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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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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.
x	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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
x	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
x	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 <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
	Our web collection on statistics for biologists contains articles on many of the points above.

Our web collection on <u>statistics for biologists</u> 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

Bioinformatics analysis of microarray data

Publicly available data were downloaded from the GEO database (GSE42405, https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi? acc=GSE42405) and then standardized and calibrated, and the log-expression matrix was extracted from MAList with R package limma (3.52.2 version). The DEGs were identified with an adjusted p-value < 0.05, absolute log2 fold-change > 1, and plotted with the R package ggplot2 (v3.3.6). Gene Ontology (GO) enrichment analysis of the upregulated DEGs was performed using the R package clusterProfiler (v4.4.4). Heat maps were generated using the pheatmap package (v1.0.12). Code to perform analysis of microarray data is available on GitHub [https://github.com/panqiu777/HE-TIPS-used-for-publication/releases/tag/v1.0].

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 raw microarray data in this study were retrieved from Gene Expression Omnibus (accession code GSE42405[https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE42405]). Source data are provided with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation)</u>, <u>and sexual orientation</u> and <u>race</u>, <u>ethnicity and racism</u>.

Reporting on sex and gender	No human participants are involved in this study.
Reporting on race, ethnicity, or other socially relevant groupings	No human participants are involved in this study.
Population characteristics	No human participants are involved in this study.
Recruitment	No human participants are involved in this study.
Ethics oversight	No human participants are involved in this study.

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 selec	one below that is the best fit for your research. If you are not sure, read the appropri	iate sections before i	making your selectic
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Life sciences Behavioural & social sciences Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see $\underline{\text{nature.com/documents/nr-reporting-summary-flat.pdf}}$

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

In general, no calculations were done to determine sample size. Sample size was chosen based on literature and variability observed in previous experience in the laboratory. In this study, sample size was determined based on the standards for cell experiments attempting to have a minimum of n=3 biological independent samples per study and animal experiments attempting to have a minimum of n=3 biological independent samples per study with sufficient reproducibility. The determination of sample size chosen in our study did not include the high-throughput experiments with big dataset from public database. The details on the sample size were included in each figure legend.

Data exclusions

No data were excluded from the analyses.

Replication

Data are are representative of three independent experiments. All attempts at replication were successful.

Randomization

All cell samples and the animals were randomly allocated to experimental groups. All animal experiments use mice with matched age.

Blinding

All the IHC staining results (Figure 6F, Supplementary Figure 1G) were reviewed independently by two pathologists blinded to the clinicopathological information. The investigators were blinded to group allocation during data collection and/or analysis.

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).

Research	samn	اد

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.

Sampling strategy

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.

Data collection

Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Timing

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.

Data exclusions

If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Non-participation

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.

Randomization

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.

Research sample

Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.

Sampling strategy

Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.

Data collection

Describe the data collection procedure, including who recorded the data and how.

Timing and spatial scale

Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken

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.

Reproducibility

Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.

Randomization

Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.

Blinding

Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

Did the study involve field work?

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Field work, collection and transport

Field conditions

Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).

Location

State the location of the sampling or experiment, providing relevant parameters (e.g., latitude and longitude, elevation, water depth).

Access & import/export

Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority,

(the date of issue, and any identifying information).	
Describe any disturbance caused by the study and how it was minimized.	

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.

system or method listed is rele	vant to your study. If you a	are not sure if a list item applies to your research, read the appropriate section before selecting a response.
Materials & experime	ntal systems	Methods
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		n/a Involved in the study ChIP-seq X Flow cytometry MRI-based neuroimaging
Antibodies		
Antibodies used Anti-His-tag (Cat# 66005-1-Polyclonal anti-FUT8 (Cat# a ab85054), anti-Ubiquitin (linform Abcam (Cambridge, Ul Technology (Danvers, MA, U (Cat# A5243), anti-JAK1 (Cat# A0816), anti-p-IRF3 (Cat# A0816), anti-p-IRF3 (Canti-CLDN-1 (Cat# A2196) a PAB47500), anti-STING (Cat Alanine Aminotransferase (A Cat# E-BC-F038. Bio-AAL wat Prof. Wenzhe Li of Dalian M		1-lg) and anti-Trim40 (Cat# 67073-1-lg) were purchased from Proteintech Group, Inc. (RoSDont, IL, USA). # ab198741), monoclonal anti-NS3 (Cat# ab13830), anti-core (Cat# ab2740), anti-HIV1 gp120 (Cat# (linkage-specific K48) (Cat# ab140601), anti-RIG-I (Cat# ab45428) and anti-VSV-G (Cat# ab309106) were UK). The anti-AKT(Cat# 4691S) and anti-pAKT(Cat# 4060S) antibody was purchased from Cell Signaling , USA). Anti-GAPDH (Cat#AC002), anti-EGFR (Cat# A11351), anti-p-EGFR-Y1068 (Cat# AP0301), anti-SNAIL Cat# A18323), anti-p-JAK1 (Cat# AP0530), anti-STAT3 (Cat# A11216), anti-p-STAT3 (Cat# AP0705), anti-IRF3 (Cat# AP0623), anti-SARS-CoV-2 Spike S (Cat# A20136), anti-CD81 (Cat# A5270), anti-OCLN (Cat# A2601), and anti-SR-B1 (Cat# A0827) antibodies were purchased from ABclonal (Wuhan, China). Anti-cGAS (Cat# at# RMAB50052), and anti-p-STING (Cat# PAB47864-P) were purchased from Bioswamp (Wuhan, China). (ALT/GPT) activity fluorometric assay kit was obtained from Elabscience Biotechnology Co., Ltd., China, was purchased from Vector Laboratories (Burlingame, CA, Cat# B-1395). Biotin-AOL was kindly provided by Medical University, China (TCI, Japan, Cat# A2659). but were used at a dilution of 1:1000~1:2000. AOL for lectin blot was used at a dilution of 1:5000.
Validation All of the antibodies in the s application in our experiment		e study were bought commercially. We provided the validation of the antibodies for the species and nents.
Eukaryotic cell lin	es	
Policy information about <u>ce</u>	ell lines and Sex and Ger	der in Research
Cell line source(s)	· · · · · · · · · · · · · · · · · · ·	HEK293T and HeLa cells were maintained in our laboratory, WT/FUT8KO HEK293 cells were given by Dr. Uiangnan University. References for these cell lines have been provided in the main text.
Authentication	All the cells were	authenticated using short-tandem repeat profiling.

