

Reporting Summary

Nature Research 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 Research policies, see [Authors & Referees](#) 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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

Microscopic data: Nikon microscope (Eclipse Ti-E, Nikon) operated by Metamorph(Molecular devices, version 7.10.3.279), CQ1 (Yokogawa) operated by CQ1 software (Yokogawa, version 1.05.01.01), FV3000 confocal microscope (Olympus) operated by FV31S-SW(version 2.3.1.163), IX81 widefield fluorescence microscope (Olympus) operated by Metamorph (Molecular devices, version 7.8.10.0), FV1000-D(Olympus)operated by FV10-ASW(version 04.02), LSM 800 (Carl Zeiss) operated by Zeiss ZEN Blue 2.6 software.
Immunoblotting data: ChemiDoc Touch Imaging System (Bio-Rad)
qPCR:ABI 7900HT RT-PCR system (Applied Biosystems), QuantStudio7(Applied Biosystems).

Data analysis

Statistical analysis: GraphPad Prism 8
Immunofluorescence staining and immunohistochemistry staining analysis: Fiji(Version 2.0.0-rc-69/1.52p), Cell Profiler(version 3.1.9)

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [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 list of figures that have associated raw data
- A description of any restrictions on data availability

Data supporting the findings of this study are available from the corresponding author on reasonable request. Source data are provided with this paper.

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	The sample size used in this study was determined based on the expense of data collection, and the need to have sufficient statistical power.
Data exclusions	No samples were excluded from analysis.
Replication	All experiments were repeated independently multiple times to ensure reproducibility of the experimental outcomes as detailed in the figure legends.
Randomization	Randomization was not relevant for cell culture study, because all cells used in this study had to be differently treated and analyzed in parallel to minimize experimental variation. Mice were randomized to receive treatments as described.
Blinding	For live imaging, data acquisition was efficiently blinded because phenotypes were not visible at the starting time point. For fixed cell imaging, cells were selected for imaging based on channel (e.g. DAPI) other than the channel used for the quantification. Cells for Western Blots were not collected or processed blindly, since knowledge of each sample identity is necessary for data generation. In all quantitative analyses of mouse histologic staining, at least 10 high-power fields were reviewed for each tissue in a blinded manner.

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
☐	☒ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used

The following antibodies and dilutions were used in this study:
 anti-Galectin 3 (rat, Santa Cruz Biotechnology, sc-23938, 1/1000),
 anti-LAMP1 (mouse, Santa Cruz Biotechnology, sc-19992, 1/2000),
 anti-LC3(rabbit, MBL, PM036, 1/1000),
 anti-ATG16L1 (rabbit, CST, #8089, 1:2000)
 anti-TFEB (rabbit, Cell Signaling Technology, #4240, 1/1000),
 anti-phospho Ser211TFEB (rabbit, Cell Signaling Technology, #37681, 1/1000),
 anti-14-3-3(rabbit, Cell Signaling Technology, #8312, 1/1000),
 anti-phospho S6K (rabbit, Cell Signaling Technology, #9205, 1/1000),
 anti-S6K (rabbit, Cell Signaling Technology, #9202, 1/1000),
 anti-phospho GSK alfa beta rabbit, Cell Signaling Technology, #9331, 1/1000),
 anti-GSK beta rabbit, Cell Signaling Technology, #9336, 1/1000),
 anti-PPP3CB (rabbit, OriGene, TA308439, 1/1000),
 anti-p62 (rabbit, MBL, PM045, 1/5000),
 anti-GAPDH (rabbit, Cell Signaling Technology, #2118, 1/20000),
 anti-LaminB (goat, SantaCruz, sc-6217, 1/1000),
 anti-TOMM20(rabbit, abcam, ab78547, 1/1000),
 anti-UQCRC1 (complexIII core subunit1) (mouse, Invitrogen, 459140, 1/1000),
 anti-TSG101(mouse, BD, 612696, 1/1000),
 anti-ALIX(rabbit, Millipore, ABC40, 1/1000),
 anti-HA (mouse, BioLegend, 901513, 1/5000),

anti-HA (rat, SIGMA, 3F10, 1/1000),
 anti-FLAG (mouse, Sigma, F1804, 1/5000),
 anti-LC3A (rabbit, Cell Signaling Technology, #4599, 1/1000),
 anti-LC3A/B (rabbit, Cell Signaling Technology, #4108, 1/1000),
 anti-GABARAP (rabbit, MBL, PM037, 1/1000),
 anti-GABARAPL1 (rabbit, abcam, ab86497, 1/1000)
 and anti-GATE-16/GABARAPL2 (rabbit, MBL, PM038, 1/1000).

