PS02.136 Rapid Mechanistic Bridging of an Alzheimer's Disease Plasma Protein Staging Panel Across Brain Proteomics Cohorts

Charles C. Kim, Meghan Kerrisk Campbell, Maximilien Burq, Aljaz Potocnik, Dejan Stepec, Cássia Maués Cuóco, Yelena Bronevetsky, Domen Zafred, Jacqueline M. Leung, Peter Cimermancic

tesorai

Background. Blood-based biomarkers are transforming Alzheimer's Disease (AD) diagnosis and staging. Recent multi-protein plasma panels accurately identify individuals with advanced Braak pathology, but whether these circulating biomarkers truly reflect the molecular remodeling underlying AD neuropathology remains unclear. Pre-existing datasets could answer such questions, but their reuse requires harmonized protein expression data, standardized sample annotations, and consistent study metadata.

Methods. A recently reported seven-protein plasma staging panel was evaluated across multiple post-mortem proteomics brain cohorts using pre-structured datasets on the Tesorai platform. Five datasets with Braak stage data were identified and re-analyzed. A linear model was used to distinguish late (V-VI) from early Braak stage (0-IV). Because phosphorylated tau 217 (p-tau217) and amyloid beta 1-40 (Aβ40) were not reported for any studies, raw spectra were reprocessed to quantify these proteoforms.

Results. Across the cohorts, the plasma-derived biomarker panel consistently discriminated early from late disease despite heterogeneous protein coverage. Reprocessing of raw spectra recovered tau phosphopeptides absent from the original protein summaries, enabling inclusion of p-tau217, while Aβ40 remained undetected. Together, these findings show that proteins comprising a recently proposed blood-based staging panel are associated with proteomic remodeling in the AD brain across independent cohorts.

Conclusions. These findings provide biological validation for a recently proposed blood-based seven-protein staging panel by demonstrating that its constituent biomarkers are associated with disease-stage proteomic changes in AD brain tissue. More broadly, re-mining legacy mass spectrometry data for disease-relevant proteoforms, combined with pre-structured datasets, can accelerate evaluation of emerging blood-based biomarkers against neuropathological and molecular features of disease.

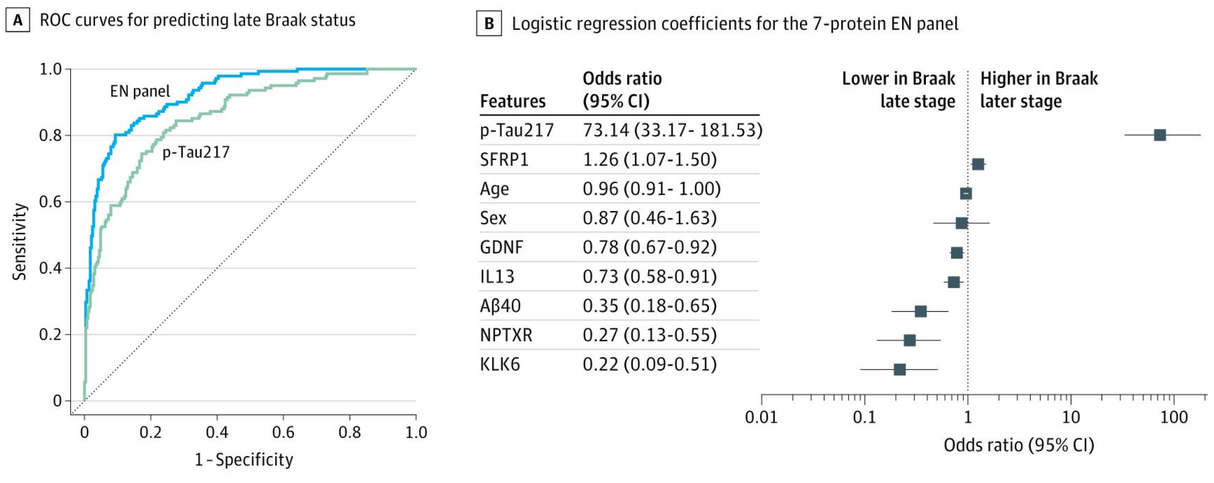


Figure 1. Recently reported results from Molfetta et al. (2026). (Left) Receiver-operating curve graph showing performance of the elastic net (EN) panel and plasma phosphorylated Tau 217 (p-tau217) for Identifying late Braak Individuals in the BioFINDER discovery cohort. (Right) Logistic regression coefficients for the 7-protein EN panel.

