Supplementary Appendix

Brain-derived tau: a novel blood-based biomarker for Alzheimer's disease-type neurodegeneration

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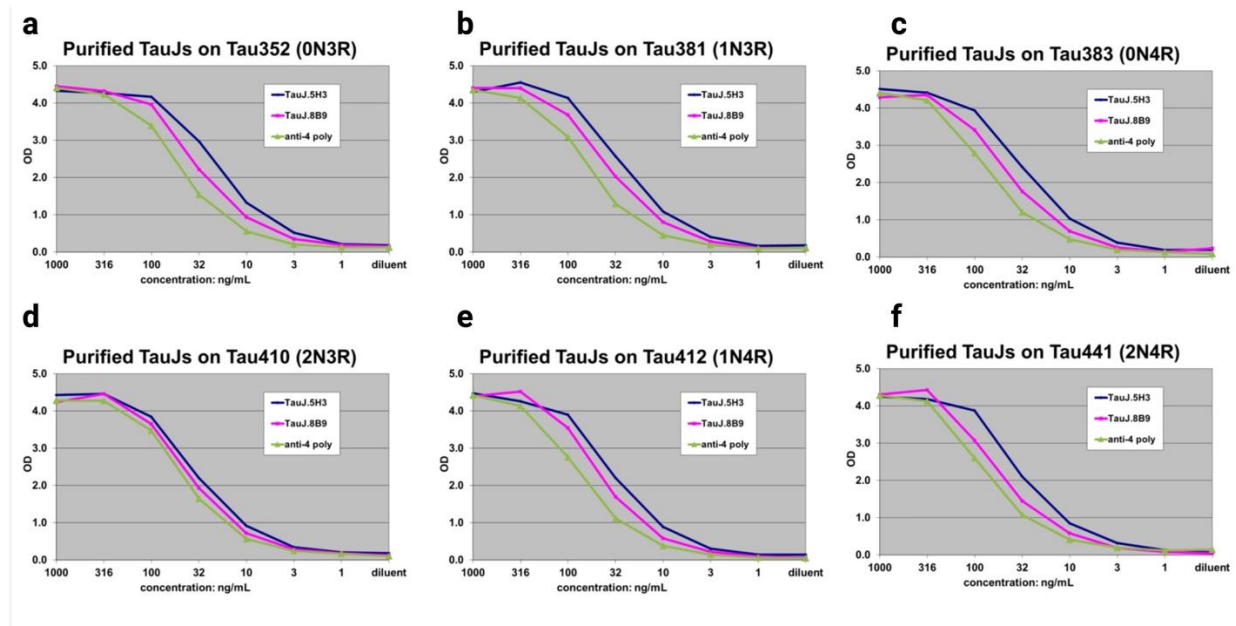
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**Running title:** Plasma BD-tau as an AD degeneration marker

Supplementary Figures

Supplementary Fig. 1. TauJ.5H3 recognizes all six tau isoforms expressed in the adult human CNS. The plots in **(A)** – **(F)** show the binding profile of the anti-BD-tau antibody TauJ.5H3 to all six isoforms of tau commonly expressed in the adult human brain. The plots start from the shortest isoform (0N3R) in **(A)** to the longest isoform (2N4R) in **(F).**
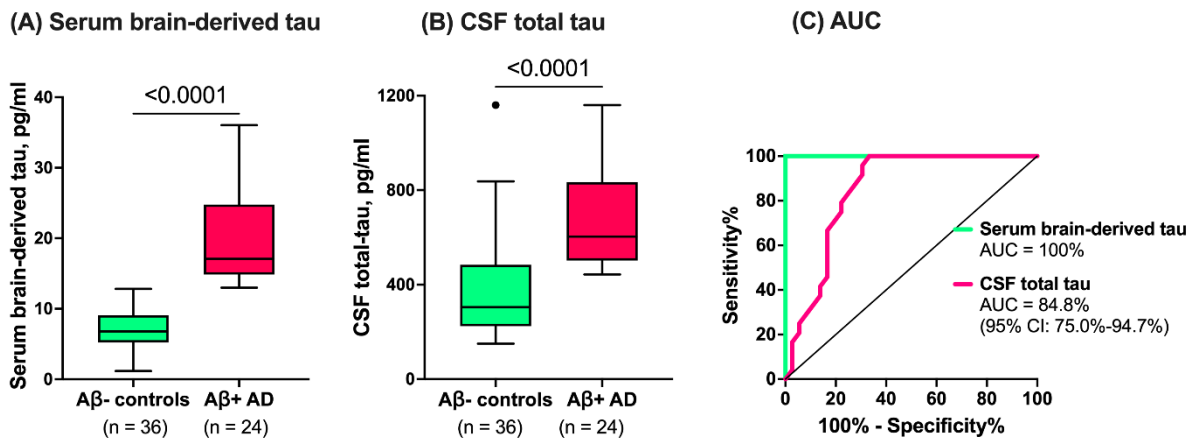
Supplementary Fig. 2. Concentrations and diagnostic accuracy of serum BD-tau versus CSF t-tau in the Neurochemical cohort. The Tukey plots in (A) show the profile of serum BD-tau in Aβ+ Alzheimer's disease and Aβ- controls. (B) ROC curve and AUC values for the discriminatory performance of serum BD-tau to separate the two groups. P values show the outcome of Mann Whitney test.