Primary antibodies used for immunohistochemical and immunofluorescence staining in mouse studies were as follows:
 anti-TFEB (Invitrogen, PA1-31552, 1:200),
 anti-Galectin-3 (Santa Cruz Biotechnology, sc-23938, 1/200),
 anti-LAMP1 (BD Biosciences, 555798, 1/200),
 and anti-LRP2/megalin (This antibody was originally developed at T. Michigami Lab and was kindly gifted from his lab, Department of Bone and Mineral Research, Osaka Medical Center and Research Institute for Maternal and Child Health, Japan, 1:40000),
 anti-THP (R&D Systems, AF5175, 1/200)
 and anti-AQP2 (Santa Cruz Biotechnology, sc-47710, 1/200).

Secondary antibodies used for Western blotting were as follows:
 HRP-conjugated goat anti-rabbit IgG (Jackson ImmunoResearch, 111-035-003, 1:5000),
 HRP-conjugated goat anti-rat IgG (Jackson ImmunoResearch, 112-035-003, 1:5000),
 HRP-conjugated goat anti-mouse IgG (Jackson ImmunoResearch, 115-035-003, 1:5000)
 and HRP-conjugated rabbit anti-goat IgG (Jackson ImmunoResearch, 305-036-003, 1:5000).

Secondary antibodies used for immunofluorescence were as follows:
 Goat anti-rabbit Alexa Fluor 488 preabsorbed (abcam, ab1500085, 1/2000),
 Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 568 (Invitrogen, A11004, 1/2000),
 and Goat anti-rat Alexa Fluor 647 preabsorbed (abcam, ab150167, 1/2000).

Validation

Most antibodies used in this study were commercially available antibodies and were validated by companies. Data sheet is available from the web links as described below. Anti-LRP2/megalin antibody was used and was validated as a marker of proximal tubules previously (Minami et al., Autophagy, 2017).

anti-Galectin 3 (rat, Santa Cruz Biotechnology, sc-23938)
<https://www.scbt.com/p/galectin-3-antibody-m3-38>

anti-LAMP1 (mouse, Santa Cruz Biotechnology, sc-19992)
<https://www.scbt.com/ja/p/lamp-1-antibody-1d4b>

anti-LC3 (rabbit, MBL, PM036)
<https://ruo.mbl.co.jp/bio/dtl/A/?pcd=PM036>

anti-ATG16L1 (rabbit, CST, #8089)
<https://www.cellsignal.jp/products/primary-antibodies/atg16l1-d6d5-rabbit-mab/8089>

anti-TFEB (rabbit, Cell Signaling Technology, #4240)
<https://www.cellsignal.jp/products/primary-antibodies/tfeb-antibody/4240>

anti-phospho Ser211 TFEB (rabbit, Cell Signaling Technology, #37681)
<https://www.cellsignal.jp/products/primary-antibodies/phospho-tfeb-ser211-e9s8n-rabbit-mab/37681>

anti-14-3-3 (rabbit, Cell Signaling Technology, #8312)
<https://www.cellsignal.com/products/primary-antibodies/14-3-3-pan-antibody/8312>

anti-phospho S6K (rabbit, Cell Signaling Technology, #9205)
<https://www.cellsignal.jp/products/primary-antibodies/phospho-p70-s6-kinase-thr389-antibody/9205>

anti-S6K (rabbit, Cell Signaling Technology, #9202)
<https://www.cellsignal.jp/products/primary-antibodies/p70-s6-kinase-antibody/9202>

anti-phospho GSK alfa beta (rabbit, Cell Signaling Technology, #9331)
<https://www.cellsignal.jp/products/primary-antibodies/phospho-gsk-3a-b-ser21-9-antibody/9331>

