

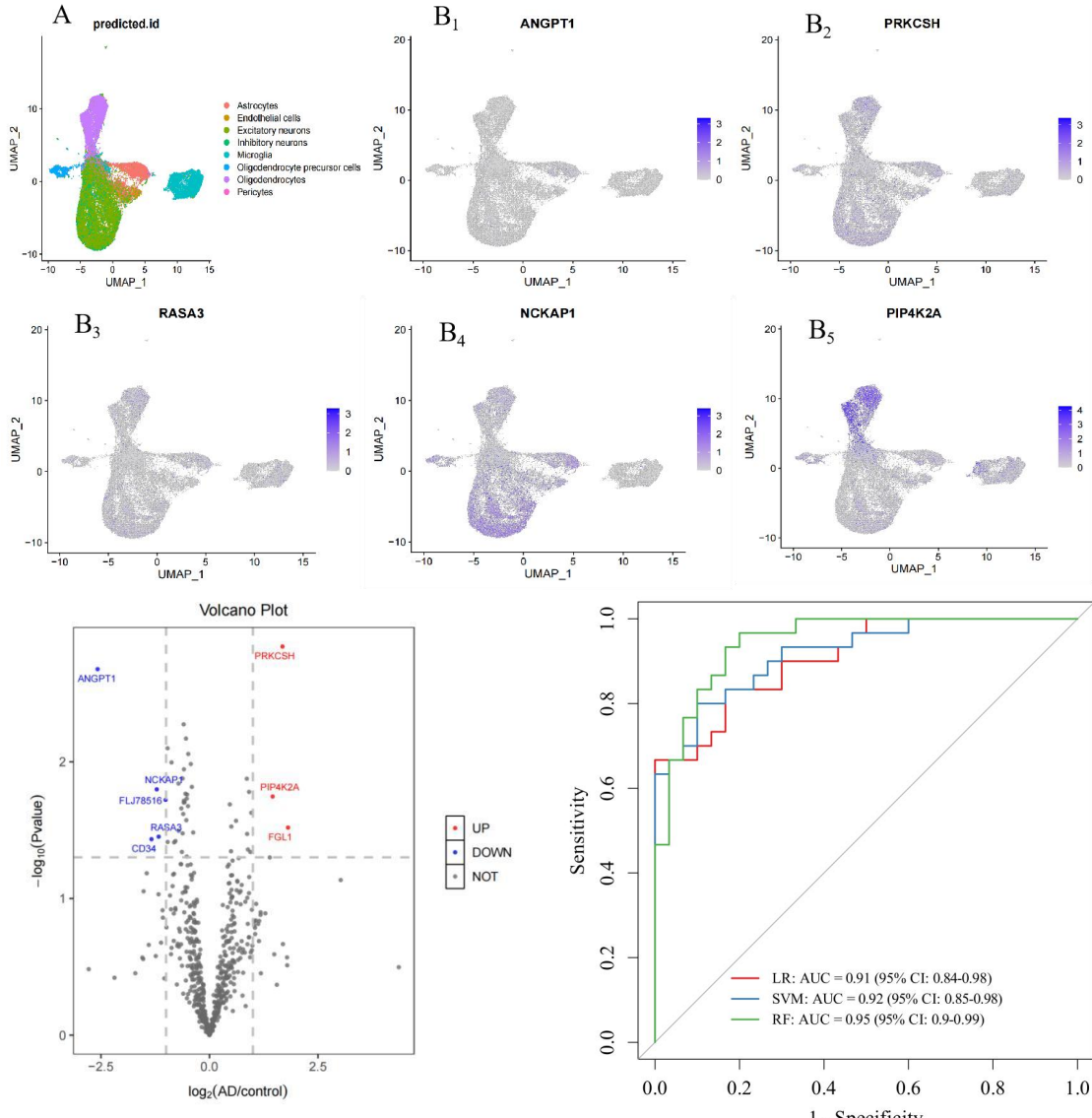
A Nested Case-Control Study of Plasma Extracellular Vesicle Biomarkers for Alzheimer's Disease: Discovery, Targeted Validation, and Cellular Origin Analysis

P2-06

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- Discovered and validated a 4-protein plasma EV panel (PRKCSH, ANGPT1, NCKAP1, FLJ78516) for AD diagnosis.
- Achieved high diagnostic accuracy (AUC 0.95, 92% sensitivity, 91% specificity) for AD.
- Biomarkers originate from brain endothelial cells & microglia, linking to AD pathology.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Early and accurate Alzheimer's Disease (AD) diagnosis is critical but challenged by invasive, costly current methods. Plasma Extracellular Vesicles (EVs) offer a non-invasive "liquid biopsy" of the brain. We aimed to identify, validate, and determine the cellular origins of a novel, highly accurate plasma EV protein biomarker panel for AD.	Study Design: Two-phase nested case-control. - Discovery (n=50): 25 AD, 25 healthy controls (HC). - Validation (n=85): 30 AD, 25 MCI, 30 HC (independent multicenter). EV Isolation & Characterization: Magnetic-bead-based enrichment; confirmed by TEM, NTA, and Western blot. Proteomics: - Discovery: Untargeted 4D label-free LC-MS/MS. - Validation: Targeted SRM-MS. Bioinformatics: Integrated Human Protein Atlas and brain single-cell RNA-seq to infer cellular origins. Statistics: Adjusted for confounders (age, systolic blood pressure). Random Forest model with 10-fold cross-validation (AUC, sensitivity, specificity).	- PRKCSH: Significantly upregulated in AD vs. HC & MCI ($p<0.001$, $p=0.02$). - ANGPT1, NCKAP1, FLJ78516: Significantly downregulated in AD vs. HC & MCI ($p<0.001$). - Diagnostic Performance (Multi-marker Random Forest model): AUC: 0.95 (95% CI: 0.91-0.99); Sensitivity: 92%; Specificity: 91% (AD vs. HC) 	We identified and validated a highly accurate, four-protein plasma EV panel (PRKCSH, ANGPT1, NCKAP1, FLJ78516) for AD diagnosis. Its origins from brain endothelial cells and microglia underscore its biological relevance. This robustly validated, non-invasive biomarker panel represents a significant advance towards a clinically applicable blood test to complement existing diagnostic strategies for Alzheimer's disease.	- Albert, M.S. et al. (2011). The diagnosis of mild cognitive impairment... <i>Alzheimers Dement</i>. - Dubois, B., et al. (2014). Advancing research diagnostic criteria for Alzheimer's disease... <i>Lancet Neurol</i>. - Kanninen, K.M., et al. (2016). Exosomes as new diagnostic tools in CNS diseases. <i>Biochim Biophys Acta</i>. - Welsh, J.A., et al. (2024). Minimal information for studies of extracellular vesicles (MISEV)... <i>J Extracell Vesicles</i>. CONTACT  扫二维码，添加我为朋友。 phoebe 浙江 杭州 Li Yang, Zhejiang Hospital, Hangzhou, China. Email: yangli84331@163.com 