nature portfolio

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Corresponding author(s): instead of author names.

Last updated by author(s): YYYY-MM-DD

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>.

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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. <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>
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes	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

Immunohistochemical images were acquired using the Olympus BX-53F microscope (Olympus, Japan). Immunofluorescence images were acquired using a confocal microscopy (Olympus, FV1000, Japan) or a confocal microscope (Leica, SP8, USA). Flow cytometry data was collected using FACS Calibur system (BD Biosciences, USA). Electron microscopy images were acquired using a transmission electron microscope (TEM, HITACHI HT7700, Japan). Serum creatinine (Cr) and blood urea nitrogen (BUN) concentrations were determined using an auto-analyzer (Beckman DXC600, USA). qPCR data was collected using Real-Time Quantitative PCR Instrument(7500, Fast).

Data analysis

Image analysis was performed using Image J software(version 1.53,USA) and specific pipelines are described in the Methods section. Statisticl analysis was performed using GraphPad Prism version 8.0 (GraphPad, USA).

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 <u>guidelines for submitting code & software</u> 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

All the data of this study are available within the article, the Supplementary Information file, and the Source data file. Source data are provided with this study.

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</u> and <u>racism</u>.

Reporting on sex and gender

- $oxed{1}$. The sex of the animals involved has been included in the Methods and Materials section as appropriate.
- 2. Regarding the study involving human renal tissue, sex and/or gender were not considered in the study design. This information is now clearly mentioned in the respective section.

Reporting on race, ethnicity, or other socially relevant groupings

All patients were Chinese.

Population characteristics

Patients with IgA nephropathy or thin basement membrane nephropathy (TBMN) (6 patients were less than 30 years old and 6 patients were over 66 years old). Eight patients who were diagnosed as IgA nephropathy or TBMN without tubular injury were designated as the control group. Nine patients who were diagnosed as acute tubular necrosis were designated as the injury group. The characteristics of the population have been provided in the manuscript in detail.

Recruitment

All human kidney biopsy samples were obtained from Department of Nephrology Nanfang Hospital from 2012-2018.

Ethics oversight

Institutional Animal Care and Use Committee of Southern Medical University. Institutional Review Board of Nanfang Hospital.

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	vour research. If you are not sure.	read the appropriate sections	before making your selection.
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X 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

The number of samples for each assay was indicated in each figure legend. For in vitro cellular and biochemical assays, the sample sizes (at least three biological replicates) were chosen. These assays yielding statistically significant difference between experimental positive and negative controls and on similar sample sizes. Results are representatives of at least three biological replicates. For in vivo assays, 6-8 mice were chosen for each condition, this sample size was determined by using power calculation for a t-test difference between two independent means based on a normally distributed population with equal variance.

Data exclusions

No data excluded.

Replication

The number of replicates are indicated in the figures and/or figure legends.

Randomization

All experiments are randomized.

Blinding

All experiments are blinding.

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,

Study description State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic Research sample 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. Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to Sampling strategy 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. If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the Data exclusions rationale behind them, indicating whether exclusion criteria were pre-established. State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no Non-participation

Ecological, evolutionary & environmental sciences study design

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if

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

Randomization

Field conditions

Location

participants dropped out/declined participation.

allocation was not random, describe how covariates were controlled.

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, Study description 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 If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, Data exclusions 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. Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were Randomization 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? Field work, collection and transport

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

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

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

Access & import/export	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).

Disturbance

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.

Materials & experime	ntal systems	Methods
n/a Involved in the study		n/a Involved in the study
Antibodies		ChIP-seq
Eukaryotic cell lines		Flow cytometry
Palaeontology and a	rchaeology	MRI-based neuroimaging
Animals and other o	rganisms	
Clinical data		
Dual use research of	concern	
⊠ Plants		
Antibodies		
Antibodies used	WB antibodies:	
	, , ,	91137S, USA)?Collagen I (1:200, Boster, BA0325, China), Fibronectin (1:200, Abcam, ab268020, USA) 300, USA) , p16 (1:1000, Cell-Signaling, 18769S, USA), p21 (1:1000, Cell-Signaling, 37543S, USA), p53
		S, USA), AQP-1 (1:1000, 20331-AP, Proteintech, China), β-Actin (1:3000, Proteintech, 66009-1, China),
		:-376230, USA), VDAC1 (1:1000, Abcam, ab14734, USA), Calnexin (1:1000, Cell-Signaling, 2679S, USA), . 4272S, USA), MCU (1:1000, Cell-Signaling, 14997S, USA), GAPDH (1:3000, Proteintech, 60004-1, China),
		A0325, China), α-SMA (1:1000, Sigma-Aldrich, A5228, USA)?β-Actin (1:3000, Proteintech, 66009- 1,
	China).	
	IF antibodies:	
	, , ,	91137s, USA), TOM20 (1:200, Proteintech, 11802-1-AP, China), p21 (1:1000, Cell-signaling, 37543s, USA), 0333-1-AP, China), Jaminin (1:250, Sigma-Aldrich, L9393, USA), CD31 (1:1000, Cell-signaling, 77699s,
	, ,	usss-1-AP, Crima) , idminin (1:250, Sigma-Aidrich, 19393, USA), CD31 (1:1000, Ceil-Signainig, 776998, gnaling, 776998, 20886-1-AP, China) .
	IIIC antibadian	
	IHC antibodies: Panx1 (1:200, Cell-Signaling,	91137S, USA) ©Collagen I (1:200, Boster, BA0325, China), Fibronectin (1:200, Abcam, ab268020, USA).
Validation	provided on the manufacture	been validated by westen blot, immunofluorescence or immunohistochemistry,etc, these data were er's website.
Eukaryotic cell lin	es	
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Policy information about ce Cell line source(s)	ell lines and Sex and Gende	er in Research oular cells (HK-2) and normal rat kidney interstitial fibroblasts (NRK-49F) were obtained from the

American Type Culture Collection(ATCC). The Panx1 knock out HK-2 cell line was produced by Vigene Biosciences (China) Authentication All cell lines have been authenticated. Mycoplasma contamination No contamination. Commonly misidentified lines There were no commonly misidentified cell lines were used in the study. (See <u>ICLAC</u> register)

Palaeontology and Archaeology

Specimen provenance

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.

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 was required and explain why not.			
Note that full information on t	the approval of the study protocol must also be provided in the manuscript.			
Animals and othe	er research organisms			
	tudies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in			
Laboratory animals	This study used male C57BL/6 mice and Panx1 knock out mice that were 8-12 weeks old and weighed 20-25g. The mice were obtained from the Guangdong Medical Laboratory Animal Center in Guangdong, China.			
Wild animals	No wild animals were used in this study.			
Reporting on sex	In general, the reason for using male mice in animal experiments is to avoid interference with the female estrous cycle. Additionally, since female hormones can affect the fibrosis progression resulting in variations. Therefore, only male mice were used in our animal studies.			
Field-collected samples	No Field-collected samples were used.			
Ethics oversight Ethical review was conducted, and all animal experiments were approved by the Institutional Animal Care and Use Comm Southern Medical University.				
Clinical data Policy information about cl				
All manuscripts should comply	with the ICMJE guidelines 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			
	ual use research of concern			
Hazards				
	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			
Any other signification	ant area			
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Doe	Does 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 For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data. May remain private before publication. Provide a list of all files available in the database submission. Files in database submission Genome browser session Provide a link to an anonymized aenome browser session for "Initial submission" and "Revised version" documents only, to (e.g. UCSC)

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

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

Cell cycle analysis: The HK-2 cells were seeded into 60-mm dishes and allowed to adhere for 24 h before adding adeno virus. Sample preparation

After 48 h, the samples were prepared for cell cycle analysis using the Cell Cycle Kit according to the manufacturer's instructions.

FACS Calibur system (BD Biosciences, USA) Instrument

FlowJo Software (10.5.3) Software

Cell population abundance No sort was performed in the study.

Initial cell populations were gated using FSC and SSC plots of unstained cell control sample to remove cell debris. Doublets Gating strategy and cell aggregates were excluded by gating in single cells (FL2-1 vs. FL2-W) in cell cycle analysis: The cell population gated in

after debris and exclusion were then used to create single-staining histograms (cell cycle based on PI).

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 anale.

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

Not used
 ■ 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

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 ana/or method and criteria for volume censoring, and state the extent of such censoring.						
Statistical modeling & inference	e						
	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	e brain ROI-based Both						
Statistic type for inference Spe	ecify 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 Carlo).						
Models & analysis							
n/a Involved in the study							
Functional and/or effective connect	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).						
Graph analysis	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, etc.).						
Multivariate modeling and predictiv	e analysis Specify independent variables, features extraction and dimension reduction, model, training and evaluation						

metrics.