(A)

(B)
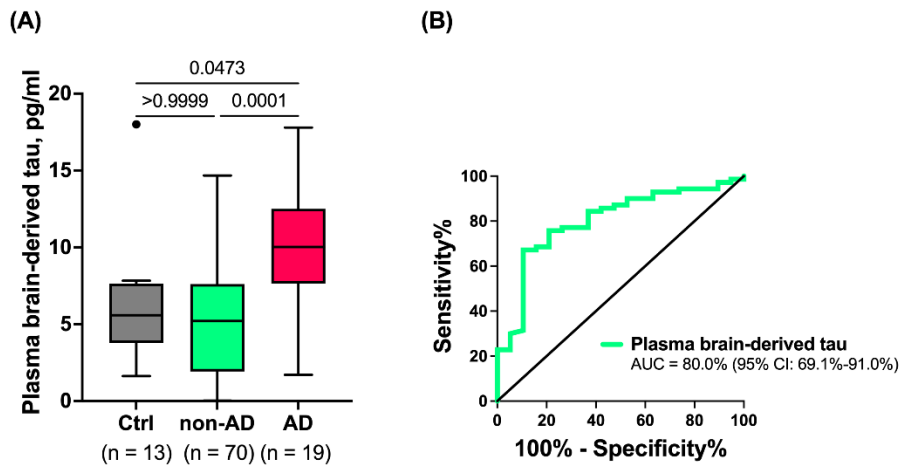
Supplementary Fig. 3. Levels and diagnostic performance of plasma BD-tau in the Memory Clinic cohort-2. **(A)** Tukey plots of plasma BD-tau levels. **(C)** ROC curve and AUC values for differentiating Alzheimer's disease (AD) from other neurodegenerative diseases (non-AD).

Supplementary Tables

Supplementary Table 1: Demographic characteristics of the Discovery and Neurochemical cohorts.

	Discovery cohort		Neurochemical cohort	
	Control	**Alzheimer's disease**	**Control**	**Alzheimer's disease**
Sample size	10	10	36	24
Age, y	58.4 ±17.1	71.4 ±7.3	65.1 ±13.7	71.1 ±8.9
Gender, F, *n (%)*	6 (60%)	7(70%)	17 (47.2%)	19 (79.1%)
CSF Aβ42, pg/ml	965 ±273.6*	453.5 ±106.3	855.6 ±346*	423 ±112.5
CSF t-tau (Innotest), pg/ml	270.2 ±104.7*	675.3 ±249.1	389.9 ±237*	689.7 ±224
CSF p-tau181 (Innotest), pg/ml	32.4 ±12.96*	95 ±28.3	53.6 ±38.6*	103.1 ±37.44
CSF BD-tau, pg/ml	101.1 ±39.8*	218.8 ±62.9	N/A	N/A
Serum BD-tau, pg/ml	3.6 ±2.5*	34.7 ±10.1	7.2 ±2.8*	22.7 ±17.5
CSF t-tau (Quanterix), pg/ml	232.5 ±86.1*	379.5 ±122.4	N/A	N/A
Serum t-tau (Quanterix), pg/ml	6.0 ±8.1	11.6 ± 16.1	N/A	N/A

*Significantly different compared with the Alzheimer's disease group (P<0.0001). Mann Whitney test.

