

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 (<i>n</i>) 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> 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 <i>d</i> , Pearson's <i>r</i>), 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.
Data analysis	Publicly available metagenomic data were analysed using R software, BBDuk, BBSplit, HUMAnN3, UniRef90 (version 201901b), ChocoPHLAn (version 30), FASTX-Toolkit, hg19, MetaPhlAn4 (version 4.0.6), MaAsLin2 and ANCOM-BC. GraphPad Prism software 9.4.1 was used for all analysis.

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](#)

Publicly available metagenomic data of both Parkinson's disease patients (n=491) and neurologically healthy elderly controls (n=234) were obtained from BioProject ID PRJNA834801

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	65 neurologically elder healthy control and 65 parkinson's disease patients and the and the demographic data including sex and age are presented in Table S1.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, or other socially relevant groupings were not considered in this study.
Population characteristics	Patients with PD were followed up for an average of 9.5 years after sampling to ensure the reliability of the diagnosis. PD was diagnosed based on the clinical diagnostic criteria of the Movement Disorders Society. Participants in the control group, who were free of PD, were enrolled from the SNUH biorepository and predominantly spouses sharing living environments with patients with PD.
Recruitment	The participants in this study were recruited from the Movement Disorders Clinic at Seoul National University Hospital (SNUH), comprising a total 130 participants.
Ethics oversight	All experimental procedures were approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2207-085-1340).

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 size was determined based on prior studies and literature in this field using similar experimental paradigms. We estimated the total number of trials by performing G*Power analysis.
Data exclusions	All relevant data are shown. No data were excluded from the analysis and raw data.
Replication	The number of the independent replications has been stated in the Figure Legends.
Randomization	We allocated cells randomly for the treatment.
Blinding	Researchers were not blind to tested groups. All statistics were performed in an unbiased manner.

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	Mouse anti-TH (1:1000) immunostar, Rabbit anti-GFAP (1:1000) abcam, Rabbit anti-Iba1 (1:1000) Wako chemicals, Rabbit anti-phospho-S6 (1:100) Cell signaling, Rabbit anti-phospho-4E-BP1 (1:100) Cell signaling, Rabbit anti-phospho- α -Synuclein (1:100) Cell signaling, Rabbit anti-MAP2 (1:100).
Validation	Validated by vendors.

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 mice
Wild animals	No wild animals were used in this study
Reporting on sex	Eight-week-old male C57BL/6N mice (Orient bio) and germ-free eight-week-old male C57BL/6N mice (CLEA Japan) were used in this study.
Field-collected samples	No field-collected samples were involved in this study
Ethics oversight	All animal experiments were conducted in compliance with ethical guidelines approved by Sungkyunkwan University Animal Care (approval number: SKKUIACUC2023-04-09-1) and the Institutional Animal Care and Use Committee (IACUC) at the POSTECH Biotech Center. We have complied with all relevant ethical regulations for animal use.

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

Plants

Seed stocks	Not applicable.
Novel plant genotypes	Not applicable.
Authentication	Not applicable.