

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 <i>P</i> 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	10X platform was used and data were deposited in GEO database.
Data analysis	R software was used and script was on GitHub.

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 datasets presented in this study can be found in online repositories, GSE221952. All codes for scRNA-seq analysis are available from the corresponding authors upon reasonable request.

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	For human eye sections, all donors was deidentified and was included without restrictions regarding gender, race, age, and socioeconomic status.
Reporting on race, ethnicity, or other socially relevant groupings	For human eye sections, all donors was deidentified and was included without restrictions regarding gender, race, age, and socioeconomic status.
Population characteristics	Not available.
Recruitment	Not available.
Ethics oversight	Not available.

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	Proposed experimental animal numbers are partially based on our previous work detecting significant differences in age-related macular degeneration and on published work detecting differences in metabolism study.
Data exclusions	Outliers were identified using Grubbs' method in GraphPad.
Replication	For animal study, all experiments were performed at least 6 mice per group. For cell culture, all experiments was performed at least 3 times with results from 3 technical replicates averaged per experiment.
Randomization	Not available.
Blinding	All in vivo analyses will be conducted by a researcher blinded to animal treatment/genotype.

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	Antibodies used in this study were listed in the supplementary table.
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Validation

All antibodies were validated by suppliers.

Eukaryotic cell lines

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

Cell line source(s)

Primary human RPE cells were purchased from Lonza (Basel, Switzerland). ARPE-19, a cell line derived from human RPE cells, was purchased from ATCC (Manassas, VA, USA).

Authentication

Well characterized by the vendor.

Mycoplasma contamination

Tested by the vendor and no contamination detected.

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

None.

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

Vldlr^{-/-} mice and WT mice on the C57BL/6J background were obtained from Jackson Laboratory (Bar Harbor, ME).

Wild animals

Not available.

Reporting on sex

Sex has not been found to contribute clearly to the choroid neovascularization; nevertheless, we will conduct all in vivo experiments using approximately equal numbers of male and female mice and will disaggregate the data to analyze the gender variable statistically. For mouse experiments, all studies using animals will be performed in accordance with the NIH Guide for the Care and Use of Laboratory Animals and AHA policies and will be approved by the Wake Forest IACUC

Field-collected samples

Not available.

Ethics oversight

Wake Forest IACUC.

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

Plants

Seed stocks

Not available.

Novel plant genotypes

Not available.

Authentication

Not available.