Supplementary Table 2. Demographic characteristics of the Memory clinic cohort-1 and Memory clinic cohort-2.

	Controls	AD	Non-AD
Memory Clinic-1			
Sample size	59	60	256
Age, years	65.3 ±12.1	75.5 ± 8.2	66.3 ± 8.1
Gender, F, *n (%)*	48 (81.3%)	41 (68.3%)	126 (49.2)
Serum BD-tau, pg/ml	3.6 ± 2	32.4 ± 141.6	4.2 ± 19.8
Serum NfL, pg/ml	15.2 ± 8	34.1 ± 22.5	40.1 ± 29.2
Memory Clinic-2			
Sample size	13	19	70
Age, y	55.7 ± 15.1	68.3 ± 6.1	62.9 ± 10.3
Gender, F, *n (%)*	8 (61.5%)	10 (52.6%)	42 (60%)
Plasma BD-tau, pg/ml	5.3 ± 2.0	9.4 ± 4.1	4.9 ± 3.4

Supplementary Table 3. Spearman correlation of serum BD-tau with other biomarkers in the Discovery and Neurochemical cohorts

Group	Serum t-tau (Quanterix)	CSF t-tau (Quanterix)	CSF BD-tau	CSF total tau (INNOTEST)	CSF p-tau181 (INNOTEST)	CSF Aβ42 (INNOTEST)
Discovery cohort						
Entire cohort	rho = 0.26 (p=0.2738)	rho= 0.75 (p=0.0002)	rho= 0.85 (p<0.0001)	rho= 0.83 (p<0.0001)	rho= 0.86 (p<0.0001)	rho= -0.73 (p=0.0003)
AD	rho= 0.08 (p=0.8382)	rho= 0.83 p= 0.0047	rho= 1.00 (p<0.0001)	rho= 0.67 (p=0.0390)	rho= 0.69 (p=0.0326)	rho= 0.18 (p=0.6136)
Controls	rho= -0.08 (p=0.8382)	rho= 0.07 p= 0.8810	rho= 0.05 (p=0.8916)	rho= 0.15 (p=0.6738)	rho= 0.19 (p=0.6073)	rho= -0.01 (p=0.8916)
Neurochemical cohort						
Entire cohort	N/A	N/A	N/A	rho=0.65 (p<0.0001)	rho= 0.64 (p <0.0001)	rho= -0.59 (p<0.0001)
AD	N/A	N/A	N/A	rho=0.59 (p=0.0024)	rho= 0.63 (p= 0.0009)	rho= -0.22 (p= 0.3056)
Controls	N/A	N/A	N/A	rho=0.28 (p=0.0996)	rho= 0.26 (p= 0.1254)	rho= -0.22 (p= 0.1979)

N/A = not available

Supplementary Table 4. Spearman correlation of plasma BD-tau with other plasma biomarkers in the Neuropathology cohort

	Plasma NfL	Plasma p-tau181	Plasma p-tau231	Plasma Aβ42/40 ratio
Entire cohort	rho=0.38 (p=0.0054)	rho= 0.69 (p<0.0001)	rho= 0.75 (p<0.0001)	rho= -0.39 (p= 0.0045)
Alzheimer's disease	rho= 0.74 (p<0.0001)	rho= 0.54 (p <0.0011)	rho= 0.69 (p<0.0001	rho= 0.03 (p= 0.8666)
Non-Alzheimer's disease	rho= 0.16 (p= 0.5153)	rho= 0.19 (p= 0.4609)	rho= 0.29 (p= 0.2431)	rho= -0.36 (p= 0.1372)

Supplementary Table 5. Spearman correlation of serum BD-tau with other blood biomarkers in the Memory Clinic cohort-1

Group	Serum NfL
Entire cohort	rho = -0.07 (p= 0.2066)
Alzheimer's disease	rho= 0.63 (p <0.0001)
Controls	rho= 0.33 (p= 0.0115)
Non-Alzheimer's diseases (combined)	rho= -0.12 (p= 0.0658)