

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 <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	Paper retrieval relies on FutureHouse's PaperQA2: https://github.com/Future-House/paper-qa. The commercial Large Language Models (LLMs) and their versions used in this study are: OpenAI 04-mini Anthropic Claude 3.7 Sonnet Google's Gemini 2.5 Pro Preview
Data analysis	Autonomous data analysis is performed using our in-house agent, Finch. The code is publicly available here: https://github.com/Future-House/finch.

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](#)

"Sample trajectories for Robin and Finch, as well as the code for Robin and ablated versions of Robin, will be available at <https://github.com/Future-House/robin>"

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

The following information was received from the Eye Bank for Sight Restoration (New York) regarding the single patient who contributed tissue which was used in this study:
sex, age, race, medical history, smoking history, date and time of death, date and time of tissue preservation.

The following information was reported about this patient in our manuscript:
"Primary RPE-SC cells were harvested from a single aged donor (>60 years old) with no known ocular conditions by the Eye-Bank for Sight Restoration, Inc. (New York)."

Reporting on race, ethnicity, or other socially relevant groupings

We use the term "aged" and define this as >60 years old. Samples from older patients are necessary as we are studying a disease of aging in this manuscript (age-related macular degeneration).

Population characteristics

For studying age-related macular degeneration, the most important variable is age. The next most important is genetic background (specifically complement factor H, CFH, and ARMS2/HTRA1 genes). Other variables thought to play a role in pathogenesis: smoking status, obesity, hypertension.

Recruitment

We were presented with a list of available tissue samples with no patient information other than age. We chose this sample based only on the age of the patient.

Ethics oversight

The project was reviewed by the Scientific Committee at the Eye Bank For Sight Restoration (New York) before samples were approved for shipping.

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

Samples sizes were determined based on pilot studies which showed 3 replicates could reliably distinguish the positive control (MFG8) from the vehicle control. For the RPE-SC phagocytosis screen a sample size of 4 was chosen to maximally utilize the available clinical material.

Data exclusions

No data was excluded.

Replication

Our initial findings in ARPE-19 cells (both phagocytosis screen and dose response) were validated by repeating the experiments in a primary human RPE cell line (RPE-SC).

Randomization

N/A

Blinding

For the human reference check (see section 3.3.1 "Crow and Falcon Ablation Experiments"), we blinded a scientist to the origin proposals (wild type Robin vs ablated Robin).

