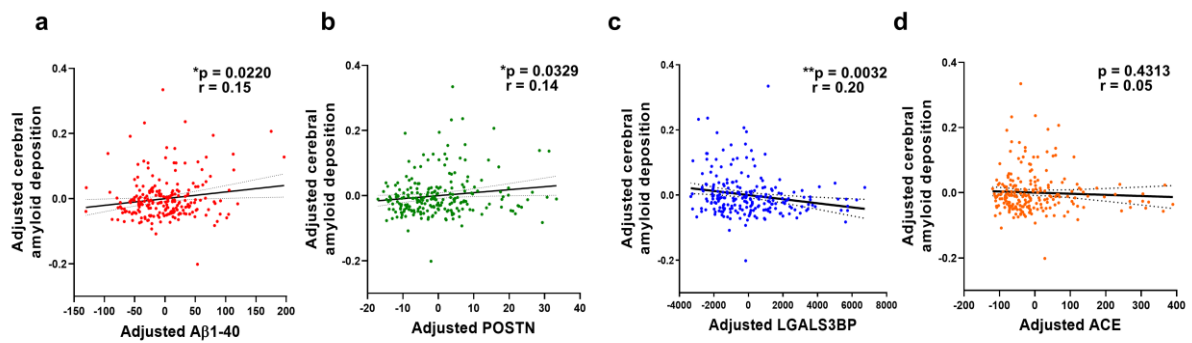


## Supplementary Information

**Application of *QPLEX*<sup>TM</sup> biomarkers in cognitively normal individuals across a broad age range and diverse regions with cerebral amyloid deposition**

Lee *et al.*



**Supplementary Fig. 1 The QPLEX™ biomarkers and cerebral amyloid deposition for all CN groups (including all age-groups) a-d** Each graph on the left shows the correlation of QPLEX™ biomarker levels with cerebral amyloid deposition for all CN groups. All graphs show the results from the partial correlation analysis with correction for age and sex. P-value cut-off,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ , and  $****p < 0.0001$ . P, partial correlation P-value; R, partial correlation coefficient. Dotted lines indicate 95% confidence intervals; CN, cognitively normal

**Supplementary Table 1. Demographic data of the participants (based on age-groups)**

Characteristics (n)	1 <sup>st</sup> tertile (47)	2 <sup>nd</sup> tertile (77)	3 <sup>rd</sup> tertile (97)	P-value
Sex, M/F	24/23	32/45	44/53	0.5871 <sup>†</sup>
Age, years, mean $\pm$ SEM (range)	32.04 $\pm$ 0.9 (21 to 42)	56.25 $\pm$ 0.7 (43 to 65)	74.06 $\pm$ 0.5 (66 to 87)	< 0.0001*
Education, mean $\pm$ SEM	15.19 $\pm$ 0.3	12.83 $\pm$ 0.5	11.39 $\pm$ 0.5	< 0.0001*
MMSE raw score, mean $\pm$ SEM	29.13 $\pm$ 0.1	28.12 $\pm$ 0.2	26.64 $\pm$ 0.2	< 0.0001*
MMSE z score, mean $\pm$ SEM	0.80 $\pm$ 0.1	0.55 $\pm$ 0.1	0.26 $\pm$ 0.1	< 0.0001*
CDR (n)	0 (47)	0 (77)	0 (97)	1
ApoE4 positivity, $\epsilon$ 4+/N (%)	13/47	15/77 (%)	24/97	0.5416 <sup>†</sup>
PiB (SUVR), mean $\pm$ SEM	1.08 $\pm$ 0.01	1.09 $\pm$ 0.01	1.29 $\pm$ 0.03	< 0.0001*
PiB positivity (- / +), n	47/0	75/2	63/34	< 0.0001 <sup>†</sup>

CN, cognitively normal; PiB, Pittsburgh compound B; - or +, PiB positivity; SEM, standard error of the mean; n, number of participants; MMSE, Mini-Mental State Examination; MMSE z score, a revised value of the MMSE score considering age, sex, and education level; CDR, Clinical Dementia Rating; ApoE, Apolipoprotein E; SUVR, standardized uptake value ratio; N, total number of participants.

- \*, significance by *t*-test; †, significance by chi-squared test.

**Supplementary Table 2. Comparison of QPLEX™ biomarker levels between CN- and CN+ (including all age-groups) with correction for age and sex**

<b>Factors</b>	<b>Mean difference</b>	<b>Std. Error</b>	<b>P<sup>a</sup></b>	<b>95% CI<sup>a</sup></b>
<b>Aβ1-40</b>	-22.3647	9.7673	0.0230	-41.6166 to -3.1128
<b>POSTN</b>	-5.1039	2.0547	0.0138	-9.1539 to -1.0540
<b>LGALS3BP</b>	1801.1584	390.4209	<0.0001	1031.6559 to 2570.6610
<b>ACE</b>	10.0631	20.1814	0.6186	-29.7177 to 49.8439

<sup>a</sup> Bonferroni corrected

**\*Abbreviations:** DF, degrees of freedom; F, F statistic; P, significance level; Std. Error, standard error; CI, confidence interval; PiB-PET, Pittsburgh compound B positron emission tomography; Aβ1-40, amyloid beta 1-40; POSTN, periostin; LGALS3BP, galectin-3 binding protein; ACE, angiotensin-converting enzyme.

