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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 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	For ATAC-seq, RNA-seq, and ChIP-seq data, FASTQ files were trimmed with fastp (version0.23.1).
Data analysis	For ATAC-seq, the reads were aligned to the mm9 by Bowtie2 (v2.3.5.1). The differential ATAC-seq peaks between normal and PVR were identified using HOMER, and annotatePeaks.pl from HOMER was utilized to associate the peaks with genomic regions and nearby genes. Using deepTools (v3.4.3), the ATAC signals were visualized as a heatmap. For ChIP-seq, the reads were aligned to the mm9 by Bowtie2 (v2.3.5.1) and SAMtools (version 1.9) was used to remove duplicated reads. HOMER was used for peak calling, annotation, and motif enrichment analysis. The deepTools (v3.4.3) was used to produce the BigWig files. For RNA-seq, HISAT2 (v2.1.0) was used to align reads to mouse reference genome, and reads were counted using featureCounts (v1.6.0). DESeq2 algorithms were used to calculate genes with differential expression. Genes with fold changes of ≤ -2 or ≥ 2 and P < 0.05 were considered as significantly differentially expressed.

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 ATAC-seq, ChIP-seq and RNA-seq data generated in this study have been deposited in the Gene Expression Omnibus (GEO) database under accession code GSE244812 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE244812]. The processed ATAC-seq, ChIP-seq and RNA-seq data are available at GEO database (GSE244812). The relevant raw data from each figure generated in this study are provided in the Supplementary Information/Source Data file. Source data are provided with this paper. The cited data used in this study are available in the GEO database under accession code GSE179603 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE179603].

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	PVR was defined according to the Retina Society Terminology Committee (PMID: 6856248). Information of age and other details are summarized in Fig. S7B.
Recruitment	Four patients diagnosed with traumatic PVR in Tianjin Medical University General Hospital and four normal control donors from the First Affiliated Hospital of Harbin Medical University were recruited in our study. Informed consent was obtained from all participants. Participants did not receive compensation.
Ethics oversight	Our study conformed to the Declaration of Helsinki. The Ethical Committee of Tianjin Medical University General Hospital approved the protocol pertaining to traumatic PVR patient samples usage (IRB2023-KY-307). The usage of control human samples followed the approval of Ethics Committee of First Affiliated Hospital of Harbin Medical University (2023JS35).

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

Life sciences study design

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

Sample size	For the animal study, we used eight-week-old C57BL/6J male mice. The choice of sample size was based on a Power analysis (PMID:24250214). In all experiments, three or more mice were used in each group for independent experiments, 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 against H3K27ac (ab4729, Abcam), H3K4me1 (ab8895, Abcam), H3K4me3 (05-745R, Millipore), H3K36me3 (ab9050, Abcam), H3K9me3 (ab8898, Abcam) and H3K27me3 (ab192985, Abcam) were used for ChIP-seq. Primary antibodies against α-SMA (A2547, Sigma), NFATc1 (ab25916, Abcam), RANK (ab200369, Abcam), p38 (8690, CST), p-p38 (4511, CST), p65 (8242, CST), p-p65 (3033, CST), Tubulin (UM4003, Utibody) and GAPDH (UM4002, Utibody) were used for western blot. Primary antibodies against α-SMA (C6198, Sigma), NFATc1 (ab25916, Abcam), ZO-1 (21773-1-AP, ProteinTech), NFATc1 (sc-7294, Santa) and RPE65 (ab231782, Abcam) were used for 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.

