

Supplementary Table 2. Association between blood p-tau and tau pathology

P-tau biomarker/ technology type	Cohort details	Diagnostic accuracy of plasma/serum P-tau (AUC-ROC analyses)	Notes and Interpretation	Accuracy of plasma/serum P-tau to identify increased amyloid pathology (AUC for Aβ+ vs Aβ-)	Association with <i>in vivo</i> amyloid pathology	Association with <i>in vivo</i> tau pathology
P-tau181						
Surface Plasmon Resonance (Serum) (Shekhar et al., 2016)	113 participants: 39 AD, 37 MCI, 37 CU	<ul style="list-style-type: none"> AD vs CU: 0.812 MCI vs CU: 0.634 	<ul style="list-style-type: none"> Serum P-tau181 ↑ in AD vs MCI and CU 			
Simoa (Plasma) (Tatebe et al., 2017)	<ul style="list-style-type: none"> Cohort 1 (n=35): 20 AD, 15 controls Cohort 2 (n=42): 22 controls, 20 Down syndrome (6 with Aβ PET) Cohort 3 (n=11): 8 AD, 1 PD, 2 VaD 	Cohort 1: AD vs controls: 0.786	<ul style="list-style-type: none"> Plasma P-tau181 ↑ in AD and Down syndrome vs controls 		Cohort 2: Plasma P-tau181 ↑ in an Aβ+ individual (n=1) versus those with less Aβ PET	Cohort 3: Correlation of plasma P-tau181 and CSF P-tau181: r= 0.673
Simoa (Plasma) (Thomas K. Karikari et al., 2020)	<ul style="list-style-type: none"> Discovery cohort (n=37): 18 CU elderly, 19 AD dementia TRIAD (n=226): <ul style="list-style-type: none"> 113 CU older adults: 91 Aβ-, 22 Aβ+ 27 Aβ- CU young adults 45 MCI: 17 Aβ-, 28 Aβ+ 33 AD: 31 Aβ+, 2 Aβ- 8 FTD: all Aβ- BioFINDER-2 cohort (n=763): <ul style="list-style-type: none"> 337 CU older adults 191 MCI 126 AD 18 bvFTD or primary progressive aphasia (PPA) 36 PD or multiple systems atrophy (MSA) 12 VaD 21 progressive supranuclear palsy (PSP) or corticobasal syndrome (CBS) Primary care cohort (n=105): 72 CU older adults, 11 CU young adults, 12 MCI, 10 AD 	<ul style="list-style-type: none"> Discovery cohort: AD vs CU: 0.901 (AUC= 0.959 when using serum) Primary care cohort: AD vs: <ul style="list-style-type: none"> CU young adults: 1.00 CU elderly: 0.844 MCI: 0.550 TRIAD cohort: Aβ+ AD vs: <ul style="list-style-type: none"> FTD: 1.00 Aβ- CU young: 0.994 Aβ- CU older adults: 0.982 Aβ+ CU older adults: 0.939 Aβ- MCI: 0.875 Aβ+ MCI: 0.849 Aβ+ MCI vs: <ul style="list-style-type: none"> Aβ- CU young: 0.922 Aβ- CU elderly: 0.864 Aβ+ CU elderly: 0.641 Aβ+ CU elderly vs Aβ- CU young: 0.899 BioFINDER-2 cohort: Aβ+ AD vs: <ul style="list-style-type: none"> Aβ- CU: 0.902 Aβ- MCI: 0.865 VaD: 0.921 PSP/CBS: 0.885 bvFTD/PPA: 0.828 PD/MSA: 0.819 	<ul style="list-style-type: none"> Discovery: in this biomarker characterised cohort, plasma and serum P-tau181 ↑ in AD vs CU In primary care cohort, P-tau181 ↑ in MCI and AD vs CU TRIAD cohort: Plasma P-tau181 ↑ in: <ul style="list-style-type: none"> Aβ+ AD vs all other diagnostic groups Aβ+ CU older adults, Aβ+ and Aβ- MCI vs Aβ- CU older adults, CU young adults and FTD BioFINDER-2 cohort: Plasma P-tau181 ↑ in: <ul style="list-style-type: none"> Aβ+ AD vs all other diagnostic groups Aβ+ MCI vs Aβ- CU, Aβ- MCI, PD/MSA, VaD and PSP/CBS Aβ+ CU vs Aβ- CU and Aβ- MCI 	TRIAD cohort: <ul style="list-style-type: none"> All: 0.881 Non-demented (Young + CU elderly + MCI): 0.797 CU (Young + CU