

Life Sciences Reporting Summary

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► Experimental design

1. Sample size

Describe how sample size was determined.

Described in "METHODS/Sample size considerations": The power calculations for sample size of the study were estimated as follows: assuming that the biomarker candidates could be used to classify PET as A β + or A β - individuals with a sensitivity of $\geq 80\%$ and a theoretical sensitivity of 50%, the sample size required to achieve a statistical power of 80% at a 5% significance level would be 20 and 20 for both A β + and A β - groups. Also, assuming the plasma biomarkers could show more than a 0.5 correlation coefficient (r) to A β -PET SUVR values or to CSF biomarker values, a total sample size of 21 would be required to achieve a statistical power of 80% at a 5% significance level. Both the NCGG and AIBL data sets, including the subpopulation having CSF data, sufficiently satisfy these numbers.

2. Data exclusions

Describe any data exclusions.

Described in "METHODS/Subjects": From 254 plasma samples of the total AIBL dataset, two outliers were excluded from the analyses because one 95 subject's abnormally high A β signals from IP-MS masked the peak of the internal standard which prevented reliable measurements, and another subject showed A β concentrations 9.2 to 20.5 times higher than the SD.

3. Replication

Describe whether the experimental findings were reliably reproduced.

Described in "METHODS/Data analyses": The findings in the NCGG dataset ($n=121$) were externally validated in the AIBL dataset ($n=252$).

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

N/A

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Described in "METHODS/Data analyses": Data analyses were performed totally in a blind and independent manner. The plasma A β measurements were performed at Koichi Tanaka Mass Spectrometry Research Laboratory (Shimadzu) without any clinical or imaging information. All of the PET imaging data were analyzed by the AIBL imaging group. The A β -PET dichotomization (A β + / A β -) and generation of SUVR were performed without any clinical or biomarker information. The NCGG group conducted statistical analyses, and all results were confirmed by two independent biostatisticians.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a Confirmed

- ☐ ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
- ☐ ☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ A statement indicating how many times each experiment was replicated
- ☐ ☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
- ☐ ☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
- ☐ ☒ The test results (e.g. P values) given as exact values whenever possible and with confidence intervals noted
- ☐ ☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
- ☐ ☒ Clearly defined error bars

See the web collection on [statistics for biologists](#) for further resources and guidance.

► Software

Policy information about [availability of computer code](#)

7. Software

Describe the software used to analyze the data in this study.

Described in "METHODS/Data analyses" and "METHODS/Imaging data": R ver. 3.3.2, SPSS ver. 21, and JMP software ver. 8., CapAIBL (<https://milxcloud.csiro.au/>), SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>)

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* [guidance for providing algorithms and software for publication](#) provides further information on this topic.

► Materials and reagents

Policy information about [availability of materials](#)

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

Described in "Data availability": Source data of graphs plotted in Table 1, Fig. 1-3, and Extended Data Figs 1-9 are available as source files. Other data are available from the corresponding author upon reasonable request.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

Described in "METHODS/Plasma A β measurements": IgG monoclonal antibody 6E10 (BioLegend, San Diego, CA, USA)

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

Described in "Supplementary Information/Cell Culture": BE(2)-C cell (CRL-2268), American Type Culture Collection

b. Describe the method of cell line authentication used.

N/A

c. Report whether the cell lines were tested for mycoplasma contamination.

Described in "Supplementary Information/Cell Culture": We routinely check mycoplasma contamination by DAPI staining and PCR analysis.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by [ICLAC](#), provide a scientific rationale for their use.

N/A

► Animals and human research participants

Policy information about [studies involving animals](#); when reporting animal research, follow the [ARRIVE guidelines](#)

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

N/A

Policy information about [studies involving human research participants](#)

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

Described in "METHODS/Subjects": The participants were aged 60 to 90 years. The discovery NCGG dataset consisted of 62 CN, 30 MCI, and 29 AD individuals (121 in total) selected from the NCGG's in-house clinical studies. The AIBL dataset for external validation consisted of 156 CN, 68 MCI, and 30 AD participants (254 in total).