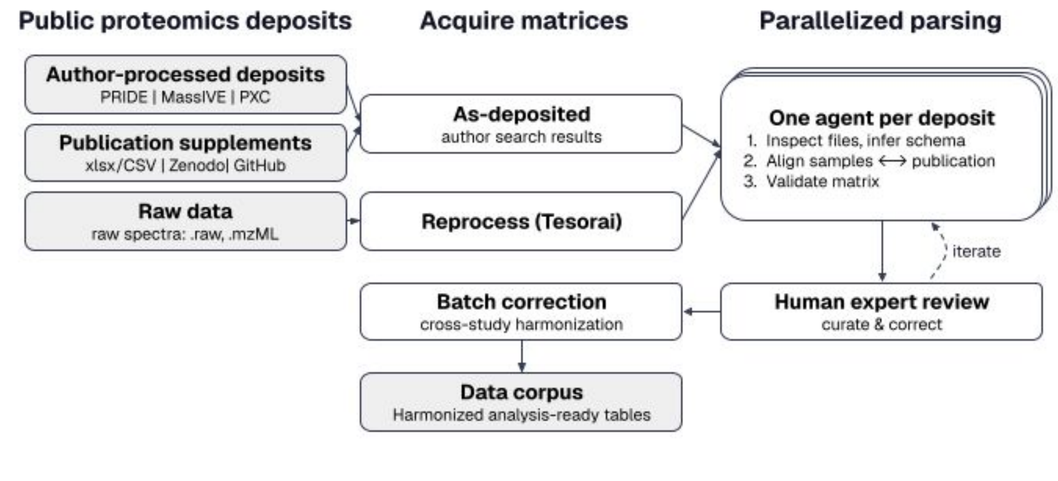
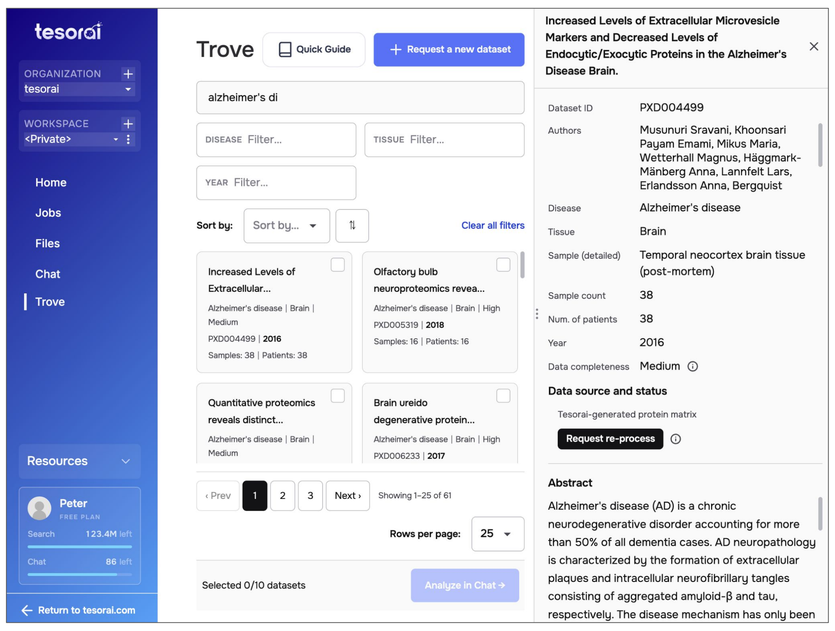


Figure 2. Tesorai's dataset structuring pipeline. Public datasets are taken as-deposited or reprocessed through Tesorai to generate quantified protein matrices. An LLM agent per deposit infers layout and links samples to the source publication, with human experts reviewing the results. Harmonized, batch-corrected tables are then made available for analysis through a chat interface.