elderly): 0.793 CU elderly: 0.772 MCI: 0.742 	<ul style="list-style-type: none"> Discovery cohort: Correlation of CSF Aβ42 and: <ul style="list-style-type: none"> Plasma P-tau181: r= -0.594 Serum P-tau181: r= -0.683 TRIAD cohort: Correlation of plasma P-tau181 and: <ul style="list-style-type: none"> CSF Aβ42 in: <ul style="list-style-type: none"> All subjects: r= -0.361 Aβ PET SUVR in: <ul style="list-style-type: none"> All subjects: r= 0.634 Aβ+ subjects: r= 0.445 Aβ- subjects: r= 0.289 CU: r= 0.405 MCI: r= 0.365 AD: r= 0.271 FTD: r= 0.048 	<ul style="list-style-type: none"> Discovery cohort: Correlation of CSF P-tau181 and: <ul style="list-style-type: none"> Plasma P-tau181: r= 0.706 Serum P-tau181: r= 0.794 TRIAD cohort: Correlation of plasma P-tau181 and: <ul style="list-style-type: none"> CSF P-tau181 (Simoa): r= 0.568 CSF P-tau181 (LUMIPULSE): r= 0.550 Tau PET SUVR (Braak I-VI) in: <ul style="list-style-type: none"> All subjects: r= 0.539 Aβ+ subjects: r= 0.628 Aβ- subjects: r= 0.164 CU: r= 0.143 MCI: r= 0.399 AD: r= 0.225 FTD: r= 0.048 Tau PET SUVR: <ul style="list-style-type: none"> Braak I-II: r= 0.564 Braak III-IV: r= 0.529 Braak V-VI: r= 0.456 BioFINDER-2 cohort: Correlation of plasma P-tau181 and Tau PET SUVR in Aβ+ subjects: <ul style="list-style-type: none"> Braak I-II: r= 0.445 Braak III-IV: r= 0.488 Braak V-VI: r= 0.446

Simoa (Serum) (Benussi et al., 2020)	417 participants: 291 FTLD ¹ , 63 AD, 63 CU ¹ FTLD included 134 bvFTD, 48 avPPA, 27 svPPA, 51 CBS, 31 PSP	<ul style="list-style-type: none"> AD vs FTLD: 0.930 Mild AD (MMSE\geq19) vs Mild FTLD (FTLD with an FTLD-modified CDR\leq5): 0.907 	<ul style="list-style-type: none"> Serum P-tau181 \uparrow in AD vs all FTLD subgroups and CU 			
Simoa (Plasma) (O'Connor et al., 2020)	70 participants: Familial AD (FAD) 27 non-carriers, 19 symptomatic, and 24 presymptomatic mutation carriers	<ul style="list-style-type: none"> Symptomatic vs Non-carriers: 0.93 Presymptomatic carriers vs Non-carriers: 0.86 	<ul style="list-style-type: none"> Plasma P-tau181 \uparrow in symptomatic and presymptomatic carriers vs non-carriers 			
Simoa (Plasma) (Lantero Rodriguez et al., 2020)	115 participants: Longitudinal blood collections with clinical evaluation at 8 (n=111), 4 (n=100) and 2 (n=87) years prior to death followed by neuropathological assessment <ul style="list-style-type: none"> Non-ADs included 4R tauopathies, cerebral amyloid angiopathy, FTD, Lewy body dementia, vascular dementia AD pathology group included AD without co-pathology, AD with cerebral amyloid angiopathy, AD with Lewy body pathology and AD with TDP43 pathology 	Using plasma collected 8 years prior to death and post-mortem diagnosis: <ul style="list-style-type: none"> AD vs Non-AD: 0.974 AD vs controls: 0.921 AD vs mixed AD: 0.573 Mixed AD vs Non-AD: 0.901 Mixed AD vs Controls: 0.841 	<ul style="list-style-type: none"> Clinical diagnosis at all 3 timepoints: Plasma P-tau181 \uparrow in AD vs controls Neuropathological diagnosis at all 3 timepoints: Plasma P-tau181 \uparrow in AD vs controls and non-AD 			At all 3 timepoints: Plasma P-tau181 \uparrow in Braak V-VI vs Braak I-II
