were used to generate phylogenetic tree of IFIT protein sequences R Studio v4.1.1, tximport v1.22.0, DESeq2 v1.34.0, OrthoFinder v2.5.2, pheatmap v1.0.12, and Phyper were used to analyze transcriptomic data for cell line stimulated with IFNb

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 transcriptomic dataset has been deposited to NCBI under the accession code PRJNA1255723. The following genomes were used as the reference to analyze the transcriptomics data: GCF_000325575.1 (Pteropus alecto), GCF_027574615.1 (Eptesicus fuscus), and GCF_000001405.40 (Homo sapiens). The raw transcriptomic data generated in this study are provided in the 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	*Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used.* *Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected.* *Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.*
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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	In vitro experiments had n>/= 3 replicates were used to enable statistical testing, The exact samples sizes can be found in the associated figure legends.
Data exclusions	*Describe any data exclusions. If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Replication	All in vitro experiments were performed at least 3 times for replication purposes, with replicates described in the associated figure legends.
Randomization	All in vitro samples were organized based on treatment and/or transfection and/or infection.
Blinding	Not applicable as no aspect of any experiment performed was subject to interpretation of the analyst.

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[x]	[ ] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used

1/1000 V5 (Abcam, #ab27671)
1/1000 or 1/200 STAT1 (BioRad, #P02-5B7)
1/1000 or 1/200 pSTAT1-Y701 (Cell Signaling Technology, #9167S)
1/1000 or 1/200 STAT2 (Cell Signaling Technology, #72604S)
1/1000 or 1/200 pSTAT2-Y690 (Cell Signaling Technology, #88410S)
1/1000 VSV-M (Kerafast, #EB0011)
1/1000 MERS-CoV N (Sino Biological, #40068-RP01-200)
1/1000 SARS-CoV-2 N (Thermo Scientific, #MA1-7403)
1/1000 Influenza A NP (Invitrogen, #PA5-32242)
1/1000 or 1/200 FLAG (Sigma-Aldrich, #F1804-200UG)
1/100 GAPDH (EMD Millipore, #MAB374)
1/5000 ACTB (Abcam, #ab8227)
1/10,000 DAPI (Thermo Scientific, #62248)
1/10,000 Goat anti-mouse IRDye680 or IRDye 800 (Licor Biosciences, #926-68070 or #926-32210)
1/10,000 Donkey anti-rabbit IRDye680 or IRDye 800 (Lior Biosciences, #926-68073 or #926-32213)
1/500 Goat anti-mouse AlexaFluor488 (Thermo Scientific, #A32728)
1/500 Goat anti-rabbit AlexaFluor594 (Thermo Scientific, #A32740)

Validation

All antibodies were validated by the manufacturer by western blot and/or immunoflourescence. Information on validation can be found on the manufacturer's website by entering in the catalog number.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

PaKiT03 cells were sourced from Dr. Linfa Wang. Efk3B cells were generated by Dr. Arinjay Banerjee during his PhD. A549 and HEK293T cells were sourced from Dr. Vikram Misra. Huh7 and A549-ACE2 cells were sourced from Dr. Che Colpitts. RPTEC-hTERT (#CRL-4031) and Vero76 cells (#CRL-1587) were sourced from ATCC. Drosophila S2 cells (#R69007) were sourced from Thermo Scientific. MDCKII cells (#00062107) were sourced from Sigma-Aldrich

Authentication

Cell lines in the laboratory are periodically authenticated by cytochrome B sequencing.

Mycoplasma contamination

All cell lines were tested regularly for Mycoplasma contamination and were negative.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used in this study.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*