

# UCSF Clinical correlations of CSF neurodegeneration biomarkers measured with aptamer proteomics in frontotemporal lobar degeneration

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## Background

- Frontotemporal lobar degeneration (FTLD) is an aggressive neurodegenerative disorder affecting cognition, behavior, and motor function
- There are currently no disease-specific diagnostic tests or therapies, and better biomarkers are needed
- Prior studies have identified several candidate CSF FTLD biomarkers
- The SomaScan® aptamer-based proteomics platform enables multiplex quantification of ~5,000 proteins in CSF
- This study evaluates whether aptamer-based measurements of known neurodegeneration biomarkers show expected clinical associations in FTLD

## Methods

- CSF samples analyzed with aptamer-based proteomics (SomaScan® v3.0, SomaLogic®)

### Study Cohorts:

- **Familial FTLD** (ALLFTD): *C9orf72*, *GRN*, *MAPT* pathogenic variant carriers (symptomatic + asymptomatic) and non-carrier controls
- **Sporadic FTLD** (UCSF): neuropathology-confirmed FTLD-tau, FTLD-TDP, and age-matched controls.
- Neurodegeneration-related biomarkers described in the literature and captured by SomaScan: NfL, NEFH, GFAP, YKL-40, NPTX2, MAPT, 14-3-3, TDP-43, SNCA, GRN, BDNF, SNAP25, SYT5, VAMP3

### Clinical metrics:

- Disease severity (CDR+NACC FTLD sum of boxes)
- Cognitive, functional, behavioral, and motor measures (MoCA, SEADL, TMT-B, UPDRS, etc.)

### Statistical Analyses:

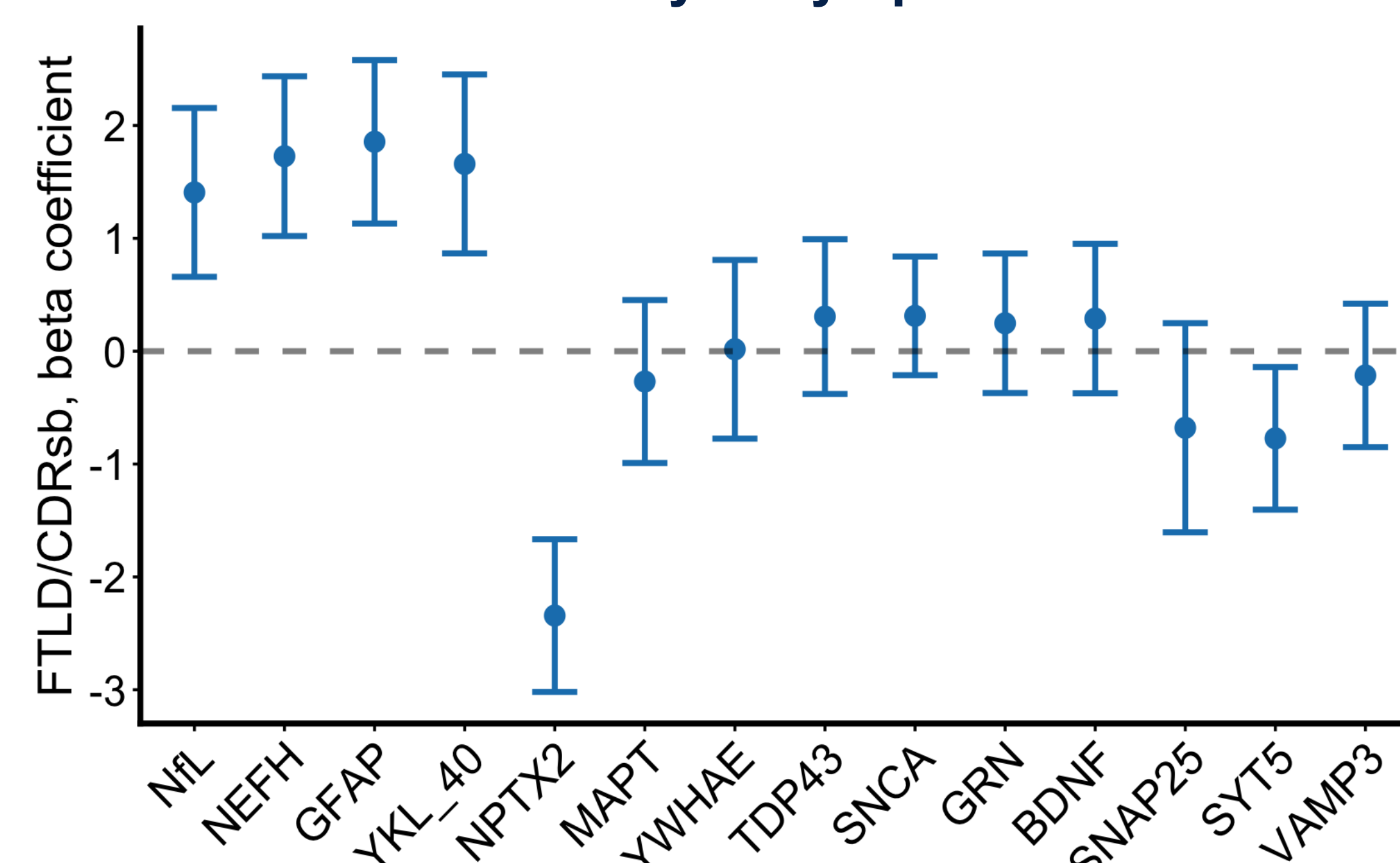
- Age and sex corrected linear regressions and mixed models, with biomarkers as predictors and clinical outcomes as dependent variables