Simoa (Plasma) (T. K. Karikari et al., 2020)	1177 participants from the ADNI cohort: <ul style="list-style-type: none"> Baseline diagnosis: <ul style="list-style-type: none"> > 400 Cognitively unimpaired (CU): 268 Aβ-, 68 Aβ+ > 558 MCI: 277 Aβ-, 209 Aβ+ > 219 AD: 41 Aβ-, 137 Aβ+ 	A β + AD vs <ul style="list-style-type: none"> Aβ- CU: 0.853 Aβ+ CU: 0.855 Aβ- MCI: 0.838 	At baseline, plasma P-tau181 \uparrow in: <ul style="list-style-type: none"> Aβ+ CU, Aβ+ MCI, Aβ+ and Aβ- AD vs Aβ- CU Aβ+ MCI and Aβ+ AD vs Aβ- CU Aβ+ MCI vs Aβ- MCI Aβ+ AD vs Aβ- AD 	<ul style="list-style-type: none"> CU: 0.704 MCI: 0.799 AD: 0.703 	Correlation of plasma P-tau181 and: <ul style="list-style-type: none"> CSF Aβ42: r= -0.39 Aβ PET SUVR: r= 0.42 Regression (adjusted for age, gender and diagnosis), association of plasma P-tau181 and: CSF A β 42 in: <ul style="list-style-type: none"> All subjects: t= -8.27 CU: t= -3.13 MCI: t= -7.51 AD (all Aβ+: t= -1.27 A β PET SUVR in: <ul style="list-style-type: none"> All subjects: t= 10.39 CU: t= 3.46 MCI: t= 10.14 AD: t= 0.73 	Correlation of plasma P-tau181 and: <ul style="list-style-type: none"> CSF P-tau181: r= 0.36 Tau PET SUVR: r= 0.26 Regression (adjusted for age, gender and diagnosis), association of plasma P-tau181 and: CSF P-tau181 in: <ul style="list-style-type: none"> All subjects: t= 8.78 CU: t= 3.09 MCI: t= 7.71 AD: t= 2.98 Tau PET SUVR in: <ul style="list-style-type: none"> All subjects: t= 4.08 CU: t= 2.06 MCI: t= 3.71
Simoa (Plasma) (Chong et al., 2021)	200 participants: <ul style="list-style-type: none"> 43 CU: 38 Aβ- and 5 Aβ+ 91 CIND (cognitive impairment no dementia): 62 Aβ- and 29 Aβ+ 44 AD: 14 Aβ-, 30 Aβ+ 22 VaD: 19 Aβ-, 3 Aβ+ 	A β + AD vs A β - VaD: <ul style="list-style-type: none"> P-tau181: 0.844 P-tau181/Aβ42 ratio: 0.903 	Plasma P-tau181, P-tau181/t-Tau ratio and P-tau181/A β 42 ratio \uparrow in: <ul style="list-style-type: none"> Aβ+ AD vs Aβ- CU, Aβ- AD and Aβ- VaD Aβ+ CIND vs Aβ- CU and Aβ- CIND 	<ul style="list-style-type: none"> All: <ul style="list-style-type: none"> > P-tau181: 0.840 > P-tau181/Aβ42 ratio: 0.889 Nondemented (CU+CIND): <ul style="list-style-type: none"> > P-tau181: 0.807 > P-tau181/Aβ42 ratio: 0.866 	Correlation of A β PET SUVR and plasma: <ul style="list-style-type: none"> P-tau181: r= 0.417 P-tau181/Aβ42 ratio: r= 0.460 Regression (adjusted for age, gender, education, APOE ϵ 4 and	

				<ul style="list-style-type: none"> • CIND: <ul style="list-style-type: none"> ➢ P-tau181: 0.820 ➢ P-tau181/Aβ42 ratio: 0.891 • Demented (AD+VaD): <ul style="list-style-type: none"> ➢ P-tau181: 0.868 ➢ P-tau181/Aβ42 ratio: 0.932 • AD: <ul style="list-style-type: none"> ➢ P-tau181: 0.906 ➢ P-tau181/Aβ42 ratio: 0.969 	<p>diagnosis), association of Aβ PET SUVR and plasma:</p> <ul style="list-style-type: none"> • P-tau181: β= 0.116 • P-tau181/Aβ42 ratio: β= 0.127 	
<p>Simoa (Plasma) (Keshavan et al., 2021)</p>	<p>441 participants:</p> <ul style="list-style-type: none"> • 359 Aβ-, 82 Aβ+ • 410 CU, 7 MCI, 24 prior neurological conditions 		<p>Plasma P-tau181 ↑ in Aβ+ group</p>	<ul style="list-style-type: none"> • All subjects: <ul style="list-style-type: none"> ➢ Plasma P-tau181: 0.707 (0.778)[#] ➢ Plasma Aβ42/Aβ40 and P-tau181: 0.696 (0.776)[#] ➢ LC-MS Plasma Aβ42/Aβ40 and Simoa Plasma P-tau181: 0.826 (0.851)[#] ➢ LC-MS Plasma composite and Simoa Plasma P-tau181: 0.829 (0.850)[#] • CU: <ul style="list-style-type: none"> ➢ Plasma P-tau181: 0.720 (0.784)[#] <p>[#] AUC after adjustment for age, gender and APOE</p>		
