

Secernin-1 As A Novel Biomarker for Alzheimer's Disease

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Background

- Our group first described, through proteomic and immunohistochemistry studies, the co-localization of this protein with dystrophic neurites and neurofibrillary tangles in Alzheimer's disease (AD), but not in other Tauopathies
- Our goal is to validate SCRN1 as a novel biomarker for AD and assess the potential correlation between SCRN1, pTau181, and other biomarkers for AD.

Results

Characterization of Secernin-1 by immunohistochemistry Secernin-1 distribution in the brain throughout the progression of AD

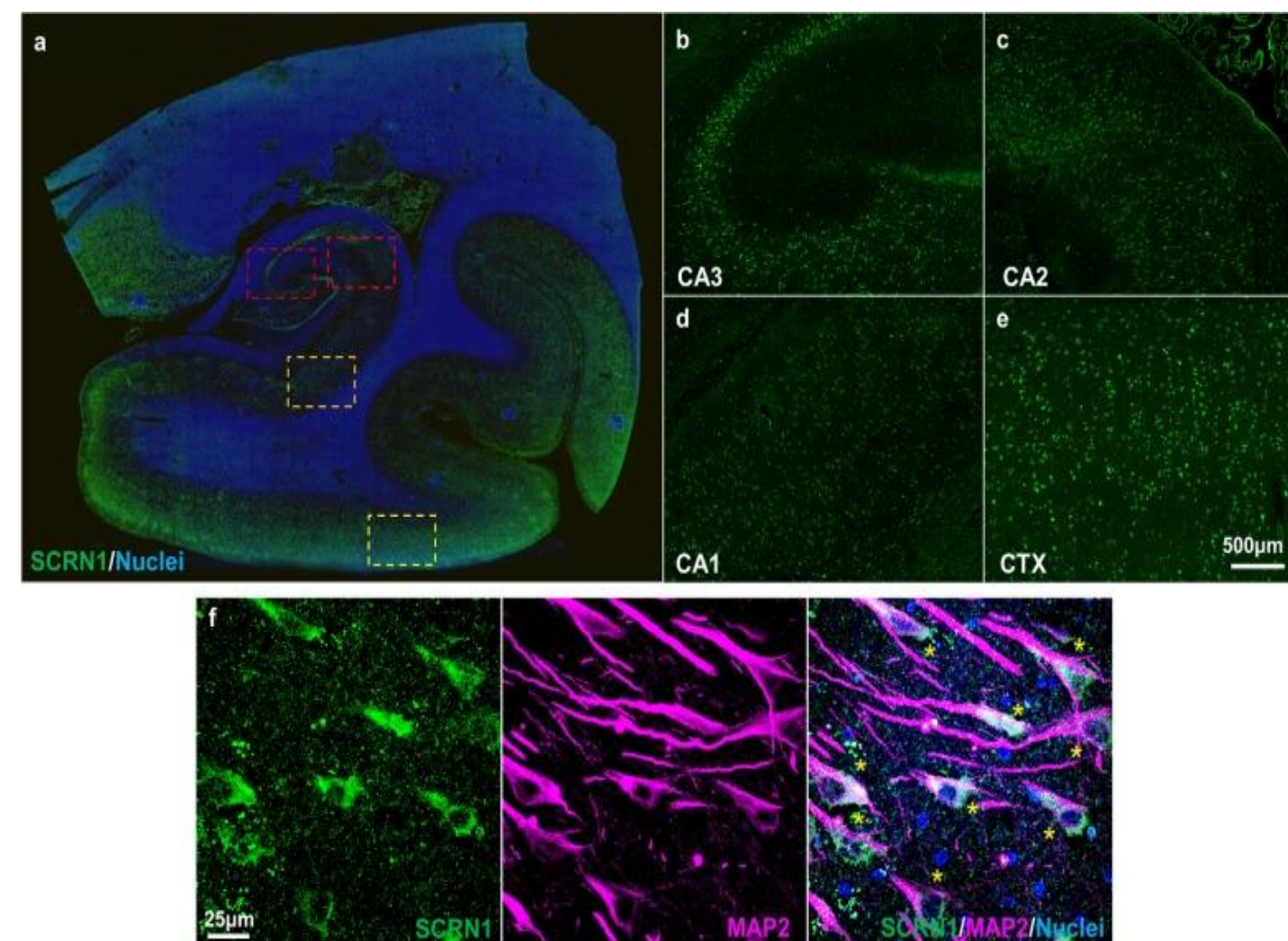


Figure 1: Secernin-1 distribution in the hippocampal section in a cognitively normal subject with no NFTs. a Whole-slide fluorescent scan of the hippocampus with α-SCRN1 antibody (green). Boxed regions shown in higher magnification images of CA3 (dark red, b), CA2 (red, c), CA1 (orange, d) and adjacent temporal cortex (yellow, e). f Double immunohistochemistry of SCRN1 with α-MAP2 antibody showing SCRN1 physiological expression in neurons (asterix) in a cognitively normal subject

