

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Data collection	No custom software or unpublished algorithms were used for data collection in this study.
Data analysis	Statistical analyses were performed using SAS version 9.4 and R version 4.2.1.

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 data supporting the findings of this study include plasma biomarker data, PET imaging data, and cognitive test data from the K-ROAD cohort. These datasets contain sensitive human participant information and carry a potential risk of participant re-identification. Due to ethical restrictions imposed by the institutional review boards and the informed consent provided by study participants, the data cannot be made publicly available without restriction. De-identified data are available to qualified researchers for research purposes upon request, subject to approval by the relevant institutional review boards and completion of an appropriate data use agreements. Requests for data access will be reviewed and responded to within 2-4 weeks of receipt. Approved data will be available for the

period specified in the data use agreement. Requests for data access should be directed to the corresponding author, SWS (sw72.seo@samsung.com). Raw LC-MS/MS acquisition files were generated at C2N Diagnostics and are not publicly available owing to commercial intellectual property restrictions; requests for access may be directed to C2N Diagnostics. Source data are provided with this paper.

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 recruited irrespective of sex, which was obtained from medical records. Sex was included as a covariate in statistical analyses where applicable. Gender identity data were not collected. Sex-specific analyses were not performed as the study was not designed to investigate sex-related differences.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity were not used as analytical variables in this study because the cohort consisted predominantly of ethnically Korean participants. Accordingly, no race- or ethnicity-based subgroup analyses were performed.
Population characteristics	Participants were recruited from the Korean Brain Aging Study for the Early Diagnosis and Prediction of Alzheimer's Disease (K-ROAD), a nationwide memory clinic–community hybrid cohort. Demographic and clinical variables including age, sex, education, APOE ϵ 4 status, clinical diagnosis, cognitive performance, and amyloid/tau PET status were collected and included in analyses as appropriate covariates.
Recruitment	Participants were recruited through memory clinics and community-based enrollment across multiple centers in South Korea. Because participants were recruited from both clinical and community settings, some degree of selection bias related to healthcare access and study participation may be present.
Ethics oversight	The study protocol was approved by the Institutional Review Board of Samsung Medical Center and the institutional review boards of participating centers. Written informed consent was obtained from all participants or their legal representatives.

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 by participant availability, plasma sample availability, and assay-specific volume requirements within the K-ROAD cohort. No formal prospective sample size calculation was performed.
Data exclusions	Outliers were excluded separately within A β -positive and A β -negative groups when values exceeded four standard deviations from the respective group mean, as predefined in the statistical analysis plan. Participants without available biomarker or PET data for a given analysis were excluded from that specific analysis only.
Replication	The robustness of the findings was assessed across clinically relevant subgroups and using complementary analytical approaches. Independent replication was not performed because key biomarkers, including eMTBR-tau243 and p-tau205, were available only in a subset of participants, limiting the feasibility of a separate replication analysis.
Randomization	This was an observational cohort study; therefore, participants were not randomized to experimental groups. Statistical models were adjusted for relevant covariates including age, sex, APOE ϵ 4 status, and education where appropriate.
Blinding	As this study did not involve experimental group allocation, blinding to group allocation was not applicable. Plasma biomarker measurements were performed by investigators blinded to clinical and imaging data.

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

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	Not applicable. This study was an observational cohort study.
Study protocol	The institutional review board of Samsung Medical Center (No. 2014-12-087, 2016-11-111, 2016-11-154, 2016-12-073, 2017-07-039, 2020-01-024, 2021-02-135, 2021-03-177, 2021-05-087, 2024-05-019) approved this study
Data collection	This study was designed as a prospective cohort study conducted in South Korea. Participants were recruited from the K-ROAD project, a nationwide genotype–phenotype cohort established in 2016 in collaboration with 25 university-affiliated hospitals to advance diagnostic and therapeutic research for Alzheimer’s disease and related neurodegenerative disorders. Clinical, neuropsychological, plasma biomarker, and PET imaging data were prospectively collected using standardized protocols.
Outcomes	Primary outcomes included associations between plasma tau biomarkers and amyloid/tau PET measures, plasma-based tau staging concordance with PET-based tau staging, and longitudinal cognitive decline assessed using CDR-SB and MMSE.

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, mosaicism, off-target gene editing) were examined.