<p>Meso Scale Discovery (MSD) (Plasma) (Mielke et al., 2018)</p>	<p>269 participants:</p> <ul style="list-style-type: none"> • 172 CU: 100 Aβ- and 72 Aβ+ • 57 MCI: 29 Aβ- and 28 Aβ+ • 40 AD: 2 Aβ- and 38 Aβ+ 		<p>Plasma P-tau181 ↑ in:</p> <ul style="list-style-type: none"> • Aβ+ AD vs Aβ+ and Aβ- CU • Aβ+ MCI vs Aβ- CU 	<ul style="list-style-type: none"> • All: 0.803 • Nondemented (CU+MCI): 0.750 • CU: 0.704 • MCI: 0.852 	<p>Regression (adjusted for age, gender and APOE), association of Aβ PET SUVR and plasma P-tau181 in:</p> <ul style="list-style-type: none"> • All subjects: β= 0.23 • CU: β= 0.10 • MCI: β= 0.17 • AD: β= 0.20 	<p>Correlation of Tau PET SUVR and plasma P-tau181 in:</p> <ul style="list-style-type: none"> • Aβ+ subjects only: r= 0.580 • Aβ- subjects only: r= 0.018 • Aβ+ CU: r= 0.287 • Aβ- CU: r= -0.057 • Aβ+ MCI: r= 0.437 • Aβ- MCI: r= 0.284 • Aβ+ AD: r= 0.125 <p>Regression (adjusted for age, gender and APOE), association of Tau PET SUVR and plasma P-tau181 in:</p> <ul style="list-style-type: none"> • All subjects: β= 0.19 • CU: β= 0.02 • MCI: β= 0.13 • AD: β= 0.18
<p>MSD (Plasma) (Janelidze et al., 2020)</p>	<ul style="list-style-type: none"> • Cohort 1 (n=182): <ul style="list-style-type: none"> ➢ 64 CU: 26 Aβ-, 38 Aβ+ ➢ 28 Aβ+ MCI ➢ 38 Aβ+ AD ➢ 52 non-AD diseases[†] • Cohort 2 (n=344): 	<ul style="list-style-type: none"> • Cohort 1: AD vs non-AD: 0.94 • Neuropathology cohort: AD vs non-AD: 0.854 	<ul style="list-style-type: none"> • Neuropathology cohort: Plasma P-tau181 ↑ in AD vs non-AD • Cohort 1: Plasma P-tau181 ↑ in: 	<ul style="list-style-type: none"> • Cohort 1: 0.79 • Cohort 2: <ul style="list-style-type: none"> ➢ P-tau181: 0.81 ➢ P-tau181 and Aβ42/Aβ40 ratio: 0.84 	<ul style="list-style-type: none"> • Cohort 1: <ul style="list-style-type: none"> ➢ Regression (adjusted for age and gender), association of Aβ PET SUVR and plasma P-tau181 in: <ul style="list-style-type: none"> ➢ All subjects: β= 0.54 ➢ Aβ+ subjects: β= 0.38 ➢ Aβ- subjects: β= 0.17 	<ul style="list-style-type: none"> • Cohort 1: <ul style="list-style-type: none"> ➢ Regression (adjusted for age and gender), plasma P-tau181 and: • CSF P-tau181 in: <ul style="list-style-type: none"> ➢ All subjects: β= 0.73 ➢ Aβ+ subjects: β= 0.73

	<ul style="list-style-type: none"> ➢ 219 CU: 126 Aβ-, 93 Aβ+ ➢ 125 MCI: 44 Aβ-, 81 Aβ+ <ul style="list-style-type: none"> • Neuropathology cohort (n=63): 16 AD, 47 non-AD[‡] <p>[‡]Non-AD diseases included 11 PD, 17 PDD, 6 PSP, 6 DLB, 6 CBS, 2 SD and 4 bvFTD</p> <p>[‡]Non-AD group included 14 controls without a major neuropathological diagnosis, 1 amyotrophic lateral sclerosis, 1 corticobasal degeneration, 2 dementia with unspecified etiology, 1 FTLD, 3 MCI, 1 multiple sclerosis, 15 PD, 2 parkinsonism, 1 primary lateral sclerosis, 2 PSP, 2 vascular cognitive impairment, 1 vascular dementia, 1 vascular