

KEY TAKEAWAYS

ENO2
top marker

ARSA
amyloid-linked protein

AUC 0.96
7-protein panel

Plasma NULISA proteomics identified plasma protein signatures linked to A β pathology, PET amyloid burden, and AD-relevant biological pathways.

BACKGROUND & METHODS

Why this study?

- Blood biomarkers are scalable tools for detecting core AD pathologies.
- Blood biomarkers also provide opportunities to investigate disease mechanisms.
- AD biology extends beyond A β and tau, requiring broader molecular profiling.
- The Nucleic acid-Linked Immuno-Sandwich Assay (NULISA) platform increased sensitivity at the attomole level for protein detection in low sample volume.

Objective

Identify plasma NULISA markers associated with A β pathology and evaluate their diagnostic and biological relevance.

Study design

Patients with cognitive impairment

PET-defined cohort
n = 153; A β + 79; A β - 74

- NULISeq CNS Disease Panel 120.
- [18F]-florbetapir PET quantified by Centiloid and regional SUVR.
- ROC analyses, LASSO regression, global and regional PET correlation analyses.

RESULT 1: DIAGNOSTIC PERFORMANCE

Individual NULISA markers distinguished A β positivity

- 37 proteins differed between A β + and A β - after FDR correction.
- Plasma ENO2 (AUC=0.92) and ARSA (AUC=0.88) showed high discriminative performance and retained diagnostic value across early clinical stages.

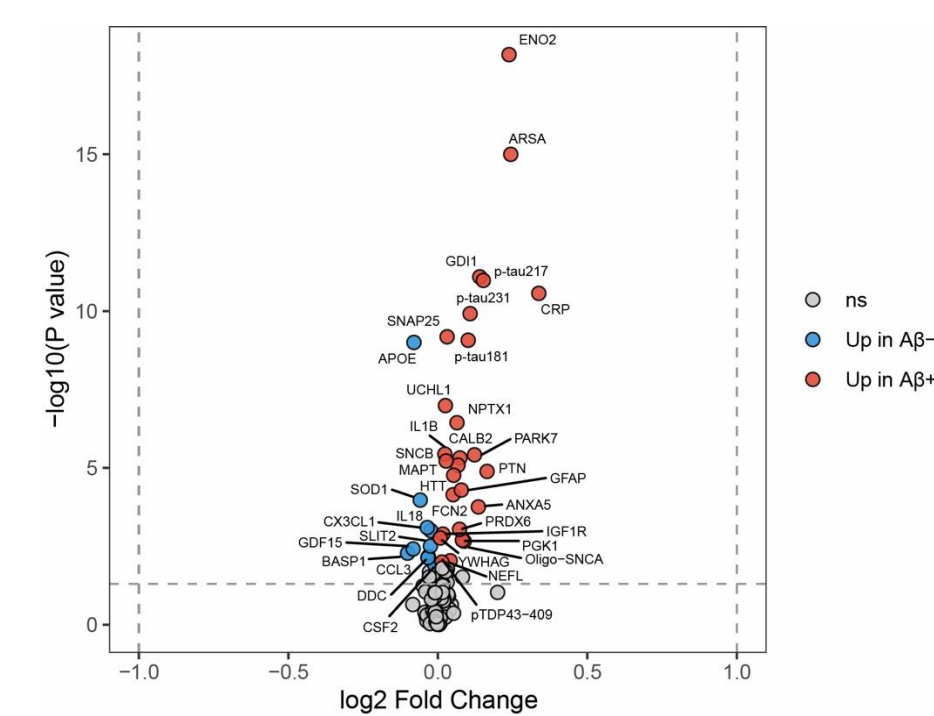


Figure 1. Volcano plot of NULISA markers.

