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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	No software were used for data collection.
Data analysis	All the software used in the analysis was described in the Methods section. Single cell RNA seq analysis was done in R (v4.0 and higher) using following packages: Seurat (v4.4.0), EnrichR (v3.2), clusterProfiler (v4.10.1), ggplot2 (v3.5.1), Enrichplot (v1.22.0), scCustomize (v2.1.2), Tidyheatmaps (v0.2.1.9), ComplexHeatmap (v2.18.0), ComplexUpset (v2.1.1), CellChat (v1.6.1). Others software used: GraphPad Prism 10, ImageJ.

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](#)

All the raw and processed scRNA seq data generated in this study have been deposited in the NIH GEO database. Wang et al., 2022 data was accessed from GEO database (GSE209872, GSM6403183, GSM6403184).

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

No human participants is involved in this study.

Reporting on race, ethnicity, or other socially relevant groupings

No human participants is involved in this study.

Population characteristics

No human participants is involved in this study.

Recruitment

No human participants is involved in this study.

Ethics oversight

No human participants is involved in this study.

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

Sample size for each experiment was mentioned in the Methods section. Sample size for scRNA seq experiments: P60: untreated- n= 24, hNPC-treated- n= 30; P90: untreated- n= 20, hNPC-treated- n= 35. Data from our previous published studies were included in visual function test data.

Data exclusions

No data was excluded.

Replication

Most experiment was repeated 2-3 times.

Randomization

Randomization was applied to the grouping of the animals. Both male and female rats were randomly allocated to each group.

Blinding

Visual function test data (OKR and ERG) was recorded by 2 blinded investigators. Image analysis was performed blindly by 2 observers.

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	Involvement 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	Involvement in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

Rabbit anti-MANF (Sigma, Cat# HPA011175), 1:200;
 Rabbit anti-MYDGF (Proteintech, Cat# 11353-1-AP), 1:200;
 Rabbit anti- KDEL (Thermo Fisher Scientific, Cat# PA5-101011), 1:200;
 Mouse anti-Human Nuclear Marker (Millipore, Cat# MAB1281), 1:300;
 Goat anti-Iba1 (FUJIFILM Wako Pure Chemical Corporation, Cat# 019-197441), 1:1000;
 Goat anti-Doublecortin (Santa Cruz, Cat# sc-8066), 1:200;
 Mouse anti-MAP2 (2a+2b) (Sigma, Cat# M1406), 1:500;
 Mouse anti-RPE65 (Sigma, Cat# MAB5428), 1:500;
 Mouse anti-AQP4 (R&D System, Cat# MAB11659-SP), 1:500;
 Rabbit anti-Collagen IV (Abcam; Cat# ab19808), 1:200;
 Mouse anti-Tenascin C (Abcam, Cat# ab86182), 1: 500;
 Rabbit anti-Cone arrestin (Millipore, Cat# AB15282), 1:1000;
 Rabbit anti-GFAP (Dako-Agilent, Cat# Z0334), 1:1000;
 Rabbit anti-Nestin (Millipore, Cat# ABD69), 1:2000
 Rabbit anti-NCAM1 (Proteintech, Cat# 14255-1-AP), 1:200;
 Rabbit anti-IMP2 (Abcam, Cat# ab272558), 1:200;
 Rabbit anti-Oligodendrocyte Specific Protein (Abcam, Cat# ab7474), 1:100;
 Rabbit anti-Recoverin (Millipore, Cat# AB5585), 1:2000;
 Rabbit anti- Sox2 (D6D9) XP (Cell Signaling, Cat# 3579), 1:400;
 Rabbit anti-TXNL6 (Proteintech, Cat# 11203-1-AP), 1:200;
 Goat anti-mouse IgG1 (γ1), CF™568 (Sigma, Cat# SAB4600314), 1:1000;
 Alexa Fluor 488 Donkey anti-rabbit IgG (H+L) (Abcam, Cat# ab150073), 1:500;
 Alexa Fluor 568 Donkey anti-goat IgG (H+L) (Abcam, Cat# ab175474), 1:500.

Validation

Antibodies were validated by respective manufacturers and available on their website.

Eukaryotic cell lines

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

Cell line source(s)

Research grade Human Neural Progenitor Cells was provided by Svendsen's Lab.

Authentication

hNPCs were authenticated by Svendsen's Lab. The GMP grade cells-CNS10-NPCs have been tested in clinical trial.

Mycoplasma contamination

Nil

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

Nil

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

The Royal College of Surgeons (RCS) rat, well-established model for retinal degeneration, were used in this study.

Wild animals

n/a

Reporting on sex

Both male and female rats were used in this study. Sex was not considered in this study as no sex-dependent differences in disease progression have been reported.

Field-collected samples

The study did not involve field-collected samples.

Ethics oversight

All animal experimental procedures were approved by Cedars-Sinai Medical Center’s Institutional Animal Care and Use Committee (IACUC 7611) and the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

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

Plants

Seed stocks

n/a

Novel plant genotypes

n/a

Authentication

n/a