parkinsonism</p>		<ul style="list-style-type: none"> ➢ Aβ+ CU, Aβ+ MCI and Aβ+ AD vs Aβ- CU and non-AD diseases ➢ Aβ+ MCI and Aβ+ AD vs Aβ+ CU <ul style="list-style-type: none"> • Cohort 2: Plasma P-tau181 ↑ in: <ul style="list-style-type: none"> ➢ Aβ+ MCI and Aβ+ CU vs Aβ- MCI and Aβ-CU ➢ Aβ+ MCI vs Aβ+ CU 		<ul style="list-style-type: none"> • Cohort 2: Regression (adjusted for age and gender), association of Aβ PET SUVR and plasma P-tau181 in: <ul style="list-style-type: none"> ➢ All subjects: β= 0.53 ➢ Aβ+ subjects: β= 0.45 ➢ Aβ- subjects: β= 0.03 	<ul style="list-style-type: none"> ➢ Aβ- subjects: β= 0.12 <p>Tau PET SUVR (Braak I-IV) in:</p> <ul style="list-style-type: none"> ➢ All subjects: β= 0.71 ➢ Aβ+ subjects: β= 0.69 ➢ Aβ- subjects: β= 0.11 <p>Tau PET SUVR (Braak I-II) in:</p> <ul style="list-style-type: none"> ➢ All subjects: β= 0.63 ➢ Aβ+ subjects: β= 0.58 ➢ Aβ- subjects: β= 0.22 <p>Tau PET SUVR (Braak III-IV) in:</p> <ul style="list-style-type: none"> ➢ All subjects: β= 0.71 ➢ Aβ+ subjects: β= 0.69 ➢ Aβ- subjects: β= 0.10 <p>Tau PET SUVR (Braak V-VI) in:</p> <ul style="list-style-type: none"> ➢ All subjects: β= 0.65 ➢ Aβ+ subjects: β= 0.63 ➢ Aβ- subjects: β= 0.08 <ul style="list-style-type: none"> • Cohort 2: Regression (adjusted for age and gender), association of plasma P-tau181 and CSF P-tau181 in: <ul style="list-style-type: none"> ➢ All subjects: β= 0.52 ➢ Aβ+ subjects: β= 0.56 ➢ Aβ- subjects: β= 0.10
MSD (Plasma) <i>(Thijssen et al., 2020)</i>	<ul style="list-style-type: none"> • Cohort 1 (n=362)[‡]: <ul style="list-style-type: none"> ➢ 69 CU: 29 Aβ-, 11 Aβ+ ➢ 47 MCI: 21 Aβ-, 18 Aβ+ ➢ 56 AD: 0 Aβ-, 51 Aβ+ ➢ 190 FTLD[‡] • Cohort 2 (n=42): Aβ+ MCI/Mild AD <p>[‡]Autopsy-confirmed cohort: Of the 362 subjects, there are 82 with autopsy-confirmed diagnosis: 15 AD, 52 FTLD-tau, 15 FTLD-TAR DNA-binding protein (FTLD-TDP)</p> <p>[‡]FTLD included 39 CBS (16 Aβ-, 3 Aβ+), 48 PSP (6 Aβ-, 0 Aβ+), 50 bvFTD (10 Aβ-, 3 Aβ+), 27 nfvPPA (5 Aβ-, 2 Aβ+), 26 svPPA (8 Aβ-, 2 Aβ+)</p>	<ul style="list-style-type: none"> • Cohort 1: Clinical AD vs FTLD: 0.894 • Autopsy-confirmed cohort: AD vs FTLD-tau + FTLD-TDP: 0.878 	<ul style="list-style-type: none"> • Cohort 1: Plasma P-tau181 ↑ in AD vs all other diagnostic groups • Autopsy-confirmed cohort: Plasma P-tau181 ↑ in AD vs FTLD-tau and FTLD-TDP 	<p>Cohort 1:</p> <ul style="list-style-type: none"> • All: 0.914 • CU: 0.859 • MCI: 0.944 	<p>Cohort 1: Regression, association of Aβ PET SUVR and plasma P-tau181: β= 0.75</p>	<ul style="list-style-type: none"> • Cohort 1: Regression, association of plasma P-tau181 and: <ul style="list-style-type: none"> CSF P-tau181 in: <ul style="list-style-type: none"> ➢ All subjects: β= 0.51 ➢ AD and MCI: β= 0.41 ➢ FTLD: β= 0.49 Tau PET SUVR: β= 0.73 • Autopsy-confirmed cohort: Plasma P-tau181 ↑ in Braak V-VI vs Braak 0, I-II and III-IV • Cohort 2: Correlation of Tau PET SUVR and plasma P-tau181: r= 0.33
Immunomagnetic reduction (IMR) (Plasma) <i>(Yang et al., 2018)</i>	<p>73 participants:</p> <ul style="list-style-type: none"> 23 CU, 29 MCI due to AD, 21 very mild AD 	<ul style="list-style-type: none"> • MCI due to AD vs HC: 0.855 • MCI due to AD vs very mild AD: 0.777 	<p>Plasma P-tau181 ↑ in:</p> <ul style="list-style-type: none"> • very mild AD and MCI due to AD vs CU • very mild AD vs MCI due to AD 			