## Results

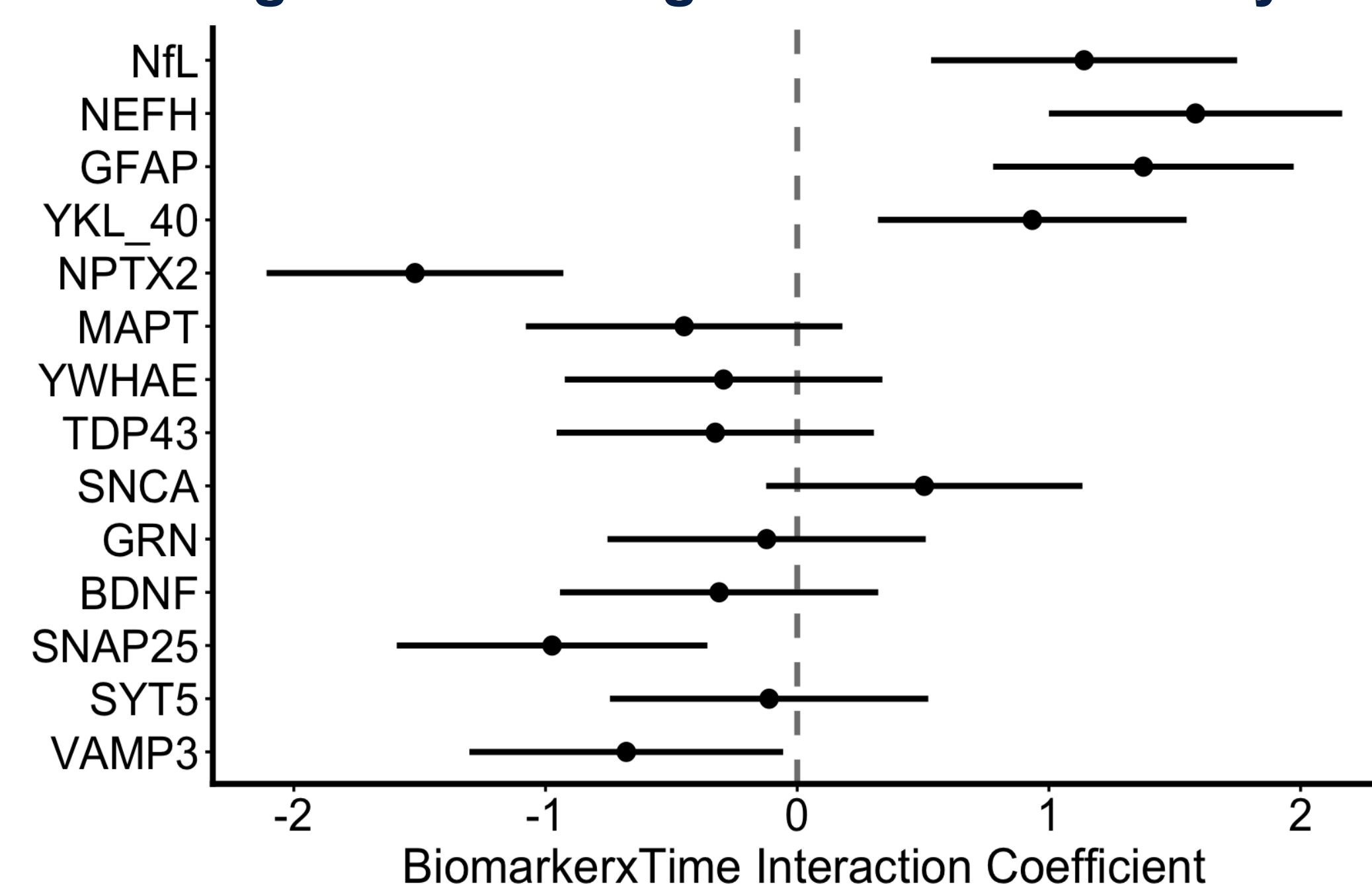
### 1. Demographics, familial and sporadic FTLD