Anti-H3K27ac (Abcam, Cat. #ab4729, Lot #GR3448944-1, 1 μg for ChIP-seq. Species reactivity: Mouse, Rat, Cow, Human. AppliCat. ion: ICC/IF, WB, IHC-P, ChIP, PepArr)
https://www.abcam.com/products/primary-antibodies/histone-h3-acetyl-k27-antibody-chip-grade-ab4729.html

Anti-H3K27me3 (Abcam, Cat. #192985, Lot #GR3264827-11, 1 μg for ChIP-seq. Species reactivity: Mouse, Rat, Human. AppliCat. ion: IHC-P, ChIP, ICC/IF, WB, PepArr, ELISA, ChIP-sequencing)
https://www.abcam.com/products/primary-antibodies/histone-h3-tri-methyl-k27-antibody-epr18607-chip-grade-ab192985.html

Anti-H3K4me1 (Abcam, Cat. #8895, Lot #GR3426435-2, 1 μg for ChIP-seq. Species reactivity: Mouse, Rat, Cow, Human. AppliCat. ion: ICC/IF, ChIP, WB, IHC-P)
https://www.abcam.com/products/primary-antibodies/histone-h3-mono-methyl-k4-antibody-chip-grade-ab8895.html

Anti-H3K4me3 (Millipore, Cat. #05-745R, Lot #4070079, 1 μg for ChIP-seq. Species reactivity: Human. This antibody has been used in previous literature to detect H3K4me3 in mice. AppliCat. ion: WB, ChIP, ChIP-seq, ELISA, PIA, Mplex, DB)
PMID: 22763441; PMID: 36681161; PMID: 27874008.
https://www.merckmillipore.com/GB/en/product/Anti-trimethyl-Histone-H3-Lys4-Antibody-clone-15-10C-E4-rabbit-monoclonal,MM_NF-05-745R

Anti-H3K9me3 (Abcam, Cat. #8898, Lot #GR3444658-1, 1 μg for ChIP-seq. Species reactivity: Mouse, Cow, Human. AppliCat. ion: ChIP, ICC/IF, IHC-P, WB)
https://www.abcam.com/products/primary-antibodies/histone-h3-tri-methyl-k9-antibody-chip-grade-ab8898.html

Anti-H3K36me3 (Abcam, Cat. #9050, Lot #GR3382010-2, 1 μg for ChIP-seq. Species reactivity: Cow, Human. Predicted to work with: Mouse, Rat. AppliCat. ion: ICC/IF, WB, ChIP)
PMID: 36424375; PMID: 36183832; PMID: 32234480; PMID: 33844685.
https://www.abcam.com/products/primary-antibodies/histone-h3-tri-methyl-k36-antibody-chip-grade-ab9050.html

Anti-Actin, α-Smooth Muscle (Sigma-Aldrich, Cat. #A2547, Lot #235414, 1:1000 dilution for WB. Species reactivity: human, mouse, rat, chicken, frog, canine, rabbit, guinea pig, goat, bovine, sheep, snake. AppliCat. ions:IHC, IF, WB)
https://www.sigmaaldrich.com/CN/zh/product/sigma/a2547

Anti-NFAT2 (Abcam, Cat. #ab25916, Lot #GR3424521-2, 1:1000 dilution for WB. Species reactivity: Mouse, Human, Chimpanzee. AppliCat. ions: ICC/IF, WB)
https://www.abcam.cn/products/primary-antibodies/nfat2-antibody-ab25916.html

Anti-RANK (Abcam, Cat. #ab200369, Lot #GR224490-39, 1:1000 dilution for WB. Species reactivity: Mouse, Human. AppliCat. ion: WB)
https://www.abcam.com/products/primary-antibodies/rank-antibody-ab200369.html

p38 MAPK (Cell Signaling Technology, Cat. #8690, Lot #9, 1:1000 dilution for WB. Species reactivity: Human, Mouse, Rat, Hamster, Monkey, Bovine, Pig. AppliCat. ions: WB, IHC, IF, F)

https://www.cellsignal.cn/products/primary-antibodies/p38-mapk-d13e1-xp-rabbit-mab/8690

Phospho-p38 MAPK (Thr180/Tyr182) (Cell Signaling Technology, Cat. #4511, Lot #13, 1:1000 dilution for WB. Species reactivity: Human, Mouse, Rat, Monkey, Mink, Pig, S. cerevisiae. AppliCat. ions: WB, IP, IHC, IF, F)
https://www.cellsignal.com/products/primary-antibodies/phospho-p38-mapk-thr180-tyr182-d3f9-xp-rabbit-mab/4511