anti-GSK beta (rabbit, Cell Signaling Technology, #9336)
<https://www.cellsignal.jp/products/primary-antibodies/phospho-gsk-3b-ser9-antibody/9336>

anti-PPP3CB (rabbit, OriGene, TA308439)
<https://www.origene.com/catalog/antibodies/primary-antibodies/ta308439/ppp3cb-rabbit-polyclonal-antibody>

anti-p62 (rabbit, MBL, PM045)
<https://ruo.mbl.co.jp/bio/dtl/A/?pcd=PM045>

anti-GAPDH (rabbit, Cell Signaling Technology, #2118)
<https://www.cellsignal.jp/products/primary-antibodies/gapdh-14c10-rabbit-mab/2118>

anti-LaminB (goat, SantaCruz, sc-6217)
<https://www.scbt.com/ja/p/lamin-b-antibody-m-20>

anti-TOMM20(rabbit, abcam, ab78547)
<https://www.abcam.co.jp/tomm20-antibody-mitochondrial-marker-ab78547.html>

anti-UQCRC1 (complexIII core subunit1) (mouse, Invitrogen, 459140)
<https://www.thermofisher.com/antibody/product/UQCRC1-Antibody-clone-16D10AD9AH5-Monoclonal/459140>

anti-TSG101(mouse, BD, 612696)
<https://wwwbdbiosciences.com/us/reagents/research/antibodies-buffers/cell-biology-reagents/cell-biology-antibodies/purified-mouse-anti-tsg101-51tsg101/p/612696>

anti-ALIX(rabbit, Millipore, ABC40)
https://www.merckmillipore.com/JP/ja/product/Anti-AIP1-Alix-Antibody,MM_NF-ABC40

anti-HA (mouse, BioLegend, 901513)
<https://www.biolegend.com/en-us/products/anti-ha-11-epitope-tag-antibody-11071>

anti-HA (rat, SIGMA, 3F10)
<https://www.sigmaaldrich.com/catalog/product/roche/roahaha?lang=ja®ion=JP>

anti-FLAG (mouse, Sigma, F1804)
<https://www.sigmaaldrich.com/catalog/product/sigma/f1804?lang=ja®ion=JP>

anti-LC3A (rabbit, Cell Signaling Technology, #4599)
<https://www.cellsignal.jp/products/primary-antibodies/lc3a-d50g8-xp-rabbit-mab/4599>

anti-LC3A/B(rabbit, Cell Signaling Technology, #4108)
<https://www.cellsignal.jp/products/primary-antibodies/lc3a-b-antibody/4108>

anti-GABARAP(rabbit, MBL, PM037)
<https://ruo.mbl.co.jp/bio/dtl/A/?pcd=PM037>

anti-GABARAPL1(rabbit, abcam, ab86497)
<https://www.abcam.co.jp/gabarapl1-antibody-ab86497.html>

and anti-GATE-16/GABARAPL2(rabbit, MBL, PM038)
<https://ruo.mbl.co.jp/bio/dtl/A/index.html?pcd=PM038>

anti-TFEB (Invitrogen, PA1-31552)
<https://www.thermofisher.com/antibody/product/TFEB-Antibody-Polyclonal/PA1-31552>

anti-LAMP1 (BD Biosciences, 555798)
<https://www.citeab.com/antibodies/2408380-555798-purified-mouse-anti-human-cd107a>

anti-THP (R&D Systems, AF5175)
https://www.rndsystems.com/products/mouse-uromodulin-antibody_af5175

and anti-AQP2 (Santa Cruz Biotechnology, sc-47710)
https://www.scbt.com/p/aqp2-antibody-e13-21?productCanUrl=aqp2-antibody-e13-21&_requestid=2821326

HRP-conjugated goat anti-rabbit IgG (Jackson ImmunoResearch, 111-035-003)
<https://www.jacksonimmuno.com/catalog/products/111-035-003>

HRP-conjugated goat anti-rat IgG (Jackson ImmunoResearch, 112-035-003)
<https://www.jacksonimmuno.com/catalog/products/112-035-003>

HRP-conjugated goat anti-mouse IgG (Jackson ImmunoResearch, 115-035-003)
<https://www.jacksonimmuno.com/catalog/products/115-035-003>