P-tau217 (and P-tau181)						
<p>MSD (Plasma) (Palmqvist et al., 2020)</p>	<ul style="list-style-type: none"> Neuropathology cohort (n=81): 47 non-AD, 34 AD BioFINDER-2 cohort (n=699): <ul style="list-style-type: none"> 301 CU: 224 Aβ-, 77 Aβ+ 178 MCI: 86 Aβ-, 92 Aβ+ 121 AD: all Aβ+ 99 other neurodegenerative diseases: 45 PD/PDD/MSA (8 Aβ+, 37 Aβ-), 21 PSP/CBS (1 Aβ+, 20 Aβ-), 12 VaD (2 Aβ+, 10 Aβ-), 21 bvFTD/PPA (4 Aβ+, 17 Aβ-) Autosomal-Dominant AD registry (n=622): <ul style="list-style-type: none"> PSEN1 E208A mutation: <ul style="list-style-type: none"> 106 CI carriers 259 CU carriers 257 non-carriers 	<ul style="list-style-type: none"> Neuropathology cohort: AD vs non-AD: <ul style="list-style-type: none"> P-tau217: 0.89 P-tau217/Aβ42 ratio: 0.90 P-tau217/t-tau ratio: 0.88 P-tau181: 0.72 BioFINDER-2 cohort (n=699): Aβ+ AD vs all other neurodegenerative diseases: <ul style="list-style-type: none"> P-tau217: 0.96 P-tau217/Aβ42 ratio: 0.94 P-tau217/t-tau ratio: 0.93 P-tau181: 0.81 Aβ+ AD vs Aβ- MCI: <ul style="list-style-type: none"> P-tau217: 0.97 Aβ+ AD vs Aβ- CU: <ul style="list-style-type: none"> P-tau217: 0.98 	<ul style="list-style-type: none"> Neuropathology cohort: Plasma P-tau217 ↑ in AD vs non-AD BioFINDER-2 cohort: Plasma P-tau217 ↑ in: <ul style="list-style-type: none"> Aβ+ AD vs all other diagnostic groups Aβ+ MCI vs Aβ- CU, Aβ- MCI, bvFTD/PPA, PD/PDD/MSA and PSP/CBS Aβ+ CU vs Aβ- CU, Aβ- MCI and PD/PDD/MSA Autosomal-Dominant AD: Plasma P-tau217 levels in mutation carriers were significantly different (†) from noncarriers at age 24.9, about 20 years before mutation carriers' median age of MCI onset. 	<p>BioFINDER-2 cohort:</p> <ul style="list-style-type: none"> P-tau217: 0.87 P-tau181: 0.76 	<ul style="list-style-type: none"> Neuropathology cohort: Correlation of NFT density score and plasma P-tau217 in: <ul style="list-style-type: none"> AD only: r= 0.64 Non-AD: r= 0.15 BioFINDER-2 cohort: Correlation of: <ul style="list-style-type: none"> Tau PET SUVR (Braak I-II) and: <ul style="list-style-type: none"> Plasma P-tau217: r= 0.59 Plasma P-tau181: r= 0.52 Tau PET SUVR (inferior temporal cortex) and: <ul style="list-style-type: none"> Plasma P-tau217: r= 0.54 Plasma P-tau181: r= 0.45 Tau PET SUVR (Braak I-IV) and: <ul style="list-style-type: none"> Plasma P-tau217: r= 0.57 Plasma P-tau181: r= 0.47 Tau PET SUVR (Braak V-VI) and: <ul style="list-style-type: none"> Plasma P-tau217: r= 0.44 Plasma P-tau181: r= 0.35 	
<p>MSD (Plasma) (Brickman et al. 2021)</p>	<p>Washington Heights-Inwood Columbia Aging Project</p> <ul style="list-style-type: none"> Neuropathology cohort (n=113): <ul style="list-style-type: none"> 33 High AD neuropathological change (ADNC) 80 all other groups (not AD, low AD, intermediate ADNC) Clinical cohort (n=300)[†]: <ul style="list-style-type: none"> 169 CU 131 AD No biomarker status; based on clinical assessment <p>[†]A subset of the clinical cohort has received amyloid PET (n=40): 8Aβ+, 32 Aβ-</p>	<ul style="list-style-type: none"> Neuropathology cohort: High ADNC vs all other groups: <ul style="list-style-type: none"> All participants (n=112): <ul style="list-style-type: none"> P-tau217: 0.84 P-tau181: 0.77 Non-Hispanic White (n=52): <ul style="list-style-type: none"> P-tau217: 0.75 P-tau181: 0.65 Non-Hispanic Black (n=31): <ul style="list-style-type: none"> P-tau217: 0.96 P-tau181: 0.94 Hispanic (n=29): <ul style="list-style-type: none"> P-tau217: 0.85 P-tau181: 0.82 Clinical cohort: AD vs CU: <ul style="list-style-type: none"> All participants (n=297): <ul style="list-style-type: none"> P-tau217: 0.63 P-tau181: 0.61 Non-Hispanic White (n=100): <ul style="list-style-type: none"> P-tau217: 0.71 	<ul style="list-style-type: none"> Neuropathology cohort: Plasma P-tau217 and P-tau181 ↑ in higher ADNC vs all other groups Clinical cohort: Plasma P-tau217 and P-tau181 ↑ in AD vs CU Subset of amyloid PET cohort: Plasma P-tau217 and P-tau181 ↑ in Aβ+ vs Aβ- groups 	<ul style="list-style-type: none"> P-tau217: 0.84 P-tau181: 0.82 	<p>Correlation of Aβ PET SUVR and plasma:</p> <ul style="list-style-type: none"> P-tau217: r= 0.48 P-tau181: r= 0.26 	

		<ul style="list-style-type: none"> ➢ P-tau181: 0.69 <p>Non-Hispanic Black (n=98):</p> <ul style="list-style-type: none"> ➢ P-tau217: 0.68 ➢ P-tau181: 0.63 <p>Hispanic (n=100):</p> <ul style="list-style-type: none"> ➢ P-tau217: 0.52 ➢ P-tau181: 0.51 				
<p>IP-MS (LC-MS/MS) (Barthélemy, Horie, Sato, & Bateman, 2020)</p>	<ul style="list-style-type: none"> • Tau SILK Discovery cohort (n=34): <ul style="list-style-type: none"> ➢ 9 young controls (Aβ-, CDR=0) ➢ 8 elderly controls (Aβ-, CDR=0) ➢ 2 non-AD MCI (Aβ-, CDR=0.5) ➢ 5 preclinical AD (Aβ+, CDR=0) ➢ 8 AD-MCI (Aβ+, CDR=0.5) ➢ 2 AD-moderate (Aβ+, CDR=1) • Aβ SILK Validation cohort (n=92) <ul style="list-style-type: none"> ➢ 31 elderly controls (Aβ-, CDR=0) ➢ 11 non-AD MCI (Aβ-, CDR=0.5) ➢ 20 preclinical AD (Aβ+, CDR=0) ➢ 24 AD-MCI (Aβ+, CDR=0.5) ➢ 6 AD-moderate (Aβ+, CDR=1) 		<ul style="list-style-type: none"> • Discovery cohort: Plasma P-tau217 ↑ in: <ul style="list-style-type: none"> ➢ Preclinical AD, AD-MCI and AD-moderate vs controls • Validation cohort: Plasma P-tau181 ↑ in: <ul style="list-style-type: none"> ➢ Preclinical AD, AD-MCI and AD-moderate vs controls 	<ul style="list-style-type: none"> • Discovery cohort: All subjects: <ul style="list-style-type: none"> ➢ P-tau217: 0.99 ➢ P-tau181: 0.95 • Validation cohort: All subjects: <ul style="list-style-type: none"> ➢ P-tau217: 0.93 ➢ P-tau181: 0.72 <p>CDR=0 only:</p> <ul style="list-style-type: none"> ➢ P-tau217: 0.86 ➢ P-tau181: 0.67 <p>CDR=0.5 only:</p> <ul style="list-style-type: none"> ➢ P-tau217: 0.93 ➢ P-tau181: 0.68 	<p>Validation cohort: In all subjects, correlation of Aβ PET and:</p> <ul style="list-style-type: none"> • Plasma P-tau217: r=0.67 • Plasma P-tau181: r=0.26 	<ul style="list-style-type: none"> • Discovery cohort: Correlation of: <ul style="list-style-type: none"> ➢ Plasma P-tau217 and CSF P-tau217 in all subjects: r=0.78 ➢ Plasma P-tau181 and CSF P-tau181 in all subjects: r=0.68 • Validation cohort: Correlation of: <ul style="list-style-type: none"> ➢ Plasma P-tau217 and CSF P-tau217 in all subjects: r=0.70 ➢ Plasma P-tau181 and CSF P-tau181 in all subjects: r=0.21