NF-κB p65 (Cell Signaling Technology, Cat. #8242, Lot #16, 1:1000 dilution for WB. Species reactivity: Human, Mouse, Rat, Hamster, Monkey, Dog. AppliCat. ions: WB, IP, IHC, IF, F, ChIP, C&R)
https://www.cellsignal.com/products/primary-antibodies/nf-kb-p65-d14e12-xp-rabbit-mab/8242

Phospho-NF-κB p65 (Ser536) (Cell Signaling Technology, Cat. #3033, Lot #19, 1:1000 dilution for WB. Species reactivity: Human, Mouse, Rat, Hamster, Monkey, Pig. AppliCat. ions: WB, IP, IF, F)
https://www.cellsignal.com/products/primary-antibodies/phospho-nf-kb-p65-ser536-93h1-rabbit-mab/3033

β-tubulin (UTIBODY, Cat. #UM4003, Lot #A0220, 1:2000 dilution for WB. Specificity: Human, Rat, Mouse. AppliCat. ions: WB, IHC, IF)
https://www.utibody.com

GAPDH (UTIBODY, Cat. #UM4002, Lot #A0819, 1:2000 dilution for WB. Specificity: Human, Rat, Mouse,Bovine,Goat. AppliCat. ions: WB, IHC, IF.) https://www.utibody.com

Anti-Actin, α-Smooth Muscle - Cy3™ antibody (Sigma-Aldrich, Cat. #C6198, Lot #0000214427, 1:200 dilution for IF. Species reactivity: human, mouse, rat, chicken, frog, canine, rabbit, guinea pig, goat, bovine, sheep, snake. AppliCat. ions: IHC, IF)
https://www.sigmaaldrich.cn/CN/en/product/sigma/c6198

Anti-NFAT2 (Abcam, Cat. #ab25916. Lot #GR3424521-2, 1:50 dilution for IF. Species reactivity: Mouse, Human, Chimpanzee. AppliCat. ion: ICC/IF, WB)
https://www.abcam.cn/products/primary-antibodies/nfat2-antibody-ab25916.html

ZO-1 Polyclonal antibody (ProteinTech, Cat. #21773-1-AP, Lot #00129646, 1:100 dilution for IF. Species reactivity: Human, Canine, Mouse, Rat, Hamster. AppliCat. ions: FC, IF, IP, WB, ELISA)
https://www.ptgcn.com/products/ZO1-Antibody-21773-1-AP.htm

NFATc1 Antibody (Santa Cruz Biotechnology, Cat. #sc-7294, Lot #H3022, 1:50 dilution for IF. Species reactivity: Mouse, Rat, Human. AppliCat. ions: WB, IP, IF, IHC, F)
https://www.scbt.com/p/nfatc1-antibody-7a6

Recombinant Anti-RPE65 antibody (Abcam, Cat. #ab231782, Lot #1001368-30, 1:100 dilution for IF. Species reactivity: Mouse, Rat, Human. AppliCat. ions: IHC-P, WB, IHC-Fr, IP, mIHC)
https://www.abcam.cn/products/primary-antibodies/rpe65-antibody-epr22579-44-ab231782.html

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	Eight-week-old C57BL/6J male mice were used in this study. 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.
Wild animals	No wild animals were used.
Reporting on sex	Sex was not taken into account in this study design. Previous research in this field has predominantly utilized male mice (PMID: 12457862; PMID: 36290802; PMID: 27569993; PMID: 18310504). Therefore, our study was conducted exclusively using male mice. This information has been included in the abstract.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	The Ethical Committee of Tianjin Medical University General Hospital approved all animal experiments in this study (IRB2023-DWFL-369). The guidelines of the ARVO (The Association for Research in Vision and Ophthalmology) Statement for the Use of Animals in Ophthalmic and Vision Research were followed.

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, 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.

The data were deposited in the Gene Expression Omnibus (GSE244812) and are available on web (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?&acc=GSE244812).