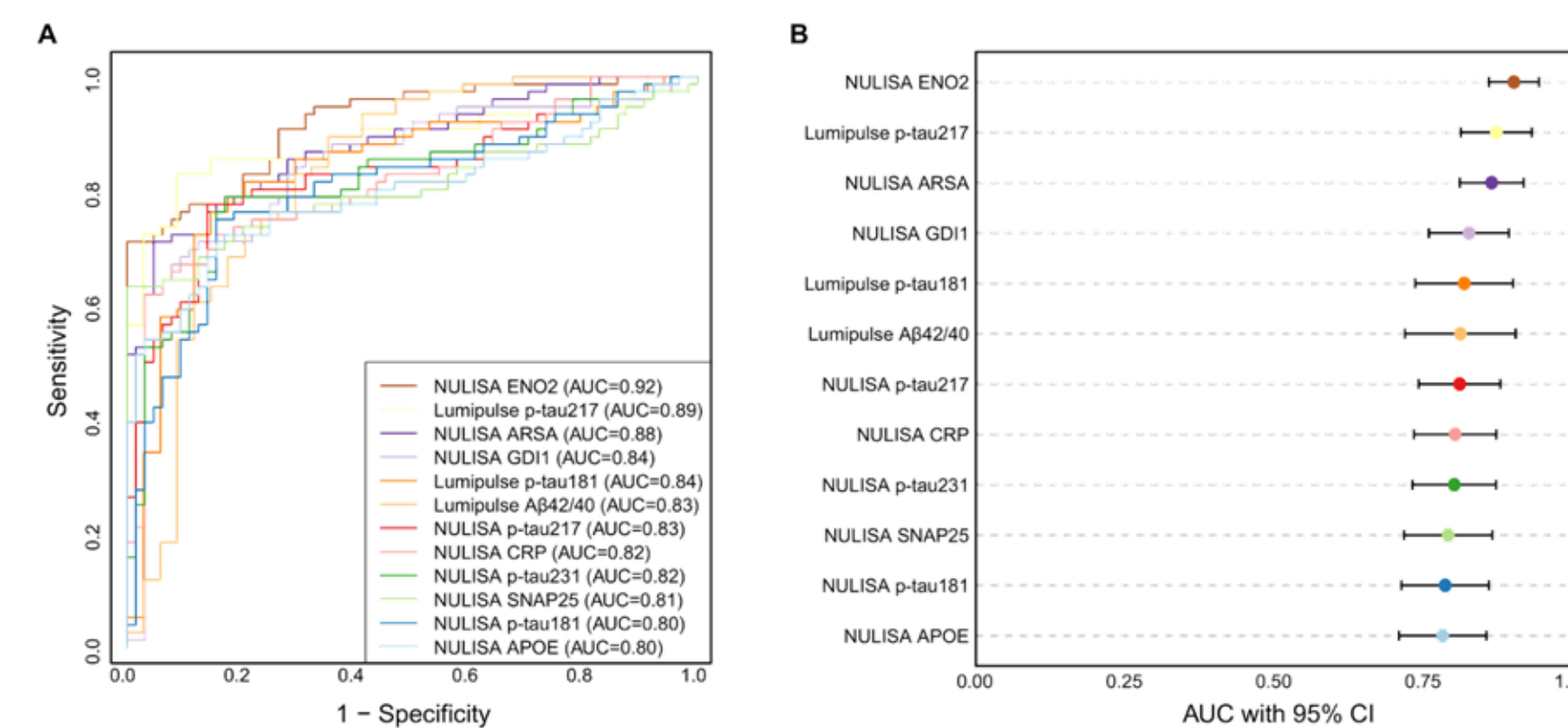


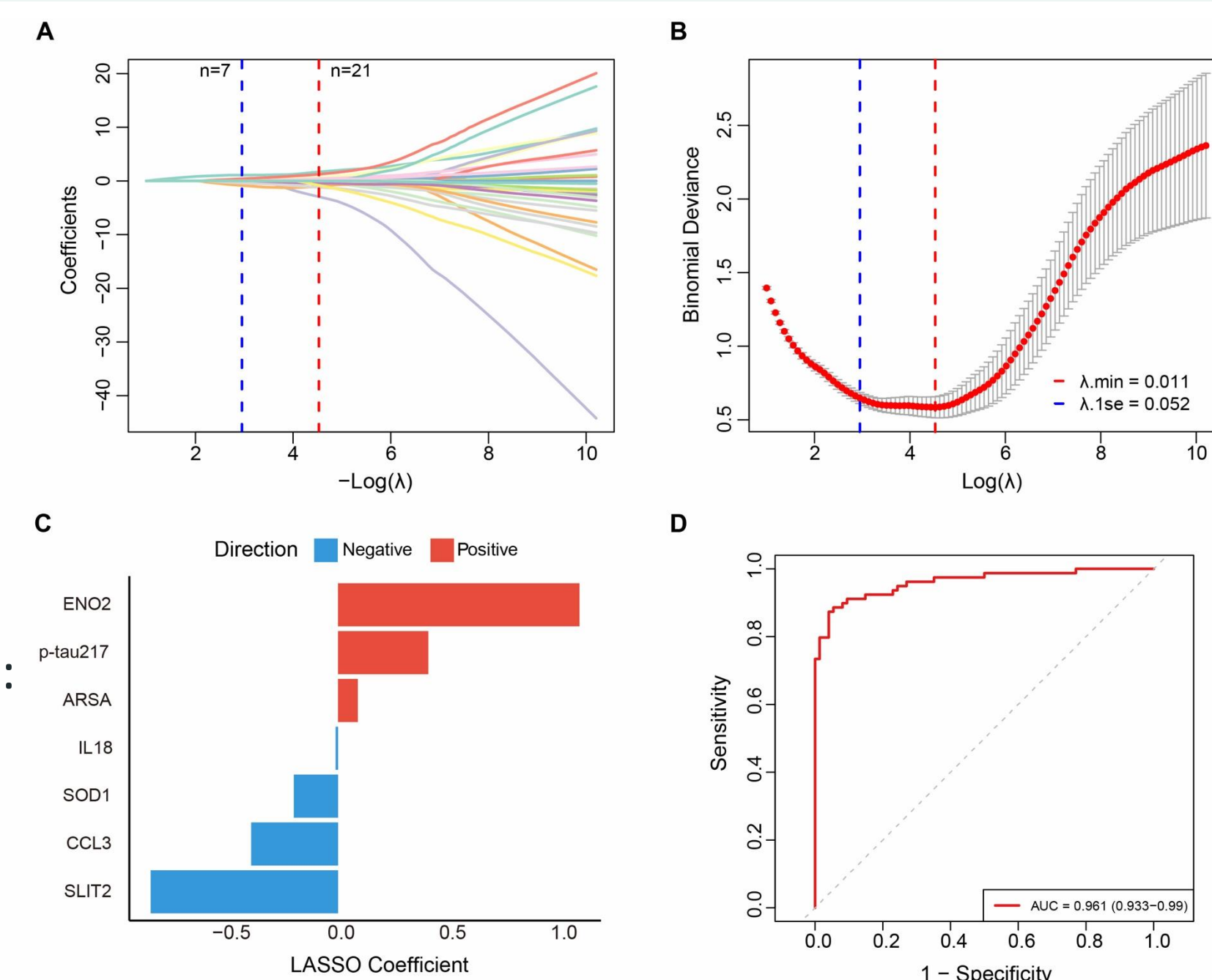
Figure 2. Diagnostic performance of plasma markers for A β positivity.

RESULT 2: MULTI-PROTEIN CLASSIFIER

Seven-protein LASSO panel

- Of the 37 NULISA markers that differed between the A β + and A β - groups, seven markers were retained following LASSO regression: ENO2, p-tau217, ARSA, IL18, SOD1, CCL3, and SLIT2.
- Seven-protein panel performance: AUC 0.96 (95% CI 0.93-0.99).

Figure 3. LASSO-based selection of plasma NULISA markers for A β positivity.