P-tau231 (and P-tau181)						
<p>Simoa (Plasma) (Ashton et al., 2021)</p>	<ul style="list-style-type: none"> • Discovery cohort (n=38): 18 CU elderly, 20 AD dementia • TRIAD (n=313): <ul style="list-style-type: none"> ➢ 32 Aβ- CU young adults ➢ 159 CU elderly: 128 Aβ-, 31 Aβ+ ➢ 54 MCI: 11 Aβ-, 43 Aβ+ ➢ 42 AD: all Aβ+ ➢ 26 Non-AD[†]: all Aβ- • Primary care cohort (n=190): <ul style="list-style-type: none"> ➢ 8 young adults ➢ 131 CU elderly ➢ 17 MCI ➢ 34 AD • Neuropathology cohort (n=47): 11 non-AD[‡], 36 AD <p>[†]Non-AD included 10 FTD, 1 PPA, 1 CBD, 2 PSP, 10 VCI, 1 hippocampal sclerosis, 1 CAA</p> <p>[‡]Non-AD included 3 PSP, 3 FTLN, 2 LBD, 2 VaD, 1 CAA</p>	<ul style="list-style-type: none"> • Discovery cohort: AD vs CU P-tau231: 0.942 • TRIAD cohort: Aβ+ AD vs Aβ- non-AD: <ul style="list-style-type: none"> ➢ P-tau231: 0.93 ➢ P-tau181: 0.94 • Aβ+ AD vs Aβ- CU elderly: <ul style="list-style-type: none"> ➢ P-tau231: 0.92 ➢ P-tau181: 0.94 • Aβ+ AD vs Aβ+ CU elderly: <ul style="list-style-type: none"> ➢ P-tau231: 0.67 ➢ P-tau181: 0.79 • Aβ+ AD vs Aβ- MCI: <ul style="list-style-type: none"> ➢ P-tau231: 0.88 ➢ P-tau181: 0.86 • Aβ+ AD vs Aβ+ MCI: <ul style="list-style-type: none"> ➢ P-tau231: 0.72 ➢ P-tau181: 0.76 • Primary care cohort: AD vs CU elderly: P-tau231: 0.75 	<ul style="list-style-type: none"> • Discovery: in this biomarker characterised cohort, plasma P-tau231 ↑ in AD vs CU • TRIAD cohort: Plasma P-tau231 ↑ in: <ul style="list-style-type: none"> ➢ Aβ+ AD vs all other diagnostic groups ➢ Aβ+ CU elderly and Aβ+ MCI vs Aβ- CU elderly, Aβ- MCI, Aβ- non-AD and Aβ- CU young adults • Primary care cohort: Plasma P-tau231 ↑ in: <ul style="list-style-type: none"> ➢ AD vs young and CU elderly ➢ MCI vs young • Neuropathology cohort: Plasma P-tau231 ↑ in AD vs non-AD 	<p>TRIAD cohort:</p> <ul style="list-style-type: none"> • CU (elderly): <ul style="list-style-type: none"> ➢ P-tau231: 0.83 ➢ P-tau181: 0.77 • MCI: <ul style="list-style-type: none"> ➢ P-tau231: 0.80 ➢ P-tau181: 0.75 	<p>TRIAD cohort: Correlation of plasma P-tau231 and:</p> <ul style="list-style-type: none"> • CSF Aβ42: r= -0.404 • Aβ PET SUVR: r= 0.623 <p>Change in plasma P-tau231 and P-tau181 as a function of Aβ PET quartiles:</p> <ul style="list-style-type: none"> • Plasma P-tau231 ↑ from Q2-Q4 Aβ PET, while P-tau181 ↑ Q4 Aβ PET 	<ul style="list-style-type: none"> • TRIAD cohort: Correlation of plasma P-tau231 and: <ul style="list-style-type: none"> ➢ CSF P-tau231: r= 0.591 ➢ Tau PET SUVR: r= 0.523 • Plasma P-tau231 and P-tau181 ↑ in Braak V-VI vs Braak 0, I-II and III-IV. • Plasma P-tau231 and P-tau181 ↑ in Braak III-IV vs Braak 0 and I-II. • Plasma P-tau231, but not P-tau181, ↑ in Braak I-II vs Braak 0. • Neuropathology cohort: Plasma P-tau231 ↑ in Braak V-VI vs Braak I-II

		MCI: P-tau231: 0.63				
		<ul style="list-style-type: none">• Neuropathology cohort: AD vs non-AD:<ul style="list-style-type: none">➤ P-tau231: 0.997➤ P-tau181: 0.929				

Significant correlation coefficients ($p < 0.05$) are in **red font**.

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