nature portfolio

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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 was used to collect data
Data analysis	Software and tools used in this study: sickle (v1.33), bowtie2 (v2.3.5.1), STAR (v2.7.4a), featureCounts (v2.0.1), RSEM (v1.3.3), RNAfold (v2.4.18), Python (v3.8.19), PyTorch (v1.12.0), JAX-RNAfold (v2.0.0-beta), R (v4.1.0), R package sva (v3.40.0), R package ggplot2 (v3.4.2), R package viridis (v0.6.4), R package ggpointdensity (v0.1.0), data.table (v1.14.4), LinearDesign (v1.0.0), CDS-fold (https://github.com/gterai/CDSfold), CodonBERT (https://github.com/Sanofi-Public/CodonBERT), Ribotree (v1.1.8). Methods/algorithms used for modeling: Batch normalization, Fast Gradient Method, dropout, Fast Gradient Method, AdamW optimizer, SmoothL1Loss function, LeakyReLU activations, activation maximization.

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 raw RNA-seq and Ribo-seq data analyzed in this study were sourced from the RPFdb database (https://sysbio.gzzoc.com/rpfdb/). The relevant sample accession codes and gene lists are provided in Supplementary Data 1. The processed datasets generated for the translation model—including gene expression counts, mRNA sequences, transcript isoform information, associated sample metadata, filtered genes, and training/test group—are publicly available on Figshare (https://doi.org/10.6084/m9.figshare.28916288.v3).
The specific mRNA sequences utilized in the experimental validations are included in Supplementary Data 2.
All source data underlying the figures and statistical analyses are available within the Supplementary Data (specifically, Supplementary Data 3 to 10).

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 or human data were involved
Reporting on race, ethnicity, or other socially relevant groupings	no human participants or human data were involved
Population characteristics	no human participants or human data were involved
Recruitment	no human participants or human data were involved
Ethics oversight	no human participants or human data were involved

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	The sample sizes for the experiments in this study were primarily chosen based on standards commonly used and accepted in the field. For example, similar studies typically employ n=3 for in vitro work and n=5-6 for in vivo experiments [1, 2]. [1] PMID: 37130545; [2] PMID: 3904551
Data exclusions	No data were excluded.
Replication	For cell-based experiments, all data were generated from at least three independent biological replicates. Quantitative results (except for Western blots) are presented in the figures as the mean ± standard deviation (SD). For all Western blot analyses, experiments were repeated three times independently with similar results, as stated in the figure legends (Legends for Figures 5a-c and 6d). For in vivo experiments, the study on NGF mRNA expression was repeated across 5 to 9 independent biological replicates (mice), and the experiment on HA mRNA was repeated 8 times. The statistically significant differences between groups, as shown in the figures 5e, 6g, and 6i. We confirm that all experiments described in this manuscript were successfully replicated.
Randomization	Animals and cells were randomly allocated into each group. No specific randomization method was used.
Blinding	For all in vitro and in vivo experiments, the researchers performing data collection and analysis were blinded to the group assignments. To ensure this, a second researcher not involved in the experimental procedures assigned anonymous codes to all samples. The decoding key was not disclosed until after all data had been collected and statistically analyzed.

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

For HA western-blot: Sigma-Aldrich, catalog #F1804, used at 1:1000 dilution.
For retinas incubating: Novus, catalog # NBP2-20112, used at 1:500 dilution Cell Signaling Technology, catalog #4413S,used at 1:1000 dilution.
For anti-NGF Antibody: Abcam, catalog #ab6199 used at 1:1000 dilution.

Validation

Primary antibodies used in NGF experiments (retinas incubating and anti-NGF) have been validated in previous literature: Circular RNA-based therapy provides sustained and robust neuroprotection for retinal ganglion cells. Molecular Therapy - Nucleic Acids 35, 102258 (2024).
Primary antibodies used in HA experiments: anti-Flag (manufacturer website: https://www.sigmaaldrich.cn/CN/zh/product/sigma/f1804).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

The HEK293T (#CRL-1573), A549 (#CCL-185), and ARPE-19 (#CRL-2302) cell lines from the American Type Culture Collection (ATCC) were used in this study.

Authentication

Cell line were not authenticated.

Mycoplasma contamination

The cells were tested negative for mycoplasma contamination. MycoBlue Mycoplasma Detector (Vazyme) was used for detection.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used.

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

For the in vivo assay of NGF mRNA, 8-week-old male C57BL/6JGpt mice were purchased from GemPharmatech.
For the in vivo assay of HA mRNA, 6-8-week-old male BALB/cAnNCrl mice were supplied by the Laboratory Animal Center of Sun Yat-Sen University.

Wild animals

The study did not involve wild animals.

Reporting on sex

Sex was not considered in study design.

Field-collected samples

All mice were group-housed (5 mice per cage) in specific pathogen-free (SPF) facilities with a 12-hour light/12-hour dark cycle, an ambient temperature of 20–26°C, and a relative humidity of 40–60%. Standard laboratory rodent chow and autoclaved water were provided ad libitum.

Ethics oversight

For the in vivo assay of NGF mRNA, 8-week-old male C57BL/6JGpt mice (RRID: N/A) were purchased from GemPharmatech. All experimental procedures involving these mice were conducted in strict accordance with the animal protocols that received approval from the Institutional Animal Care and Use Committee (IACUC) at the Zhongshan Ophthalmic Center, Sun Yat-Sen University, under the animal ethics approval number Z2021067.
For the in vivo assay of HA mRNA, 6-8-week-old male BALB/cAnNCrl mice were supplied by the Laboratory Animal Center of Sun Yat-

Sen University. All experimental procedures were conducted in strict accordance with the animal protocols that received approval from the Animal Care and Use Committee Institutional at the Sun Yat-Sen University, under the animal ethics approval number 2022002794.

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

Plants

Seed stocks	The study did not involve plants.
Novel plant genotypes	The study did not involve plants.
Authentication	The study did not involve plants.