

Lipid Nanoprobe-Based Isolation of Plasma Extracellular Vesicles Enables Detection of CNS-Derived Alzheimer's Disease Biomarkers

Jadranka Milosevic (PhD)¹, Zeng, Xuemei (PhD)^{2,3}, Leonardo D'Aiuto (PhD)², Siyang Zheng (PhD)⁴, Thomas K Karikari (PhD)^{2,3}, Hongzhang He (PhD)^{1*}.

¹Captis Diagnostics Inc, Pittsburgh, PA, USA (email: simonhe@captisdx.com).

²University of Pittsburgh, Department of Psychiatry, School of Medicine, Pittsburgh, PA, USA.

³Alzheimer's Disease Research Center, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

⁴Carnegie Mellon University, Biomedical Engineering, Pittsburgh, PA, USA.

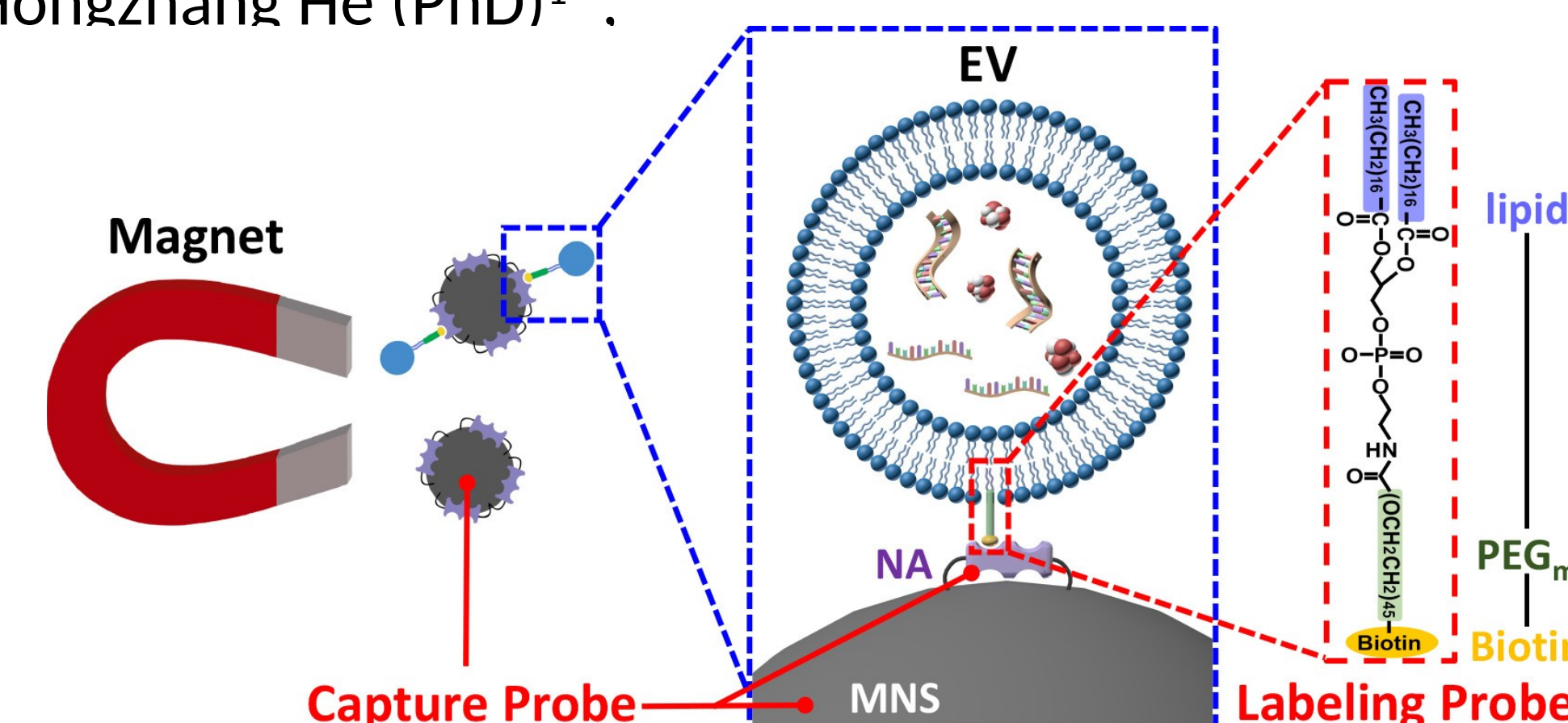


Fig. 1 LNP with labeling probe and capture probe for EV isolation from plasma samples.

