nature portfolio

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Last updated by author(s): Sep 22, 2025

# 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<br>*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<br>*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 | Illumina Miseq and Miniseq platform were used to collect the targeted deep sequencing data |
| Data analysis | CRISPR RGEN Tools program was used to quantifying edited reads and to search and identify potential off-target sites. Microsoft Excel and Graphpad prism were used to analyze the targeted deep sequencing data |

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 authors declare that all data supporting the findings of this study are available in the article and its supplementary information files. All other data supporting the findings of this study are available from the corresponding author on request. Targeted deep sequencing data files will be uploaded at the National Center for Biotechnology information (NCBI) before publication.

## 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 | N/A |
| Reporting on race, ethnicity, or other socially relevant groupings | N/A |
| Population characteristics | N/A |
| Recruitment | N/A |
| Ethics oversight | N/A |

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 | Sample sizes were determined based on literature precedence for genome editing experiments. |
| Data exclusions | No data was excluded |
| Replication | All experiments were repeated |
| Randomization | All experimental conditions were assigned randomly |
| Blinding | Blinding was used for histological quantifications (H&E staining, OCT measurements, immunofluorescence, and immunohistochemistry). Images were analyzed by investigators blinded to group allocation. No blinding was applied for other assays. |

# 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 | Anti-Brn3a primary antibody (Santa Cruz, sc-8429) and goat anti-mouse secondary antibody(Jackson, 111-545-146), Anti-RBPMS primary antibody (Abcam, ab152101), Cleaved Caspase-3 (Cell Signaling, 9664s), Anti-GFAP primary antibody (Abcam, ab7260), Anti-LC3B antibody (Abcam, ab192890), Anti-CD15-PE (BioLegend, 125606), Anti-CD48-PE (BioLegend, 103424), Anti-CD57 (Sigma, |

| | |
|---|---|
| | C6680-100TST), Anti-CD90.2-AF700 (BioLegend, 105320), and BV421 goat anti-mouse secondary antibody (BioLegend, 405317). |
| Validation | Antibody was validated by antibody suppliers |

## Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

| | |
|---|---|
| Cell line source(s) | B16F10, NIH3T3 cells were obtained from ATCC, Mouse Embryonic Fibroblast (generate), Human Urine-derived Cell from Seoul National University Bundang Hospital. |
| Authentication | The cell lines used were not laboratory authenticated after purchase or generated. |
| Mycoplasma contamination | No mycoplasma was detected in the cell lines used |
| Commonly misidentified lines (See ICLAC register) | Misidentified cell lines were not 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 | C57BL/6N and ICR mice used in the experiment were purchased from Orient Bio (Republic of Korea) |
| Wild animals | No wild animals were used |
| Reporting on sex | Histological analyses were performed on male mice. Behavioral tests and genotyping were conducted without sex-based stratification. |
| Field-collected samples | No field-collected samples were used |
| Ethics oversight | All animal procedures were conducted with guidelines from Institutional Animal Care and Use Committee of Korea University (KOREA-2024-0019) |

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

## Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

| | |
|---|---|
| Clinical trial registration | Patient urine-derived primary cells were collected under Institutional Review Board approval (IRB-B-2211-794-301) with informed consent. |
| Study protocol | This study did not involve a clinical trial. Experiments using patient-derived primary cells were conducted under Institutional Review Board approval (IRB-B-2211-794-301); therefore, no clinical trial protocol is applicable. |
| Data collection | N/A |
| Outcomes | N/A |

## 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 | Retinas were dissociated into single-cell suspensions by gently pressing through a 70-µm nylon cell strainer and stained with anti-mouse CD15-PE (BioLegend, 125606), CD48-PE-Cy7 (BioLegend, 103424), CD57 (Sigma, C6680-100TST), and CD90.2-AF700 (BioLegend, 105320)) followed by goat anti-mouse secondary antibody (BioLegend, 405317). |
| Instrument | Data were acquired using a BD FACSAria III (BD Biosciences, USA) equipped with 355 nm UV, 405 nm violet, 488 nm blue, and 640 nm red lasers. |
| Software | Acquisition was performed with BD FACSDiva software (v6.1.3; BD Biosciences). |
| Cell population abundance | Not applicable. Flow cytometry was used only for RGC isolation prior to genotyping; no abundance or purity data are included in the manuscript. |
| Gating strategy | Cells were gated on FSC/SSC to exclude debris, singlets were identified using FSC-H vs FSC-A, and RGCs were enriched as $CD90^{+}CD48^{-}CD15^{-}CD57^{-}$ subsets, following established protocols (Chintalapudi et al., JoVE, 2017). |

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