HRP-conjugated rabbit anti-goat IgG (Jackson ImmunoResearch, 305-036-003)
<https://www.jacksonimmuno.com/catalog/products/305-036-003>

Goat anti-rabbit Alexa Fluor 488 preabsorbed (abcam, ab1500085)
<https://www.abcam.co.jp/goat-rabbit-igg-hl-alex-fluor-488-preadsorbed-ab1500085.html>

Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 568(Invitrogen, A11004)
<https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11004>

Goat anti-rat Alexa Fluor 647 preabsorbed (abcam, ab150167)
<https://www.abcam.co.jp/goat-rat-igg-hl-alex-fluor-647-preadsorbed-ab150167.html>

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	HeLa Kyoto cells were kindly provided by the laboratory of Prof Shuh Narumiya(Kyoto University). MEF cells were kindly provided by the laboratory of Prof. Masahiro Yamamoto (Osaka University). PTECs were established in our lab previously (Takahashi et al., Am J Pathol, 2012). Plat-E cells were kindly provided from the laboratory of Prof. Toshio Kitamura(The University of Tokyo).
Authentication	All KO cell lines established in our lab were authenticated by PCR using sequence specific primer and subsequent sequencing to confirm the deletion and/or insertion at the intended genome locus. Cell lines obtained from other sources were not authenticated by us.
Mycoplasma contamination	We confirmed there was no mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell 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	Stated in Methods under " Mouse studies". 1) Conditional kidney proximal tubular epithelial cell (PTEC)-specific Atg5-deficient mice were generated as follows: First, we generated a transgenic mouse that expresses Cre recombinase under control of the promoter of KAP, the kidney androgen-regulated protein gene (KAP-Cre transgenic mice). The KAP-Cre mice were used after backcrossing with C57BL/6 mice more than 10 times. We then crossed the KAP-Cre transgenic mice with mice bearing an Atg5 flox allele. 2) Conditional PTEC-specific Tfeb-deficient mice were generated by crossing mice bearing a Tfeb flox allele with KAP-Cre transgenic mice. Mice were housed in box cages, maintained on a 12-h light/12-h dark cycle, and fed a normal fat chow diet. The ambient temperature and humidity was $23\text{C} \pm 1.5\text{C}$ and $45\% \pm 15\%$, respectively. 8- to 10-week-old male mice received a single intraperitoneal injection of 75 mg/kg of sodium oxalate and were sacrificed after indicated time periods.
Wild animals	Study did not involve wild animals.
Field-collected samples	Study did not involve samples collected from the field.
Ethics oversight	All animal experiments were approved by the institutional committee of the Animal Research Committee of Osaka University and the Japanese Animal Protection and Management Law (No. 25).

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

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics	All kidney specimens were obtained from living patients by fine needle aspiration. Control specimens were derived from tissue sections with no significant abnormal changes. Crystal nephropathy diagnoses included acute phosphate nephropathy, calcium oxalate nephropathy, and monoclonal light chain tubulopathy. The followings are the detailed population characteristics of human research participants. The information is shown as the following order: Group, Age (years), Gender, BUN (mg/dL), Cr (mg/dL), Diagnosis Control, 40, Female, 18, 0.91, no significant abnormal changes Control, 15, Male, 13, 0.77, no significant abnormal changes Control, 21, Male, 15, 1.05, no significant abnormal changes Crystal Nephropathy, 70, Male, 14, 2.98, Acute phosphate nephropathy Crystal Nephropathy, 74, Female, 40, 3.78, monoclonal light chain tubulopathy Crystal Nephropathy, 52, Female, 54, 5.57, calcium oxalate nephropathy
Recruitment	Patients who underwent kidney biopsy in osaka university hospital and japan community health care organization osaka hospital and were diagnosed as no significant abnormal changes or crystal nephropathy were enrolled. In the crystal nephropathy group, kidney function is significantly exacerbated compared to control group and we could not rule out the possibility kidney function affects TFEB activity. Control group is relatively young compared to the crystal nephropathy group and there might be a potential influence of aging on TFEB expression.
Ethics oversight	All studies were approved by the Institutional Review Board of Osaka University Hospital (IRB number 16554).

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