Palaeontology and Archaeology

Specimen provenance

(See <u>ICLAC</u> register)

Mycoplasma contamination

Commonly misidentified lines

Disturbance

Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.

Specimen deposition

Indicate where the specimens have been deposited to permit free access by other researchers.

All cell lines were tested negative for mycoplasma contamination.

No commonly misidentified cell lines were used in the study.

Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.	
Tick this box to confir	m that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance on the study protocol, OR state that no ethical approval or guidance o		
Note that full information on t	the approval of the study protocol must also be provided in the manuscript.	
Animals and other	or recearch organisms	
	tudies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in	
Laboratory animals	Male C57BL/6J mice and ICR mice (6-8 weeks old) were obtained from Center for Animal Experiments at Wuhan University. All mice were kept under specific-pathogen free conditions in Animal Facility of Center for Animal Experiments at Wuhan University. They were kept in an animal room with a 12-h light-dark cycle at a temperature of 20-25 °C with 40-60% humidity.	
Wild animals	No wild animals were used in the study.	
Reporting on sex	In the case of virus infection mice models, male mice were used since male mice are not subject to hormonal cycles.	
Field-collected samples No field collected samples were used in the study.		
Ethics oversight All animal experiments were approved by the Center for Animal Experiments at Wuhan University (No. S01319070T). All mice we specific pathogen free and housed under controlled temperature and light conditions following institutional animal care guidelin.		
Clinical data Policy information about <u>cl</u> All manuscripts should comply	linical studies v with the ICMJEguidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.	
Clinical trial registration	Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.	
Study protocol	Note where the full trial protocol can be accessed OR if not available, explain why.	
Data collection	Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.	
Outcomes	Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.	
Dual use research	n of concern	
Policy information about <u>d</u>	ual use research of concern	
Hazards		
Could the accidental, del	iberate or reckless misuse of agents or technologies generated in the work, or the application of information presented a threat to:	
No Yes		
Public health		
National security		
Crops and/or lives	tock	
Ecosystems		

Any other significant area

Experiments of concern

Doe	s the work involve any of these experiments of concern:
No	Yes
	Demonstrate how to render a vaccine ineffective
	Confer resistance to therapeutically useful antibiotics or antiviral agents
	Enhance the virulence of a pathogen or render a nonpathogen virulent
	Increase transmissibility of a pathogen
	Alter the host range of a pathogen
	Enable evasion of diagnostic/detection modalities
	Enable the weaponization of a biological agent or toxin
	Any other potentially harmful combination of experiments and agents

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.

ChIP-seq

Data deposition

Confirm that both raw and final processed data have been deposited in a public database such as GEO.

Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

May remain private before publication.

For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.

Files in database submission

Provide a list of all files available in the database submission.

Genome browser session (e.g. <u>UCSC</u>)

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates

Describe the experimental replicates, specifying number, type and replicate agreement.

Sequencing depth

Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.

Antibodies

Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.

Peak calling parameters

Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files

Data quality

Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.

Software

Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

Flow Cytometry

Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- x The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- 🗶 All plots are contour plots with outliers or pseudocolor plots.
- 🗶 A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation

The Huh 7 cells were infected with HCV (MOI = 10) for indicated time. And then cells were gently scraped off the bottom of the cell dish into the PBS using a cell scraper. For cell-surface staining, cell suspensions were washed twice in PBS and stained with indicated antibodies for 30 min on ice and washed with PBS. For intracellular staining, the cells were fixed using fixation buffer (Cat# 420801; BioLegend, San Diego, CA) and permeabilized using the Perm Wash Buffer (Cat# 421002; BioLegend, San Diego, CA).

Instrument

CytoFlex (Beckman)

Software

FlowJo_V10

Cell population abundance

No cell sorting was performed in the study.

Gating strategy

For all experiments, cells were first gated by FSC/SSC to exclude debris. Then, target positive cell population for further analysis were gated by cell surface or intracellular staining (e.g. E2/EGFR). For surface marker and intracellular staining, isotype control antibodies were used to define background and non-specific binding signal.

 $\boxed{\mathbf{x}}$ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type

Indicate task or resting state; event-related or block design.

Design specifications

Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.

Behavioral performance measures

State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)

Specify: functional, structural, diffusion, perfusion.

Field strength

Specify in Tesla

Sequence & imaging parameters

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.

Area of acquisition

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Diffusion MRI

Used

 $ec{\;\;\;\;}$ Not used

Preprocessing

Preprocessing software

Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

Normalization

If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.

Normalization template

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.

Noise and artifact removal	fact removal Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).				
Volume censoring	Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.				
Statistical modeling & infe	rence				
Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).				
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.				
Specify type of analysis:	Whole brain	ROI-based Doth			
Statistic type for inference Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.					
(See Eklund et al. 2016)					
Correction Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Correction)		of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).			
Models & analysis					
n/a Involved in the study Functional and/or effect Graph analysis Multivariate modeling of	,				
		Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).			

Multivariate modeling and predictive analysis

Graph analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency,