nature portfolio

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Last updated by author(s): Oct 31, 2025

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

The frozen sample was taken out to a 1.5 ml centrifuge tube and 300 µl of a lysate containing a protease inhibitor was added. Ultrasonic disruption on ice, centrifugation to remove the supernatant, and repeat the operation once. Acetone was added to the supernatant, and the precipitate was collected by centrifugation at -20 ? overnight. After drying at room temperature, it is dissolved in SDS, and the mixture is centrifuged at room temperature, and the supernatant is centrifuged, and the operation is repeated once. The supernatant is the total protein solution of the cells, and the protein is quantified by BCA, and the enzymatic hydrolysis is carried out by the FASP method. After enzymatic hydrolysis, the peptide was dissolved in 0.1% TFA and desalted using a RP-C18 solid phase extraction column.
The hydrolyzed products were analyzed by LC-MS/MS, and each sample was analyzed three times. Separation was carried out using a nanoliter flow rate HPLC liquid phase system (EASY-nLC1000). The digested product was separated and analyzed using an LTQ Orbitrap Velos Pro mass spectrometer. The first- and second-stage mass spectra were collected using profile and centroid methods to reduce the data file size.
The original file of the library LC-MS/MS was searched using Maxquan software for analysis. The uniprot database and the protein information were further analyzed by MaxQuant software, and the identification ratio was calculated from all the identified peptides. Further use the OmicsBean cloud platform to screen the differential proteins for gene function annotation (GO), analyze the subcellular localization of differential proteins, molecular functions and specific functions of biology; then perform differential protein analysis by KEGG to analyze protein expression.

Data analysis	The original file of the library LC-MS/MS was searched using Maxquan software for analysis. The uniprot database and the protein information were further analyzed by MaxQuant software, and the identification ratio was calculated from all the identified peptides. Further use the OmicsBean cloud platform to screen the differential proteins for gene function annotation (GO), analyze the subcellular localization of differential proteins, molecular functions and specific functions of biology; then perform differential protein analysis by KEGG to analyze protein expression. The signal path that may be involved in the function.

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 label free proteomic data has been uploaded to iProX database (Project ID: IPX0011230000). All other data are presented in manuscript or the supplemental complete materials and methods. Please request material sharing associated with this study from the corresponding author Yi Li (liyisn@med.uestc.edu.cn).

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	Demographic information of patients was collected, including age and sex. Sex and gender were not considered in the study design. And sex and/or gender of participants was not determined based on self-report or assigned.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, or other socially relevant groupings were not considered in the study design. And participants wit race,ethnicity, or other socially relevant grouping were not determined based on self-report or assigned.
Population characteristics	Patients who admitted in Nephrology Department of Sichuan Provincial People's Hospital during June to December, 2018 were included in this study. Patients who admitted in Nephrology Department of Sichuan Provincial People's Hospital during June to December, 2018 were included in this study. Patients with confirmed diagnosis of end stage kidney disease (defined as eGFR<15 mL/min/1.73 m2) at admission were excluded. Demographic information of patients was collected, including age and sex. Fast serum samples were taken 48 hours after admission or earlier if needed. The samples were stored at -20 ? before measurements. Kidney biopsies of acute tubular necrosis (ATN) patients were collected with the clinical information showed in Supplementary table 2. Normal renal tissue surrounding tumor (ST) from patients with renal carcinoma were collected as the normal control.
Recruitment	AKI was defined by the Kidney Disease: Improving Global Outcomes (KDIGO) definition as an increase in serum creatinine by > 26.5 µmol/L within 48 h or > 1.5 times baseline within 7 days [1]. At confirmation of AKI, AKI stages were further defined as KDIGO definition: Stage 1: increase in serum creatinine by ≥ 26.5 µmol/L within 48 hours or > 1.5 times baseline within 7 days; Stage 2: increase in serum creatinine by 2 to 2.9 times baseline within 7 days; Stage 3: increase in serum creatinine by ≥ 3.0 times baseline or increase in serum creatinine by > 353.6 µmol/L or initiation of renal replacement therapy (RRT). The baseline creatinine was defined as creatinine level measured at admission. The level of SRP14 in the fast serum samples at diagnosis of AKI was determined using ELISA kit (#ZC-54503, Zhuochai biology, Shanghai, China). Routine indexes were also measured concurrently with the determination of occurrence of AKI, including uric acid, serum albumin, hemoglobin, triglyceride, and total cholesterol. eGFR was calculated using CKD-EPI equation [2]. Patients who developed AKI within 48 hours after admission were included in the AKI group, whereas patients without AKI were included in the control group. [1]Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl. 2:1–138. [2]Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro III AF, Feldman HI et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration): a new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-12.
Ethics oversight	Written informed consents were obtained from patients before conducting any study procedure. All the procedure followed the Declaration of Helsinki and approved by the ethics committee of Sichuan Provincial People's Hospital (No.2018-176 and No. 2018-284).

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

Life sciences study design

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

Sample size	Serum SRP14 was tested in 45 candidates, among which 29 candidates were AKI patients. H&E, PAS staining, and immunohistochemistry measuring SRP14 and RPS7 in human renal tissues. Renal tissue specimens from patients with acute tubular necrosis (ATN) (n = 5) and Normal renal tissue surrounding the tumor (ST) (n = 4) from patients with renal carcinoma were collected. Male wild type C57 BL/6 mice and SRP14-/-, Ggt-Cre mice subjected to clamping bilateral renal arteries with artery clamps at 37 ? for 45 min and reperfusion for 24 hours to establish the murine AKI model induced by IRI. Wild type C57 BL/6 mice and SRP14-/-, Ggt-Cre mice in the sham group subjected to the same procedure without clamp (n = 6). AAV-SRP14 shRNA was delivered into the kidney of C57 BL/6 male mice by intrarenal injection. Some of the mice subjected to intrarenal injection of the hRPS7 recombinant protein injection. The mice subjected to bilateral renal arteries with artery clamps at 37 ? for 45 min and reperfusion for 24 hours to establish the murine AKI model induced by IRI. Mice in the sham group received the same procedure without clamp (n = 6). We respectively treated mice with 25 mg/kg.d and 50 mg/kg.d Nafamostat mesilate upon renal IRI. The mice subjected to clamping bilateral renal arteries with artery clamps at 37 ? for 45 min and reperfusion for 24 hours to establish the murine AKI model induced by IRI (n = 6). Mice in the sham group subjected to the same procedure without clamp (n = 6). CCK-8 determining cell viability for SRP14 and RPS7 silenced HK2 cells upon H/R. Six biologically independent experiments for CCK-8 measurement. Flowcytometry detecting Annexin V-FITC/PI of HK2 cells following H/R treatment. Three biologically independent experiments for Flowcytometry detecting Annexin V-FITC/PI. Western blot measuring SRP14, RPS7, p53, MDM2, cleaved Caspase3, Bax, and beta-actin in HK2 cells with H/R treatment and SRP14 silencing. Three biologically independent experiments for western blot. Screening for RPS7 associated molecule from a compound library involving apoptosis containing 356 FDA-approved compounds.
Data exclusions	Patients who admitted in Nephrology Department of Sichuan Provincial People's Hospital during June to December, 2018 were included in this study. Patients with confirmed diagnosis of end stage kidney disease (defined as eGFR<15 mL/min/1.73 m2) at admission were excluded.
Replication	CCK-8 determining cell viability for SRP14 and RPS7 silenced HK2 cells upon H/R. Six biologically independent experiments for CCK-8 measurement. Flowcytometry detecting Annexin V-FITC/PI of HK2 cells following H/R treatment. Three biologically independent experiments for Flowcytometry detecting Annexin V-FITC/PI. Western blot measuring SRP14, RPS7, p53, MDM2, cleaved Caspase3, Bax, and beta-actin in HK2 cells with H/R treatment and SRP14 silencing. Three biologically independent experiments for western blot.
Randomization	Mice were randomized into control and intervention groups to ensure comparable baseline characteristics.
Blinding	All outcome assessments were performed by investigators blinded to the experimental groups.

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
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	The renal tissue slices were respectively incubated with anti-SRP14 antibody (1:100, #NBP2-94184, Novus, USA) and anti-RPS7 antibody (1:50, #SC-100834, Santa Cruz, USA) at 4 ? overnight. After cleaning, the sections were incubated with appropriate horseradish peroxidase labeled secondary antibody (#K5007, Dako Producs, Denmark) at 37 ? for one hour. The multiplex immunofluorescence staining was performed on 2 μm renal tissue paraffin sections from human and mice by Opal 4 color Manual IHC staining Kit (Akoya Bioscience, USA). Primary antibodies including anti-SRP14 antibody (1:100, #NBP2-94184, NOVUS, USA), anti-RPS7 antibody (1:50, #SC-100834, Santa Cruz, USA), and anti-KIM-1 antibody (1:400, #NBP-43761, NOVUS, USA) were used for multiplex immunofluorescence staining. For immunoprecipitation, 20 μL protein A/G agarose was added to each sample and incubated for 1 h at room temperature. The total cell lysates with 500 μg were immunoprecipitated with RPS7 antibody (#SC-100834, Santa Cruz, USA) or SRP14 antibody (#SC-377012, Santa Cruz, USA) overnight at 4 ?. For western blot analysis, the protein bands were detected using the ?-actin (1:1000, #6008, Proteintech, China) protein levels were used as a loading control. Primary antibodies included SRP14 (1:1000, #NBP2-94184, NOVUS, USA), RPS7 (1:1000, #PA5-77005, Invitrogen, USA), Bax (1:1000, #ab182733, Abcam, Britain), Cleaved Caspase3 (1:1000, #9664s, Cell signaling technology, USA), p53(1:1000, #ab131442, Abcam, Britain), MDM2(1:1000, #ab259265,

	Abcam). The secondary antibodies included HRP-labeled Goat Anti-Rabbit (1:5000, #511203, ZENBIO, China) and HRP-labeled Goat Anti-Mouse (1:10000, #511103, ZENBIO, China).
Validation	All antibodies used are from commercial sources as described. Only antibodies that have been validated by the vendor with in vitro and in situ experiments (for IHC and IF, with images available on the websites) and/or heavily used by the community with publication in several references were used. The validation and references for each are publicly available on the respective vendor websites that can reached via the catalog numbers listed above.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Human renal cortex proximal tubular epithelial cell line HK2 cells were bought from National Collection of Authenticated Cell Cultures (#GNHu47, National Collection of Authenticated Cell Cultures, Shanghai, China).
Authentication	Human renal cortex proximal tubular epithelial cell line HK2 cells were bought from National Collection of Authenticated Cell Cultures (#GNHu47, National Collection of Authenticated Cell Cultures, Shanghai, China).
Mycoplasma contamination	Cell lines were tested for mycoplasma contamination by National Collection of Authenticated Cell Cultures when we received the cells. And the cells were not infected by mycoplasma.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Male C57 BL/6 mice aged from 6 to 8 weeks and weighed from 18 to 22 g were purchased from Chengdu Dossy experimental animals co., LTD (Chengdu, China). Male tubule specific SRP14 knockout (SRP14-/-, Ggt-Cre) mice were obtained by Cyagen biosciences (Suzhou, China).
Wild animals	The study did not involve wild animals.
Reporting on sex	Male C57 BL/6 mice aged from 6 to 8 weeks and weighed from 18 to 22 g were purchased from Chengdu Dossy experimental animals co., LTD (Chengdu, China). Male tubule specific SRP14 knockout (SRP14-/-, Ggt-Cre) mice were obtained by Cyagen biosciences (Suzhou, China).
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animals were housed in the animal center of Sichuan provincial people's hospital under a specific pathogen free condition with a 12-hour light/dark cycle, humidity from 40 % to 70 %, and ambient temperature from 18 to 22 ?. The mice were allowed to freely get food and water. All the animal studies were approved by the ethics committee of Sichuan provincial people's hospital (No.2018-176 and No. 2020-215).

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

Clinical data

Policy information about clinical studies

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	As a small-scale, exploratory prospective analysis, this study was not submitted to a clinical cohort registry.
Study protocol	AKI was defined by the Kidney Disease: Improving Global Outcomes (KDIGO) definition as an increase in serum creatinine by > 26.5 μmol/L within 48 h or > 1.5 times baseline within 7 days [1]. At confirmation of AKI, AKI stages were further defined as KDIGO definition: Stage 1: increase in serum creatinine by ≥ 26.5 μmol/L within 48 hours or > 1.5 times baseline within 7 days; Stage 2: increase in serum creatinine by 2 to 2.9 times baseline within 7 days; Stage 3: increase in serum creatinine by ≥ 3.0 times baseline or increase in serum creatinine by > 353.6 μmol/L or initiation of renal replacement therapy (RRT). The baseline creatinine was defined as creatinine level measured at admission. The level of SRP14 in the fast serum samples at diagnosis of AKI was determined using ELISA kit (#ZC-54503, Zhuochai biology, Shanghai, China). Routine indexes were also measured concurrently with the determination of occurrence of AKI, including uric acid, serum albumin, hemoglobin, triglyceride, and total cholesterol. eGFR was calculated using CKD-EPI equation [2]. Patients who developed AKI within 48 hours after admission were included in the AKI group, whereas patients without AKI were included in the control group. [1] Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl. 2:1–138. [2] Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro III AF, Feldman HI et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration): a new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-12.
Data collection	Demographic information of patients was collected, including age and gender. All the procedure followed the Declaration of Helsinki and approved by the ethics committee of Sichuan Provincial People's Hospital (No.2018-176 and No. 2018-284).

Outcomes	Confirmation of AKI

Plants

Seed stocks	The study did not involve plants.
Novel plant genotypes	The study did not involve plants.
Authentication	The study did not involve plants.

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

Sample preparation	2×105 HK2 cells were seeded into six well plates and respectively transfected with SRP14 siRNA and RPS7 siRNA before hypoxia/reoxygenation.
Instrument	Becton Dickinson FAC Sort cytometer (For Annexin V, excitation: 633 nm; emission, 660 nm. For Propidium Iodide, excitation: 488 nm; emission, 580 nm.)
Software	Becton Dickinson FAC Sort cytometer (For Annexin V, excitation: 633 nm; emission, 660 nm. For Propidium Iodide, excitation: 488 nm; emission, 580 nm.)
Cell population abundance	BD FACSDiva Software
Gating strategy	For Annexin V, excitation: 633 nm; emission, 660 nm. For Propidium Iodide, excitation: 488 nm; emission, 580 nm.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.