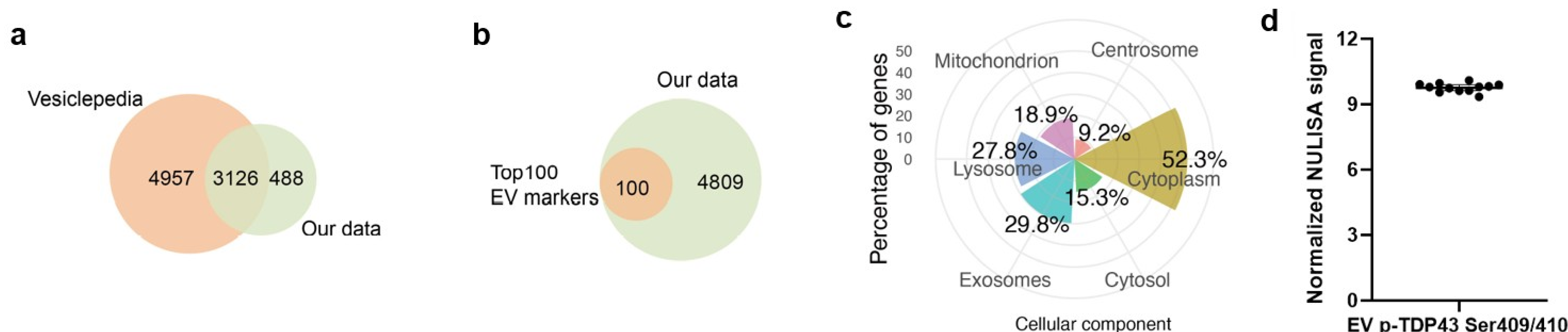


Fig. 2 Plasma proteins identified by different blood proteomic methods. **a)** Overlap of proteins identified from our dataset using EV method with the Vesiclepedia database. **b)** The top 100 recognized EV marker proteins were all identified in our dataset using EV method. **c)** GO (Gene Ontology) analysis of identified proteins based on cellular components. **d)** Quantification of EV-associated phosphorylated TDP-43 (p-TDP43 Ser409/410) in EVs from plasma using the NULISA platform.

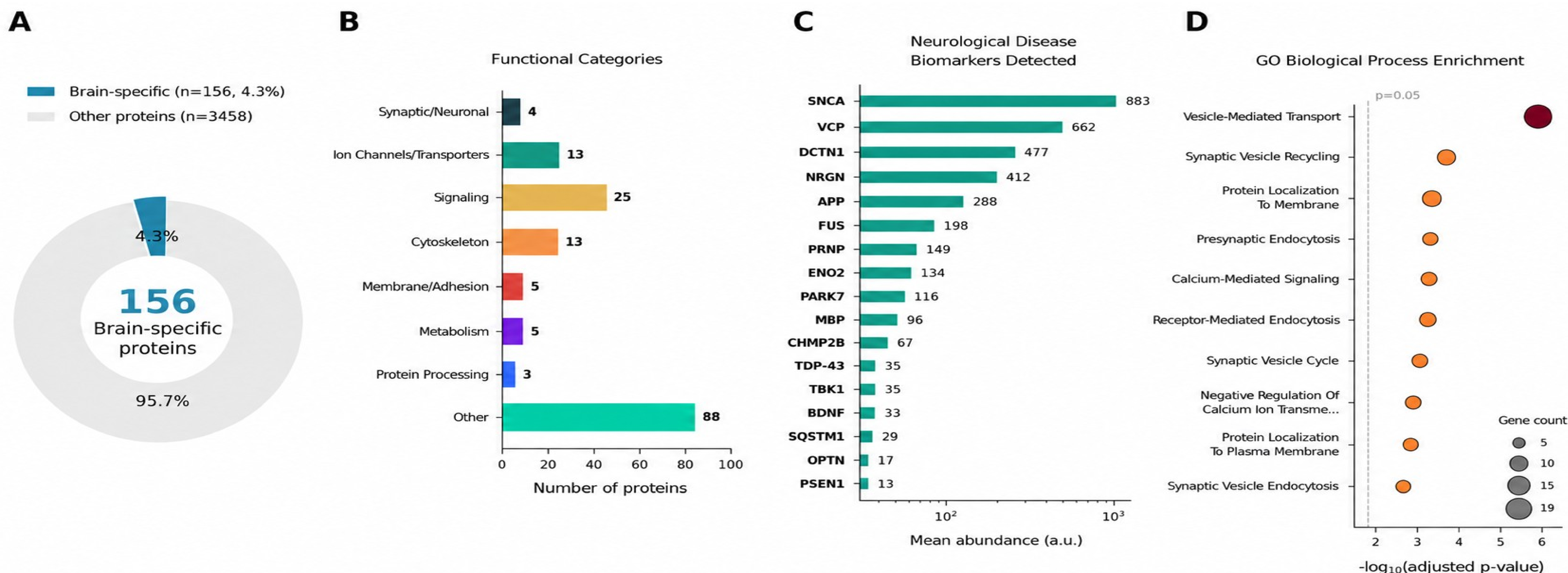


Fig 3. Brain-derived proteins identified in plasma EVs isolated by LNP. (A) Proportion of brain-specific proteins detected in plasma EVs. Of 3,614 quantified proteins, 156 (4.3%) were classified as brain-specific based on tissue-enhanced or tissue-enriched expression in the Human Protein Atlas. **(B)** Functional categorization of brain-specific proteins. **(C)** Detection of established neurological biomarkers in plasma EVs.. **(D)** Gene Ontology Biological Process enrichment analysis. Dot plot showing the top 10 enriched GO terms among brain-specific proteins.