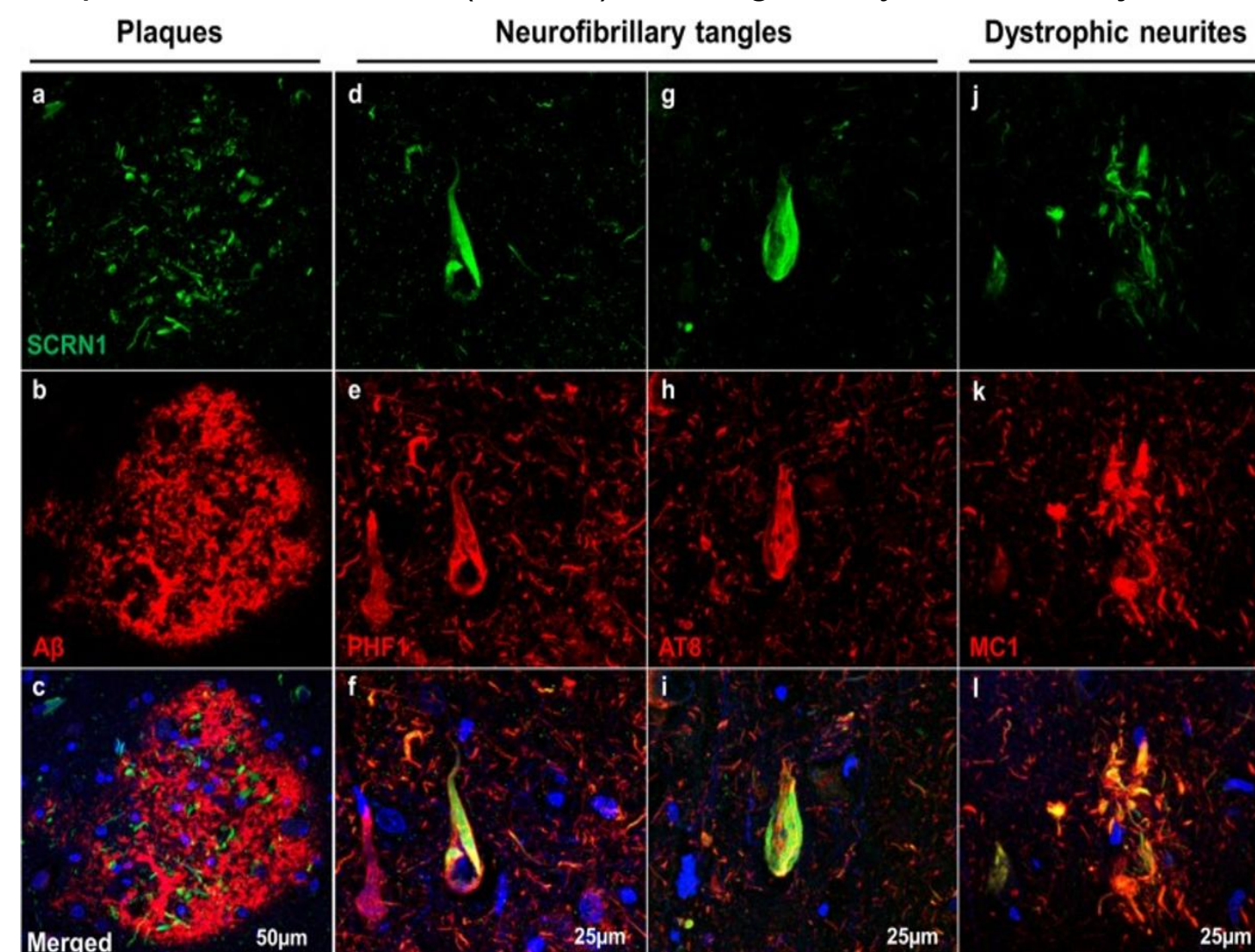


Figure 2: Secernin-1 significantly accumulates in neurofibrillary tangles and dystrophic neurites in AD. Hippocampus sections were immunostained with α-SCRN1 (green) and PHF1 antibody (red) in all three groups