**Supplementary Table 3. Multiple regression analysis on the 3rd tertile group (>65 years)**

<b>QPLEX™ markers</b>							
<b>Dependent Y</b>							<b>Cerebral amyloid deposition (SUVR)</b>
<b>Sample size</b>							94
<b>Coefficient of determination R<sup>2</sup></b>							0.2437
<b>R<sup>2</sup>- adjusted</b>							0.2097
<b>Multiple correlation coefficient</b>							0.4937
<b>Residual standard deviation</b>							0.2791
<b>Ind. variables</b>	<b>Coefficient</b>	<b>Std. Error</b>	<b>t</b>	<b>P</b>	<b>r<sub>partial</sub></b>	<b>r<sub>semipartial</sub></b>	<b>VIF</b>
<b>(Constant)</b>	1.3670						
<b>Aβ1-40</b>	0.0008808	0.0005743	1.534	0.1286	0.1605	0.1414	1.165
<b>LGALS3BP</b>	-0.00005646	0.00001641	-3.440	0.0009	-0.3426	0.3171	1.214
<b>ACE</b>	-0.0008850	0.0004007	-2.209	0.0298	-0.2280	0.2036	1.506
<b>POSTN</b>	0.01381	0.003477	3.973	0.0001	0.3882	0.3663	1.492
<b>QPLEX™ markers + Sex + Age</b>							
<b>Dependent Y</b>							<b>Cerebral amyloid deposition (SUVR)</b>
<b>Sample size</b>							94
<b>Coefficient of determination R<sup>2</sup></b>							0.2468
<b>R<sup>2</sup>- adjusted</b>							0.1948
<b>Multiple correlation coefficient</b>							0.4968
<b>Residual standard deviation</b>							0.2817
<b>Ind. variables</b>	<b>Coefficient</b>	<b>Std. Error</b>	<b>t</b>	<b>P</b>	<b>r<sub>partial</sub></b>	<b>r<sub>semipartial</sub></b>	<b>VIF</b>
<b>(Constant)</b>	1.2060						
<b>Aβ1-40</b>	0.0009375	0.0005877	1.595	0.1143	0.1686	0.1484	1.198
<b>LGALS3BP</b>	-0.00005411	0.00001703	-3.178	0.0021	-0.3225	0.2957	1.282
<b>ACE</b>	-0.0008844	0.0004051	-2.183	0.0317	-0.2279	0.2031	1.511
<b>POSTN</b>	0.01317	0.003694	3.565	0.0006	0.3570	0.3317	1.653
<b>Sex</b>	-0.02716	0.06029	-0.450	0.6535	-0.04824	0.04191	1.064
<b>Age</b>	0.002239	0.005912	0.379	0.7058	0.04057	0.03523	1.108
<b>QPLEX™ markers + Sex + Age + ApoE genotype</b>							
<b>Dependent Y</b>							<b>Cerebral amyloid deposition (SUVR)</b>
<b>Sample size</b>							94
<b>Coefficient of determination R<sup>2</sup></b>							0.2778
<b>R<sup>2</sup>- adjusted</b>							0.2190
<b>Multiple correlation coefficient</b>							0.5270
<b>Residual standard deviation</b>							0.2775
<b>Ind. variables</b>	<b>Coefficient</b>	<b>Std. Error</b>	<b>t</b>	<b>P</b>	<b>r<sub>partial</sub></b>	<b>r<sub>semipartial</sub></b>	<b>VIF</b>
<b>(Constant)</b>	1.3271						
<b>Aβ1-40</b>	0.0008562	0.0005804	1.475	0.1438	0.1571	0.1352	1.204
<b>LGALS3BP</b>	-0.00005650	0.00001682	-3.360	0.0012	-0.3406	0.3079	1.289
<b>ACE</b>	-0.0007833	0.0004025	-1.946	0.0549	-0.2054	0.1784	1.537
<b>POSTN</b>	0.01257	0.003652	3.442	0.0009	0.3480	0.3154	1.665
<b>Sex</b>	-0.02361	0.05941	-0.397	0.6921	-0.04281	0.03642	1.065
<b>Age</b>	0.0004404	0.005897	0.0747	0.9406	0.008053	0.006844	1.137
<b>ApoE</b>	0.1317	0.06859	1.921	0.0581	0.2028	0.1760	1.061

\***Abbreviations:** SUVR, standardized uptake value ratio; Ind., independent; VIF, variance inflation factor; Aβ1-40, amyloid beta 1-40; LGALS3BP, galectin-3 binding protein; ACE, angiotensin-converting enzyme; POSTN, periostin; ApoE, apolipoprotein E.