RESULT 3: AMYLOID BURDEN & BIOLOGY

Global cerebral amyloid burden

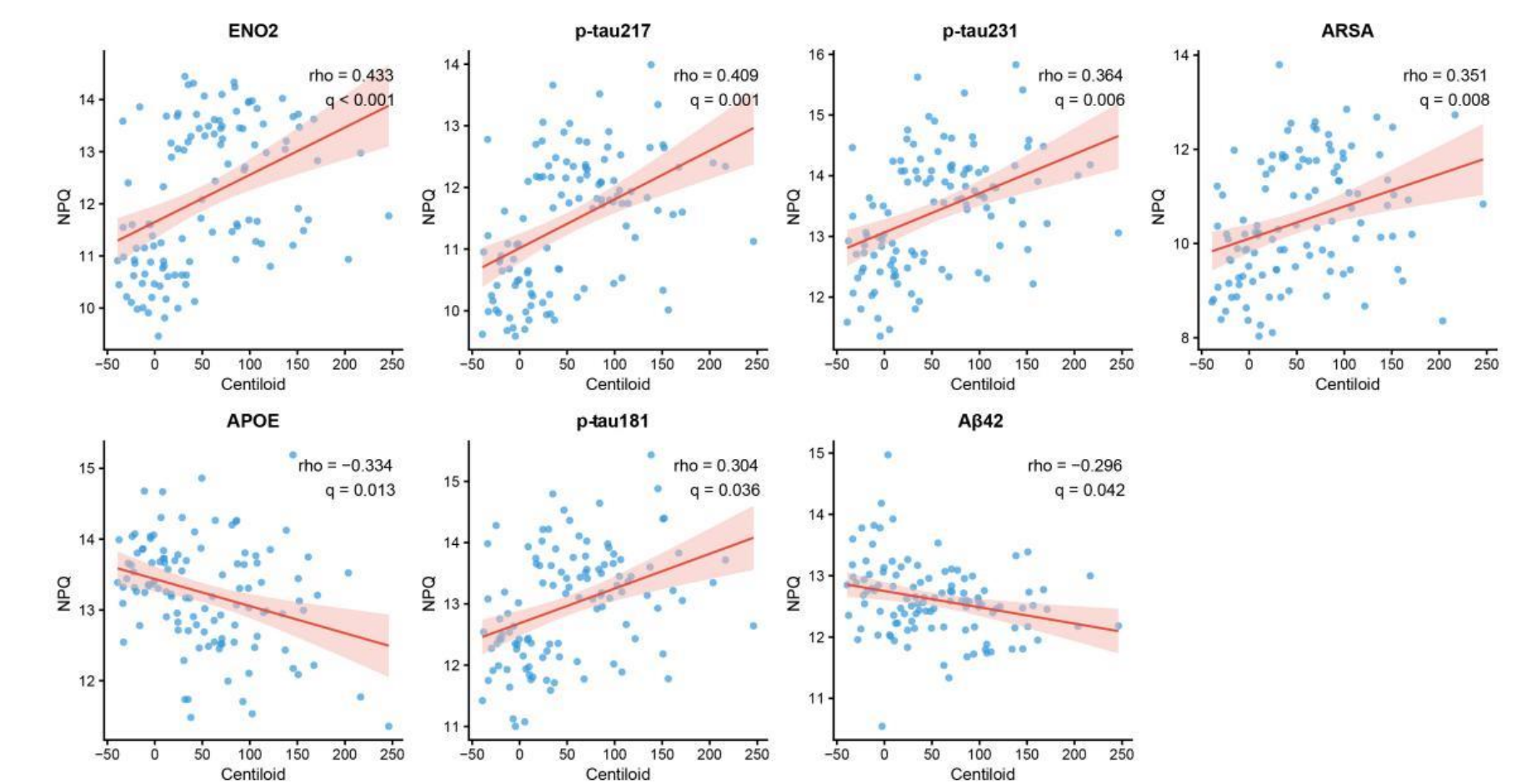


Figure 4. Association of NULISA markers with Centiloid value.

Regional cerebral amyloid burden

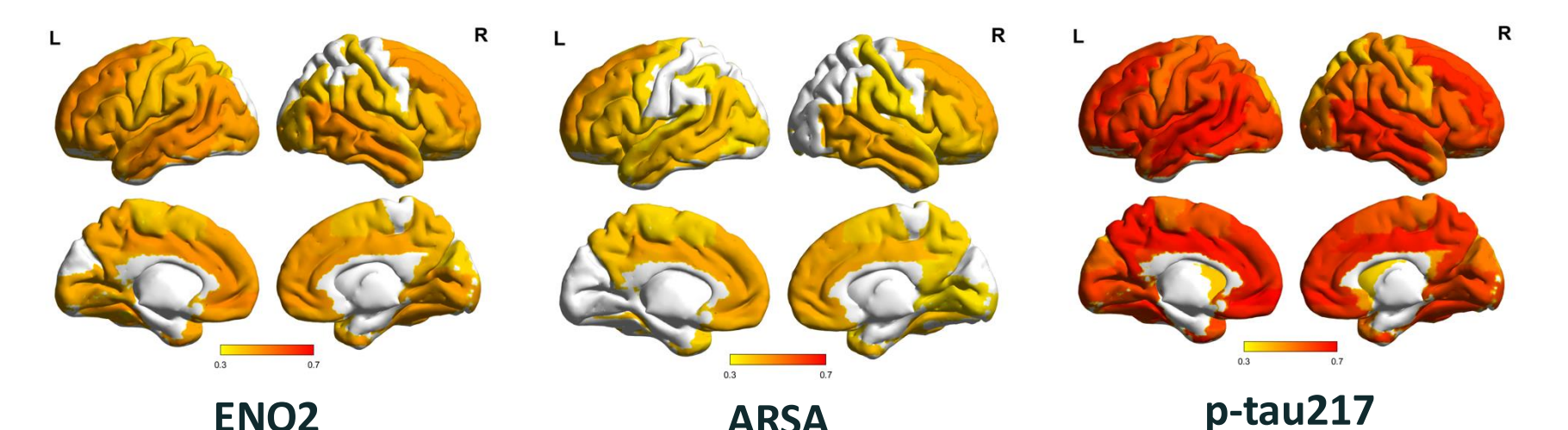


Figure 5. Correlations between plasma NULISA markers (ENO2, ARSA, p-tau217) and A β -PET SUVR across cortical regions.

CONCLUSIONS

ENO2 and ARSA emerged as candidate plasma biomarkers for A β pathology.

- Seven-protein panel improved A β -status classification.
- Proteomic signatures linked diagnosis to inflammatory and neuronal processes.