

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 (<i>n</i>) 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. <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>
☒	☐ 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 <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.

Software and code

Policy information about [availability of computer code](#)

Data collection	For RNA-seq data, sequencing was performed by Novogene facility (Beijing, China) on Illumina Hiseq platform according to the manufacturer's guide (Illumina, San Diego, CA, USA).FASTQ files were trimmed with fastp (version 0.23.1).
Data analysis	For RNA-seq data, expression changes between groups were calculated with DESeq2 package(Love et al., 2014). For Bioinformatic Analysis, Enrichr (https://maayanlab.cloud/Enrichr/) were used for pathway enrichment analysis, and BiNGO plugin in Cytoscape 3.9.1 was used to perform the network generation. The resulting MS/MS data were analyzed using Proteome Discoverer 2.4 software. Other data was analyzed using GraphPadPrism Version 9.0. Image was analyzed by ImageJ 1.53c.

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 all data supporting the findings of this study are available within article and its Supplementary Information and Source data. The RNA-seq raw data files are deposited in the Gene Expression Omnibus (GEO) database with the accession number GSE266071 and GSE266072.

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	Sex and/or gender are not relevant for any findings in this study and were therefore not considered in our study design, and participants was not determined based on self-report nor assigned.
Reporting on race, ethnicity, or other socially relevant groupings	The samples used in this paper are from xanthoderm.
Population characteristics	Information of age and other details are summarized in Methods.
Recruitment	Our study complied with all relevant ethical regulations and the Declaration of Helsinki. The Ethical Committee of Tianjin Medical University General Hospital approved the protocol for patient sample usage in ELISA (Approval No. IRB2019-WZ-099). Eye samples from PDR patients and age-matched controls for immunohistochemistry were obtained from the National Disease Research Interchange, with storage in accordance with the UK Human Tissue Act (2004). Ethical approval for the research was also obtained from the Ethical Review Boards of Queen's University Belfast. Our study does not involve any self-selection bias.
Ethics oversight	Study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Tianjin Medical University General Hospital (NO. IRB2019-WZ-099), and the Ethical Review Boards of Queen's University Belfast.

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

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.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	No statistical method was used to predetermine sample size. Sample size was determined according to previous publications where at least three animals per group were analyzed. Information of sample size are detailed in Methods. Moreover, sample sizes are indicated in the figures, legends and supplementary information. All experimental results showed statistically significant differences, with $P < 0.05$.
Data exclusions	No data were excluded.
Replication	We can confirm that all replication attempts were successful. Consistent results were obtained in more than three independent experiments, each with more than three biological replicates for every assessment or measurement, and all experimental outcomes are documented in the manuscript.
Randomization	The samples were randomly designated into experimental groups.
Blinding	Throughout the data collection and analysis processes, all researchers maintained blinding to group allocation.

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

Primary antibodies:

Anti-O-Linked N-Acetylglucosamine [RL2](Abcam, #2739), Mouse monoclonal [RL2] to O-Linked N-Acetylglucosamine. 1:1000 in WB and 1:200 in immunofluorescence.

anti-pYAP-S397 (Cell Signaling Technology, #13619), Phospho-YAP (Ser397) (D1E7Y) Rabbit mAb, 1:1000 in WB.

anti- Flag (Proteintech, # 66008-4ig), Mouse / IgG2b, 1:1000 in WB.

anti-OGT (Ptm-biolab, #PTM-5497), Mouse mAb, 1:1000 in WB.

anti-OGA ((Cell Signaling Technology, #60406), Rabbit IgG, 1:1000 in WB.

anti-GFPT1 (Abcam, #125069), Rabbit monoclonal [EPR4854] to GFPT1, 1:1000 in WB.

anti-β-TRCP (Cell Signaling Technology, #4394), (D13F10) Rabbit mAb, 1:1000 in WB.

anti-Ubiquitin (Cell Signaling Technology, #3936), (P4D1) Mouse mAb, 1:1000 in WB.

anti-YAP/TAZ (Cell Signaling Technology, #8418), Rabbit IgG, 1:1000 in WB and 1:200 in immunofluorescence.

anti-CD31 (BD biosciences, #557355), Rat LEW, also known as Lewis IgG2a, κ, h, 1:150 in immunofluorescence.

anti-TER119 (R&D, #MAB1125), Monoclonal Rat IgG2B Clone # TER-119, 1:200 in immunofluorescence.

anti-Desmin (Abcam, #15200, 1:200), Rabbit polyclonal to Desmin - Cytoskeleton Marker, 1:200 in immunofluorescence.