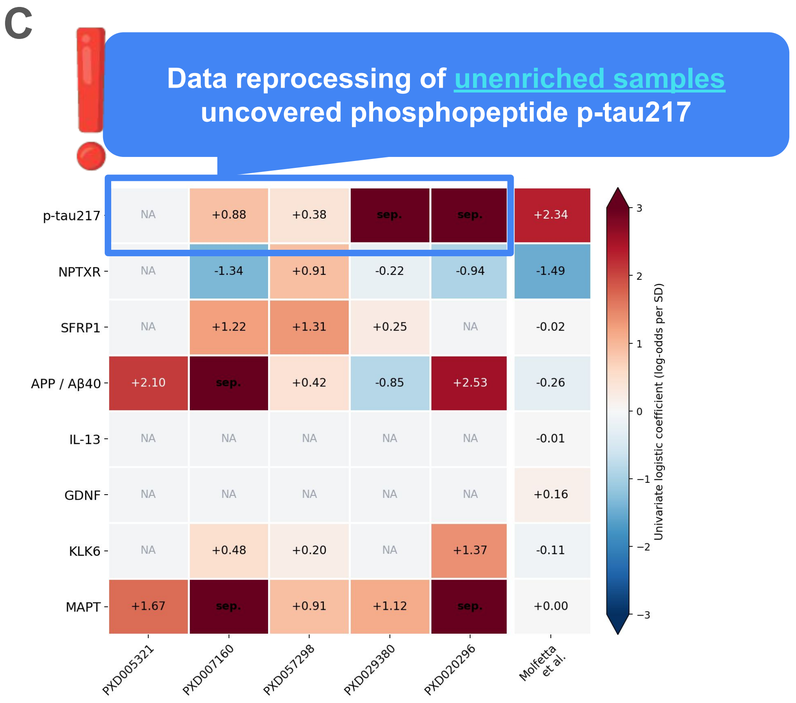
A



B

PXD ID	S#	P#	Proteins detected from 7-protein panel
PXD005321	35	35	2/7: MAPT, APP
PXD007160	80	49	5/7: MAPT, NPTXR, SFRP1, APP, KLK6
PXD020296	27	27	4/7: MAPT, NPTXR, APP, KLK6
PXD057298	72	72	5/7: MAPT, NPTXR, SFRP1, APP, KLK6
PXD029380	37	37	4/7: MAPT, NPTXR, SFRP1, APP

C



D

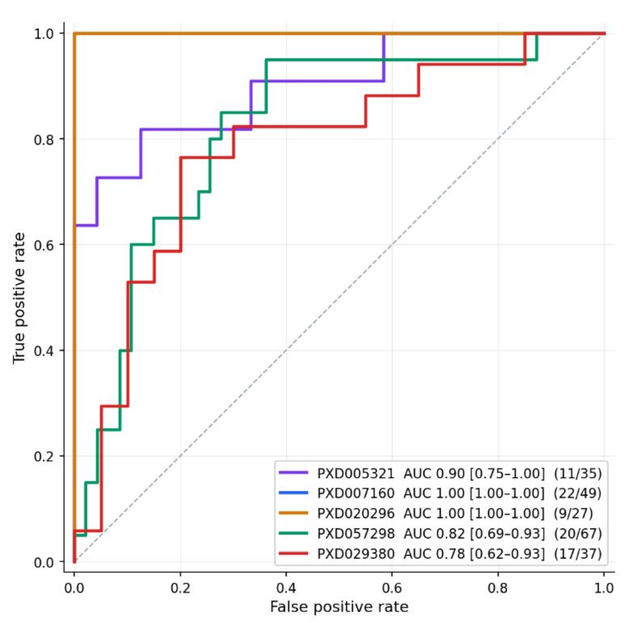


Figure 3. Tesorai Trove for rapid analysis of existing source data. (A) Tesorai Trove. A structured, searchable collection of public life-science datasets, integrating data from repositories, publications, supplements, and raw MS files into harmonized, analysis-ready datasets. (B) Public AD proteomics datasets selected for validation of the plasma multi-protein staging panel. (C) Consistency of individual biomarker associations across independent brain proteomics cohorts. (D) Receiver operating characteristic of the plasma tau-staging panel across five brain proteomics cohorts. The line for PXD007160 is obscured by the line for PXD020296 due to both curves having an AUC of 1.00

References

Di Molfetta, G.; Brum, W. S.; Pola, I.; Tan, K.; Benedet, A. L.; Sauer, M.; Montoliu-Gaya, L.; Janelidze, S.; Mattsson-Carlgren, N.; Rahmouni, N.; Chan, T.; Denkinger, M. N.; Proitsi, P.; Zetterberg, H.; Hansson, O.; Rosa-Neto, P.; Ashton, N. J. Plasma Biomarkers for Neocortical Tau Burden. JAMA Neurol. 2026, e262650.

Burq, M.; Cimermancic, P.; Kim, C.; Stepec, D. Single-Cell Foundation Models Benefit from Cross-Modal Training: Adding Proteomics Data Beats Parameter Scaling. bioRxiv August 19, 2026, p 2026.08.14.744845.

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