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<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 | EDMS-Online ver.3.1 |
| Data analysis | Brain images were processed using Functional Magnetic Resonance Imaging of the Brain (FMRIB) Sofrware Library (FSL 5.3) and Statistical Parametric Mapping 12 (SPM12, Release 7219). Statistical analyses of clinical data were conducted using SAS software (version 9.4, SAS Institute), and statistical analysis of animal experiments were performed using GraphPad Prism (version 10.3.1, GraphPad Software). |

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 relevant data from this trial are included in the article and Supplementary Material.

## 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 | Participants were enrolled irrespective of their sex. Data are provided in Extended Data Table 1. |
| Reporting on race, ethnicity, or other socially relevant groupings | Participants were enrolled irrespective of their race/ethnicity. |
| Population characteristics | Data are provided in Extended Data Table 1 |
| Recruitment | A public call was made by website, press conference. Patients were selected from among those who wished to participate, after consultation by a selection committee in accordance with the selection criteria. Potential biases (placebo effect and observer bias) are noted in the discussion. |
| Ethics oversight | The protocol was reviewed and approved by Kyoto University Hospital Institutional Review Board (K044). |

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 | Based on the results of the monkey study (Kikuchi et al Nature 2017), we calculated number of samples for which safety could be assessed. Details are given in the Statistic Analysis Plan p 3. "Target sample size". |
| Data exclusions | No data were excluded. |
| Replication | We replicated the transplantation of iPSC-derived dopaminergic progenitors in a total of 7 participants. We confirmed all attempts were successful. |
| Randomization | This trial was not randomized. When selecting patients, the male/female ratio (4:3) and HLA match or incompatibility (3:4) were not biased among patients who met the selection criteria. |
| Blinding | This trial was a single-arm trial. |

# 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 | Primary antibodies used are as follows: FOXA2 (goat, R&D systems, AF2400, 1:500), NURR1 (mouse, Perseus Proteomics, PP-N1404-00, 1:300), HNA (mouse, Millipore, MAB1281, 1:500, KI67 (rabbit, Abcam, Ab16667, 1:1,000), 5-HT (rat, Millipore MAB352, 1:100), and TH (rabbit, Millipore, AB152, 1:400). Secondary antibodies are as follows: Alexa Fluor 488 anti-Mouse IgG, (donkey, ThermoFisher, A21202, 1:400), Alexa Fluor 594 anti-Goat IgG (donkey, ThermoFisher, A11058, 1:2,000), Alexa Fluor 594 anti-Rabbit IgG (donkey, ThermoFisher, A21207, 1:400), and Alexa Fluor 594 anti-Rat IgG (donkey, ThermoFisher, A21209, 1:400). |
| Validation | Antibodies are used under validation using adequate negative and positive control samples.<br>We confirmed the staining by using animal samples when possible, or we rely on the stained samples presented in manufacturer's website (FOXA2 from R&D, HNA from Millipore, KI67 from Abcam, and 5-HT and TH from Millipore). |

## Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

| | |
|---|---|
| Cell line source(s) | iPSCs are derived from human peripheral blood cells, donated by healthy volunteer.<br>QHJI01s04 is provided by Center for iPS cell Research and Application (CiRA), Kyoto University, Japan. MCB003 is provided by Sumitomo Pharma (Tokyo, Japan). |
| Authentication | The STR (short tandem repeat) pattern of iPSCs coincide with that of donor cells. |
| Mycoplasma contamination | All cells are negative for mycoplasma contamination. |
| Commonly misidentified lines<br>(See ICLAC register) | Nothing. |

## 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 | Adult (9-week-old) male nude rats (F344/NJcl-rnu/rnu, CLEA, Japan) were used for this study. |
| Wild animals | The study did not involve wild animals. |
| Reporting on sex | In this study, only male rats were used to precisely examine the effect of transplanted cells by excluding effects of the female's sexual cycle on the survival or maturation of dopaminergic neurons. |
| Field-collected samples | The study did not involve samples collected from the field. |
| Ethics oversight | The study protocol is approved by the ethical committees of Kyoto University and Sumitomo Pharma. |

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 | jRCT2090220384, UMIN000033564 |
| Study protocol | The study protocol was provided in the supplementary material. |
| Data collection | This trial was conducted at Kyoto University Hospital. Patients are recruited from Aug. 1, 2018 to May 19, 2021. Data are collected from Sep. 25, 2018 to Jan. 18, 2024. |
| Outcomes | Primary end points included the adverse-event profile and secondary end points involved the safety and efficacy at 24 months |

## Plants

Seed stocks — *Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes — *Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication — *Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

## Magnetic resonance imaging

### Experimental design

Design type — This was not an fMRI study.

Design specifications — This was not an fMRI study.

Behavioral performance measures — This was not an fMRI study.

### Acquisition

Imaging type(s) — T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and T2*-weighted images

Field strength — 3 Tesla scannar

Sequence & imaging parameters — Whole brain

Area of acquisition — *State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☒ Not used

### Preprocessing

Preprocessing software — Functional Magnetic Resonance Imaging of the Brain (FMRIB) software

Normalization — Normalization was not conducted.

Normalization template — Not applicable

Noise and artifact removal — Not applicable

Volume censoring — Not applicable

### Statistical modeling & inference

Model type and settings — Not applicable

Effect(s) tested — Not applicable

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016) — Not applicable

Correction — Not applicable

## Models & analysis

| n/a | Involved in the study |
|---|---|
| ☐ | ☐ Functional and/or effective connectivity |
| ☐ | ☐ Graph analysis |
| ☐ | ☐ Multivariate modeling or predictive analysis |

| | |
|---|---|
| Functional and/or effective connectivity | *Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).* |
| Graph analysis | *Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).* |
| Multivariate modeling and predictive analysis | *Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.* |