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	Bestrophin-1 Monoclonal antibody; Target: BEST1; Vendor: Proteintech; Catalog number: 60326-1-Ig; Dilution: 1:200. MERTK Polyclonal antibody; Target: MERTK; Vendor: Proteintech; Catalog number: 27900-1-AP; Dilution: 1:200. Anti-Integrin alphaBeta5 Antibody, clone EM09902, ZooMAb® Rabbit Monoclonal; Target: $\alpha\beta 5$; Vendor: Sigma-Aldrich; Catalog number: ZRB1191-25UL; Dilution: 1:100. Anti-RPE65 Rabbit Polyclonal Antibody; Target: RPE65; Vendor: Proteintech; Catalog number: 17939-1-AP; Dilution: 1:100. Anti-MiTF antibody [EPR26363-10]; Target: MiTF; Vendor: Abcam; Catalog number: ab303530; Dilution: 1:50. Otx2 Polyclonal Antibody; Target: OTX2; Vendor: Thermo Fisher Scientific; Catalog number: PA5-39887; Dilution: 1:20. Donkey Anti-Mouse IgG H&L (Alexa Fluor 647); Target: Mouse IgG; Vendor: Abcam; Catalog number: ab150107; Dilution: 1:500. Goat Anti-Rabbit IgG H&L (Alexa Fluor 647); Target: Rabbit IgG; Vendor: Abcam; Catalog number: ab150079; Dilution: 1:500. Donkey Anti-Goat IgG H&L (Alexa Fluor 647), preadsorbed; Target: Goat IgG; Vendor: Abcam; Catalog number: ab150135; Dilution: 1:500.
Validation	**Bestrophin-1 Monoclonal antibody** (Proteintech, catalog no. 60326-1-Ig): According to the manufacturer's website and online antibody databases, this antibody is validated for use in Western Blot, ELISA, Immunocytochemistry, Immunoprecipitation, and Immunohistochemistry, demonstrating cross-reactivity with human, mouse, rat, and canine samples (such as positive Western blot detection in human Y79 cells). **MERTK Polyclonal antibody** (Proteintech, catalog no. 27900-1-AP): Proteintech validates this antibody for Western Blot, Immunohistochemistry, Immunofluorescence, Intracellular Flow Cytometry, and ELISA across human, mouse, and rat tissues. It is widely cited in peer-reviewed literature, including recent 2024 studies characterizing MERTK expression in hepatocellular carcinoma mouse models. **Anti-Integrin $\alpha\beta 5$ Antibody, clone EM09902, ZooMAb® Rabbit Monoclonal** (Sigma-Aldrich, catalog no. ZRB1191-25UL): The manufacturer's profile states this recombinant antibody is validated for Flow Cytometry, Immunocytochemistry, Immunohistochemistry, and Western Blot. Sigma-Aldrich specifically notes its high affinity for human Integrin $\alpha\beta 5$ (EC50 = 5 ng/mL) and heavily enhanced validation for specificity, showing low cross-reactivity to the closely related $\alpha\beta 3$ integrin. **Anti-RPE65 Rabbit Polyclonal Antibody** (Proteintech, catalog no. 17939-1-AP): The manufacturer verifies this antibody for Western Blot, Immunohistochemistry, Immunofluorescence, and ELISA in human, mouse, and rat models. It is well-documented in the SciCrunch research resource registry (RRID:AB_2285290) and features dozens of literature citations validating its use in retinal pigment epithelium studies. **Anti-MiTF antibody [EPR26363-10]** (Abcam, catalog no. ab303530): Abcam's database highlights that this rabbit monoclonal antibody has undergone strict knockout (KO) validation. It is validated for Immunocytochemistry/Immunofluorescence, Immunohistochemistry, Western Blot, Immunoprecipitation, and Flow Cytometry in human, mouse, and rat samples, and appears frequently in recent proteogenomic literature. **Otx2 Polyclonal Antibody** (Thermo Fisher Scientific, catalog no. PA5-39887): Thermo Fisher and online registries (such as SciCrunch RRID:AB_2556436) indicate this antibody is validated for Immunocytochemistry/Immunofluorescence, Immunohistochemistry, and Western Blot targeting human, mouse, and rat OTX2. It has been actively cited in recent 2024 and 2025 publications, including benchmark studies utilizing human cerebellar organoids.

Eukaryotic cell lines

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

Cell line source(s)	ARPE-19 - ATCC RPE-SC - Eye Bank For Sight Restoration New York
Authentication	ARPE-19 cells - immunocytochemistry, brightfield RPE-SC - immunocytochemistry, brightfield, VEGF polarization assay
Mycoplasma contamination	All cell lines tested negative for mycoplasma.

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

None.

Plants

Seed stocks

N/A

Novel plant genotypes

N/A

Authentication

N/A

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

For flow cytometry, samples were prepared as follows:

1. Drug Treatment: ARPE-19 cells or RPE-SC were incubated with test compounds or a vehicle control for 60 minutes.
2. Bead Addition: pHrodo beads or ROS were added, and the plates were incubated for 3 hours.
3. Dissociation: Cells were treated with TrypLE Express for 10 minutes to detach them.
4. Suspension: Cells were washed and resuspended in FACS buffer (1% BSA and 500 ng/ml DAPI or 1ug/ml Hoechst 33342 in PBS) before being transferred to the flow cytometer.

Instrument

Attune NxT flow cytometer with autosampler

Software

Either Finch (agent analysis) or FlowJo (human analysis).

Cell population abundance

After passing all gates, there was between 2000 and 6000 cells in the final population (apart from the Cytochalasin D negative control and 4-phenylbutyric acid test condition which showed some cytotoxicity and had <1000 cells in the final population).

Gating strategy

ARPE-19 with pHrodo beads: (i) cell population gated in the FCS vs SSC plot, (ii) singlet gate (iii) live/dead gate on DAPI (iv) the Alexa 647 background signal was removed using the no-bead control (V) take the geometric mean of the pHrodo fluorescence

RPE-SC with pHrodo-labelled ROS: (i) cell population gated in the FCS vs SSC plot, (ii) A histogram of the Hoechst 33342 signal was used to exclude the bovine rod outer segments (ROS), which were Hoechst negative. (iii) Measure the geometric mean of the Hoechst positive population.

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