|                  | Overall       | Familial      |               |               | Sporadic     |              |              |
|------------------|---------------|---------------|---------------|---------------|--------------|--------------|--------------|
|                  |               | Control       | Asymptomatic  | Symptomatic   | Control      | FTLD-tau     | FTLD-TDP     |
| n                | 272           | 47            | 52            | 78            | 28           | 54           | 13           |
| sex = Female (%) | 139 (51.1)    | 26 (55.3)     | 26 (50.0)     | 41 (52.6)     | 16 (57.1)    | 25 (46.3)    | 5 (38.5)     |
| Age (mean (SD))  | 56.10 (14.56) | 44.17 (12.30) | 43.57 (13.31) | 56.35 (10.31) | 69.11 (3.18) | 69.14 (6.86) | 65.71 (6.81) |
| CDR+NACC/FTLDSb  | 3.01 (4.18)   | 0.00 (0.00)   | 0.00 (0.00)   | 5.15 (4.49)   | 0.00 (0.00)  | 5.81 (3.60)  | 7.96 (4.56)  |
| MoCA score       | 24.06 (6.02)  | 27.37 (2.08)  | 27.26 (2.42)  | 20.76 (6.84)  | 27.25 (2.11) | 17.67 (6.77) | 19.33 (4.18) |
| Mutation (%)     |               |               |               |               |              |              |              |
| C9               | 49 (18.0)     | 0             | 25 (48.1)     | 24 (30.8)     | 0            | 0            | 0            |
| GRN              | 32 (11.8)     | 0             | 9 (17.3)      | 23 (29.5)     | 0            | 0            | 0            |
| MAPT             | 37 (13.6)     | 0             | 18 (34.6)     | 19 (24.4)     | 0            | 0            | 0            |