Validation

All antibodies utilized in this research were acquired from commercial suppliers, and their validation statements can be found on the manufacturer's website. The manufacturer's websites provide details regarding validations and associated reference publication. Anti-O-Linked N-Acetylglucosamine [RL2]: <https://www.abcam.cn/products/primary-antibodies/o-linked-n-acetylglucosamine-antibody-rl2-ab2739.html>.

anti-pYAP-S397 , <https://www.cellsignal.cn/products/primary-antibodies/phospho-yap-ser397-d1e7y-rabbit-mab/13619>,
 anti- Flag, <https://www.ptgcn.com/products/Flag-tag-Antibody-66008-4-Ig.htm>,
 anti-OGT, <http://www.ptm-biolab.com.cn/productDetail.html?id=5243>,
 anti-OGA , <https://www.cellsignal.cn/products/primary-antibodies/mgea5-oga-e9c5u-rabbit-mab/60406>,
 anti-GFPT1, <https://www.abcam.cn/products/primary-antibodies/gfpt1-antibody-epr4854-ab125069.html>,
 anti-β-TRCP, <https://www.cellsignal.cn/products/primary-antibodies/b-trcp-d13f10-rabbit-mab/4394>,
 anti-Ubiquitin, <https://www.cellsignal.cn/products/primary-antibodies/ubiquitin-p4d1-mouse-mab/3936>,
 anti-YAP/TAZ, <https://www.cellsignal.cn/products/primary-antibodies/yap-taz-d24e4-rabbit-mab/8418>,
 anti-CD31, <https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-rat-anti-mouse-cd31.557355>,
 anti-TER119, https://www.rndsystems.com/cn/products/mouse-ter-119-antibody-ter-119_mab1125,
 anti-Desmin, <https://www.abcam.cn/products/primary-antibodies/desmin-antibody-cytoskeleton-marker-ab15200.html>,

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

HEK 293T cell line (ATCC CRL-3216, female) was used in the study.

Authentication

No authentication was performed.

Mycoplasma contamination

The cells were tested negative for mycoplasma contamination.

Commonly misidentified lines
(See [ICLAC](#) register)

This study doesn't involve commonly misidentified cell lines.

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

Ogtfl/fl mice (Jackson Laboratory 004860) were crossed with Cdh5-Cre mice (Zhao et al., 2023) or Cdh5-(PAC)-CreERT2 mice (Wang et al., 2010) to generate Ogt Δ EC line or Ogt i Δ EC line to specifically deleted Ogt in the endothelium. Yap fl/fl; Taz fl/fl mice (Xin et al., 2013) were crossed with Cdh5-(PAC)-CreERT2 mice (Wang et al., 2010) to specifically delete YAP/TAZ in the endothelium. All mouse lines were C57BL/6J background. In OIR model, neonatal C57BL/6J mouse pups with the nursing mother on day P7 were exposed to hyperoxia (75% O₂) for 5 days. Mice were returned to room air on P12. On P17, the mice were sacrificed and the retinas were harvested for analysis. For STZ model, Hyperglycemia was induced in male adult (8-weeks-old) mice via 5-consecutive-day intraperitoneal injection of STZ (50 mg/kg, in trisodium citrate buffer, pH 4.5; Sigma Aldrich, #S0130). Control animals were administered with an equivalent volume of the vehicle.

Wild animals

The study did not involve wild animals.

Reporting on sex

In our study design, male mice were selected in the STZ model based on the previous study that only 50% of female mice were responding to the streptozotocin treatment (PMID: 37730757). While in OIR model and P6 mice, Sex are not relevant for any findings therefore male and female mice were both involved.

Field-collected samples

Mice were maintained under a 12-hour light-dark cycle at a temperature of 21-25°C with humidity level between 30 to 70%, and were provided unrestricted access to food and water. The mice were then randomly designated into experimental groups.

Ethics oversight

All study protocols involving the use of animals were approved by the Institutional Animal Care and Use Committee of Tianjin Medical University (TMUaMEC 2020006).

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

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, mosaicism, off-target gene editing) were examined.