Comparative Analysis of Blood-Based Proteomic Biomarkers for Genetic Frontotemporal Dementia Using NULISA and Simoa Platforms

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Background

- Blood-based biomarkers, including neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), show promise for improving differential diagnosis across heterogeneous Frontotemporal Dementia (FTD) disorders
- NfL is consistently elevated in symptomatic mutation carriers, rising prior to phenoconversion, whilst GFAP is increased in specific FTD subgroups, particularly in progranulin (GRN) mutation carriers
- Cross-platform validation is essential for diagnostic accuracy, disease monitoring, and evaluation of emerging therapies

Aim

To assess cross-platform agreement and diagnostic performance of plasma NfL and GFAP measured using NULISA and Simoa in a genetic FTD cohort (GENFI)

Methods

- Comparative analysis of plasma NfL and GFAP in a genetic FTD cohort (GENFI, n=448)
- Comparing Alamar's nucleic acid linked immuno-sandwich assay (NULISA) and Quanterix's Single Molecule Array (Simoa)
- Grouped by genetic mutation, genetic status, and symptom status on the CDR + NACC FTLD rating scale

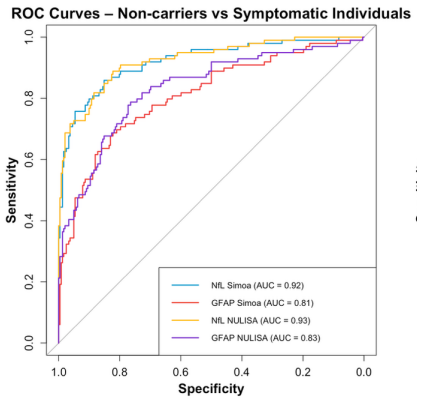


Figure 4. ROC curves comparing non-carriers and symptomatic individuals. *Comparison for NfL and GFAP measured using NULISA and Simoa platforms, with corresponding AUCs.*

Results

- NfL and GFAP showed strong agreement (ρ = 0.84-0.98)
- Correlations increased with clinical severity (NfL ρ = 0.87-0.96; GFAP ρ = 0.82-0.93)
- Highest correlations observed in GRN mutation carriers (ρ = 0.98)
- Stronger correlations in mutation carriers vs non-carriers (NfL ρ = 0.96 vs 0.91; GFAP ρ = 0.92 vs 0.84)
- ROC analyses showed strong discrimination between non-carriers vs symptomatic individuals (AUC 0.82–0.93)

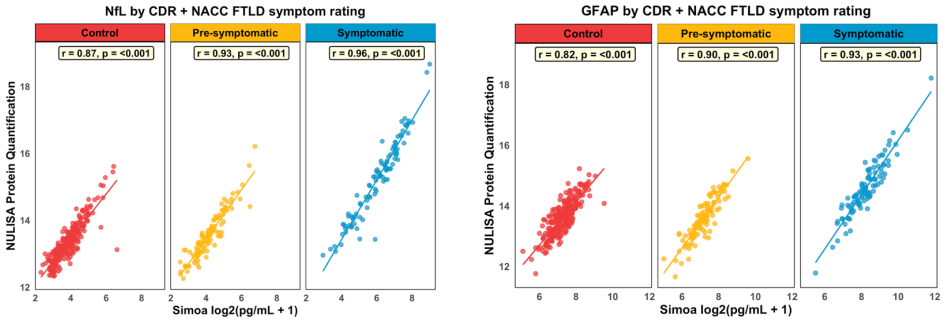


Figure 1. NULISA vs Simoa correlations by clinical stage. *Cross-platform correlations for plasma NfL and GFAP stratified by clinical stage (control, presymptomatic, symptomatic on the CDR+NACC FTLD scale)*

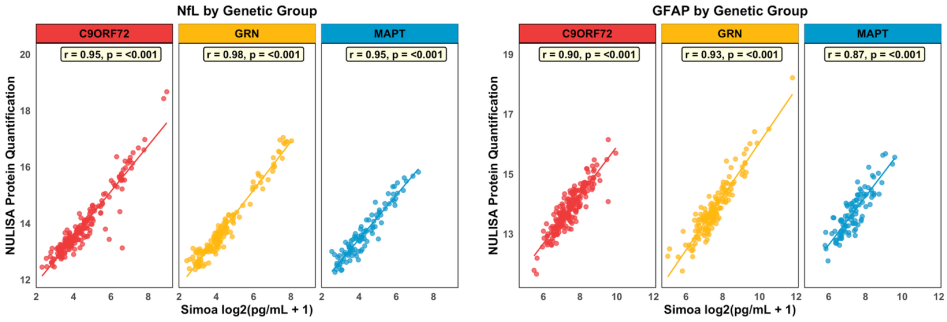


Figure 2. NULISA vs Simoa correlations by genetic subgroup. *Cross-platform correlations for plasma NfL and GFAP stratified by mutation group (C9ORF72, GRN, MAPT)*

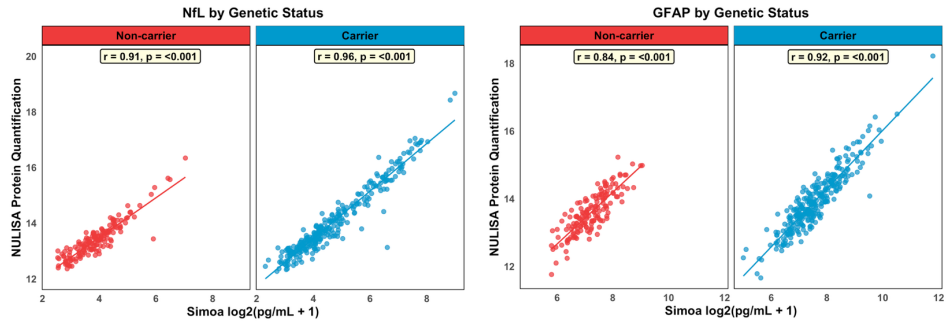


Figure 3. NULISA vs Simoa correlations by genetic subgroup. *Cross-platform correlations for plasma NfL and GFAP stratified by genetic status (Non-carrier vs mutation carrier)*

Conclusions

- NULISA and Simoa exhibited strong platform correlations for NfL and GFAP
- Concordance increases with clinical severity, supporting stage-specific diagnosis
- ROC analysis confirmed excellent accuracy in distinguishing symptomatic individuals
- Findings support NfL and GFAP as robust biomarkers for FTD diagnosis and monitoring, with clinical and research applications

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