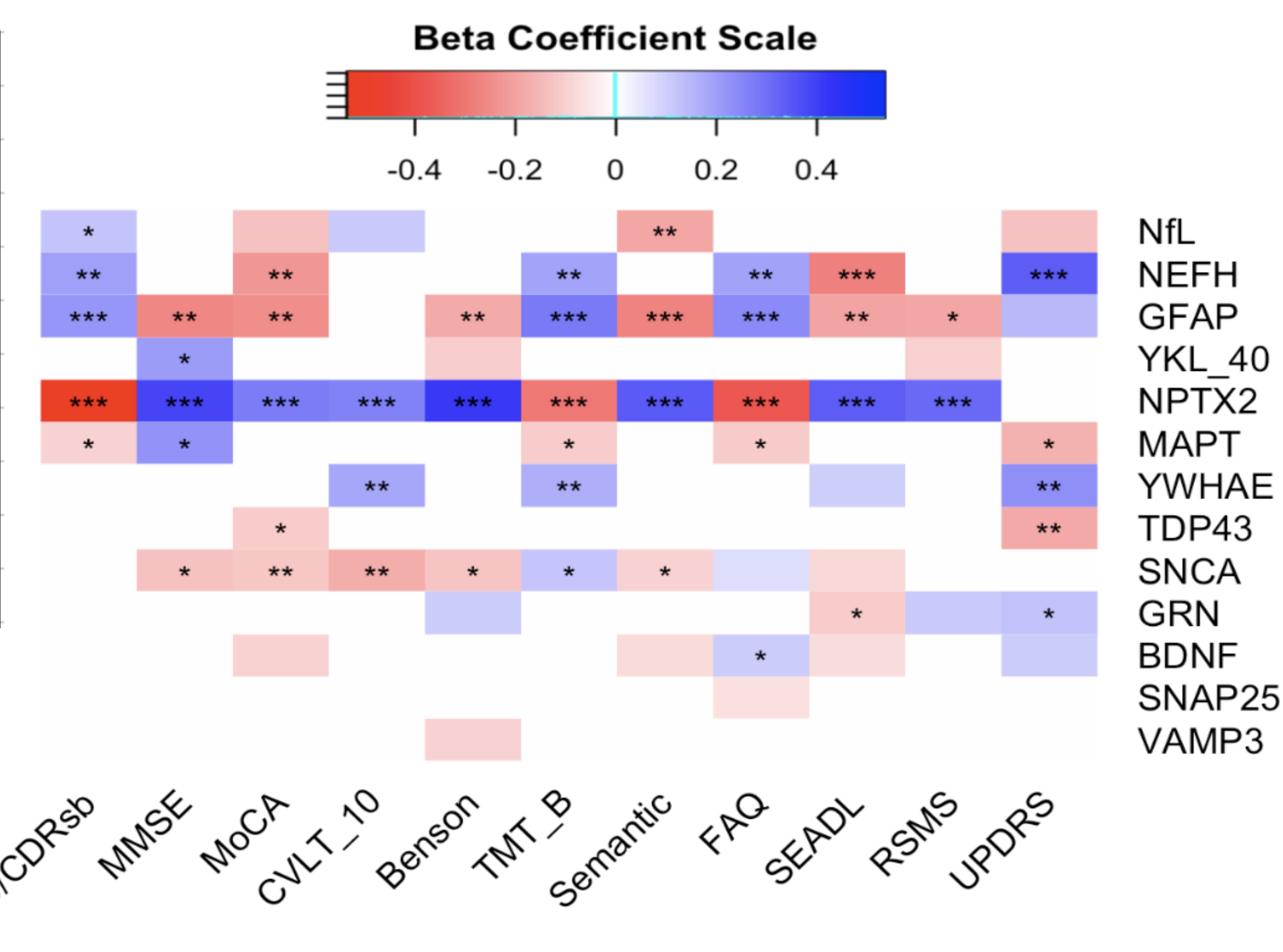
### 2. Biomarkers showed strong baseline associations with disease severity in symptomatic disease