Files in database submission

GSM7830180 Normal_K27ac
GSM7830181 Normal_K27me3
GSM7830182 Normal_K4me1
GSM7830183 Normal_K4me3
GSM7830184 Normal_K36me3
GSM7830185 Normal_K9me3
GSM7830186 PVR_K27ac
GSM7830187 PVR_K27me3
GSM7830188 PVR_K4me1
GSM7830189 PVR_K4me3
GSM7830190 PVR_K36me3
GSM7830191 PVR_K9me3
GSM8174689 Normal_K27ac_2
GSM8174690 Normal_K27me3_2
GSM8174691 Normal_K4me1_2
GSM8174692 Normal_K4me3_2
GSM8174693 Normal_K36me3_2
GSM8174694 Normal_K9me3_2
GSM8174695 Normal_K27ac_3
GSM8174696 Normal_K27me3_3
GSM8174697 Normal_K4me1_3
GSM8174698 Normal_K4me3_3
GSM8174699 Normal_K36me3_3
GSM8174700 Normal_K9me3_3
GSM8174701 PVR_K27ac_2
GSM8174702 PVR_K27me3_2
GSM8174703 PVR_K4me1_2
GSM8174704 PVR_K4me3_2
GSM8174705 PVR_K36me3_2
GSM8174706 PVR_K9me3_2
GSM8174707 PVR_K27ac_3
GSM8174708 PVR_K27me3_3
GSM8174709 PVR_K4me1_3
GSM8174710 PVR_K4me3_3
GSM8174711 PVR_K36me3_3
GSM8174712 PVR_K9me3_3
GSM8174713 Normal_Input_1
GSM8174714 PVR_Input_1
GSM8174715 Normal_Input_2
GSM8174716 PVR_Input_2
GSM8174717 Normal_Input_3
GSM8174718 PVR_Input_3

Genome browser session (e.g. UCSC)	All raw (fastq) and processed data (bigwig) are available in GEO.

Methodology

Replicates	We performed 3 replicates
Sequencing depth	ChIP-seq: pair-end 150 bp. ChIP-seq raw read counts of normal RPE cells: The unique reads numbers for three H3K27me3 ChIP samples are 13649307, 14387414, and 15769376, respectively. The unique reads numbers for three H3K27ac ChIP samples are 45153217, 13958500, and 31073780, respectively. The unique reads numbers for three H3K4me3 ChIP samples are 10245530, 11362838, and 12192694, respectively. The unique reads numbers for three H3K4me1 ChIP samples are 12184898, 16953308, and 14241918, respectively. The unique reads numbers for three H3K9me3 ChIP samples are 11524512, 19585700, and 11680198, respectively. The unique reads numbers for three H3K36me3 ChIP samples are 19142936, 12145112, and 16940340, respectively. ChIP-seq raw read counts of PVR RPE cells: The unique reads numbers for three H3K27me3 ChIP samples are 16996231, 15327388, and 24880188, respectively. The unique reads numbers for three H3K27ac ChIP samples are 38934240, 15334206, and 18143284, respectively. The unique reads numbers for three H3K4me3 ChIP samples are 13698210, 8844826, and 13912238, respectively. The unique reads numbers for three H3K4me1 ChIP samples are 11559726, 13766549, and 17800506, respectively. The unique reads numbers for three H3K9me3 ChIP samples are 20436352, 10009282, and 12576274, respectively. The unique reads numbers for three H3K36me3 ChIP samples are 13326652, 11564806, and 14238094, respectively.
Antibodies	1 µg antibody of H3K27ac (ab4729, Abcam), H3K4me1 (ab8895, Abcam), H3K4me3 (05-745R, Millipore), H3K36me3 (ab9050, Abcam), H3K9me3 (ab8898, Abcam) or H3K27me3 (ab192985, Abcam) were used for ChIP-seq.
Peak calling parameters	findPeaks <histone tag directory> -style histone -o auto -i <input tag directory> -F 2 -P 0.05
Data quality	ChIP-seq quality control was performed by fastp (version0.23.1) software.
Software	Bowtie (v2.3.5.1), SAMtools (version 1.9), deepTools (v3.4.3), and HOMER.