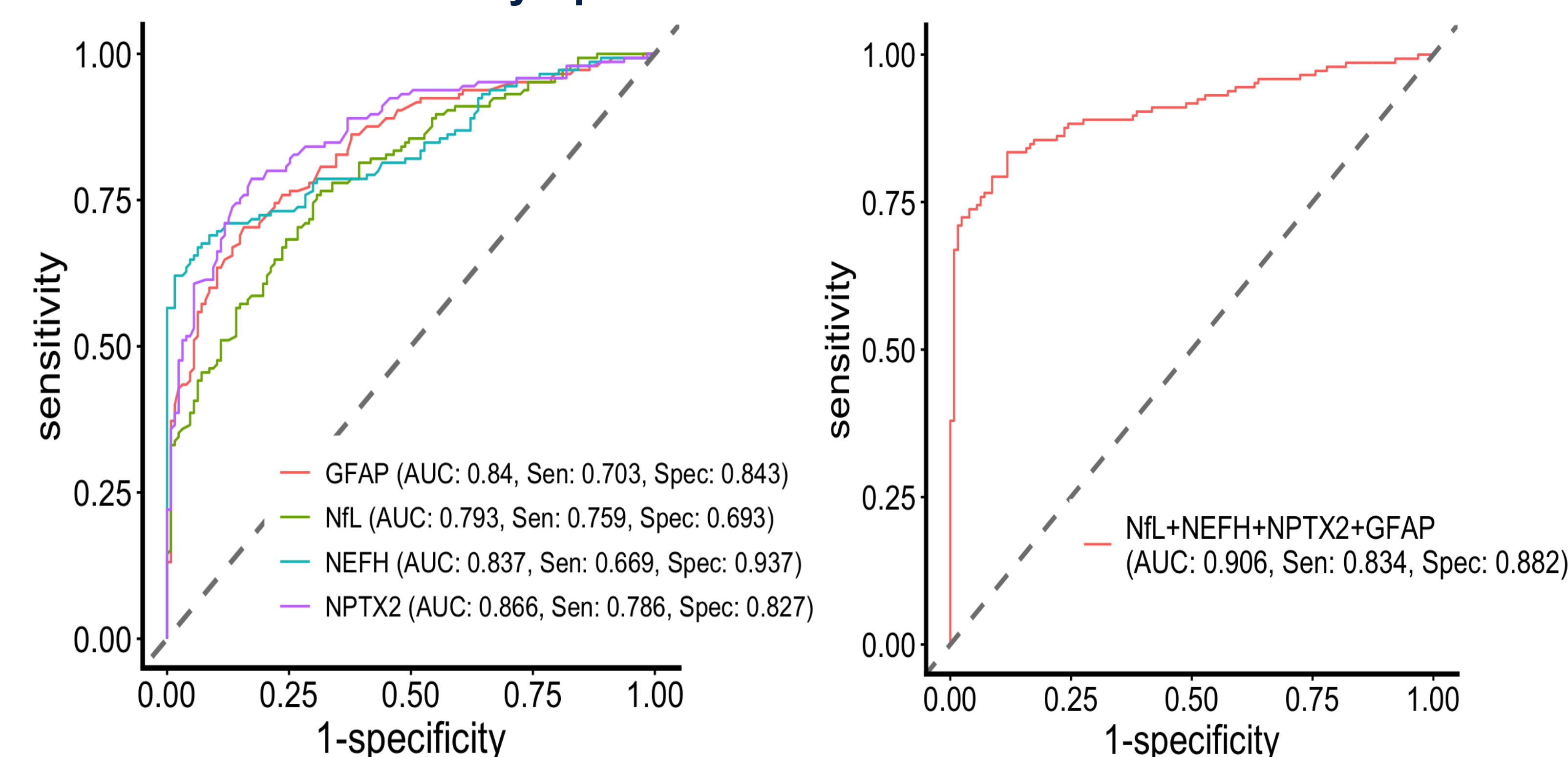
### 3. Baseline biomarkers correlated with longitudinal change in disease severity



### 4. Baseline biomarkers correlated with additional clinical scales of disease severity



### 5. Biomarkers discriminated symptomatic individuals from asymptomatic carriers + controls



## Conclusion

CSF neurodegeneration biomarkers measured by aptamer proteomics, in particular NfL, NEFH, GFAP and NPTX2, have associations with disease severity in FTLD and had added diagnostic performance as a biomarker panel.

### Acknowledgements

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