SCRN1 staining in Neurofibrillary tangles and in neuritic plaques

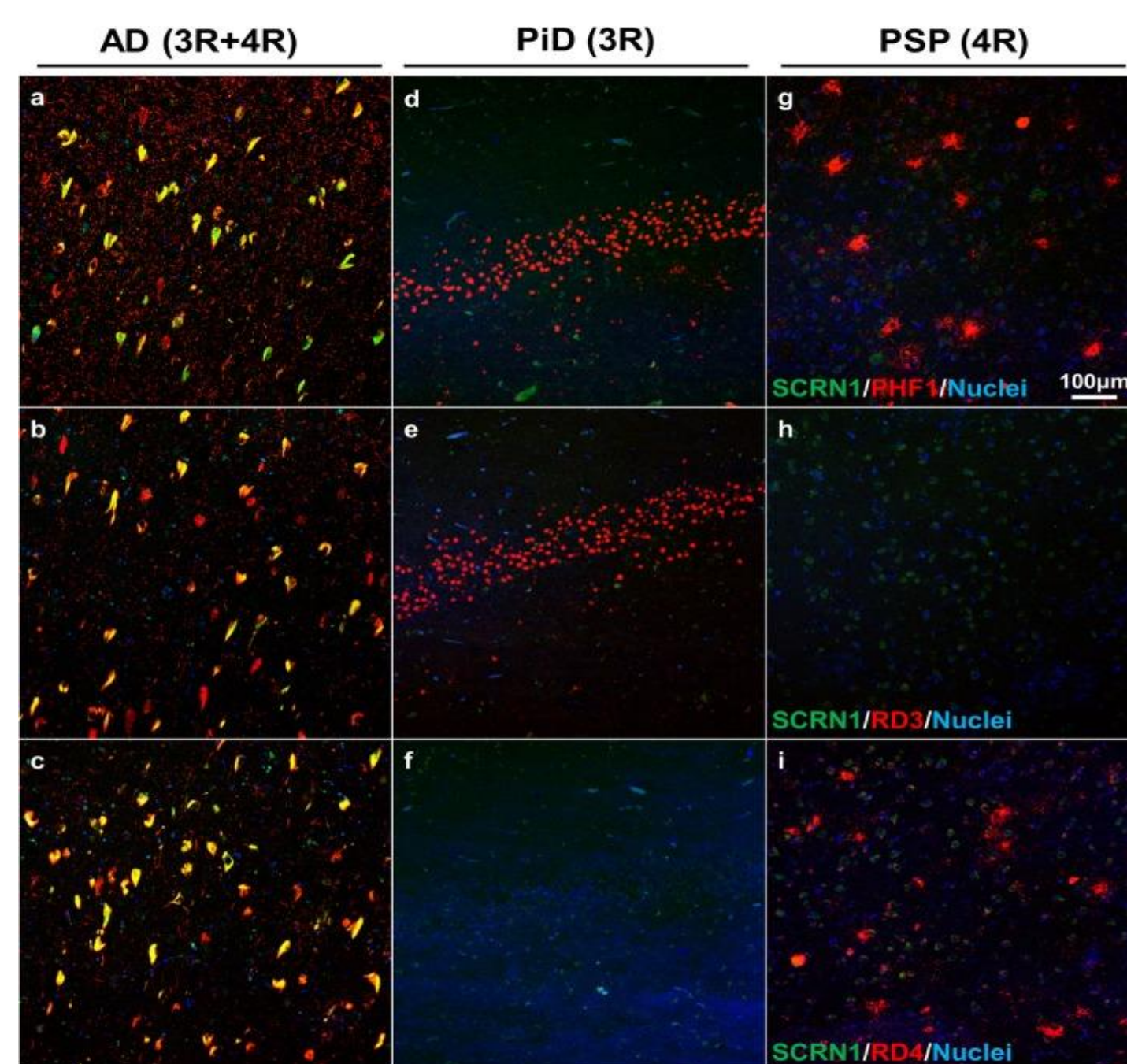


Figure 3: Secernin-1 accumulation in NFTs and dystrophic neurites in AD. Sections were immunostained with α-SCRN1 and 4G8/6E10 (aβ, a-c) or the pTau markers PHF1 (d-f), AT8 (g-i) and MC1 (j-l)

Secernin-1 does not accumulate in pTau-positive lesions in 3R-tau and 4R-tau specific tauopathies

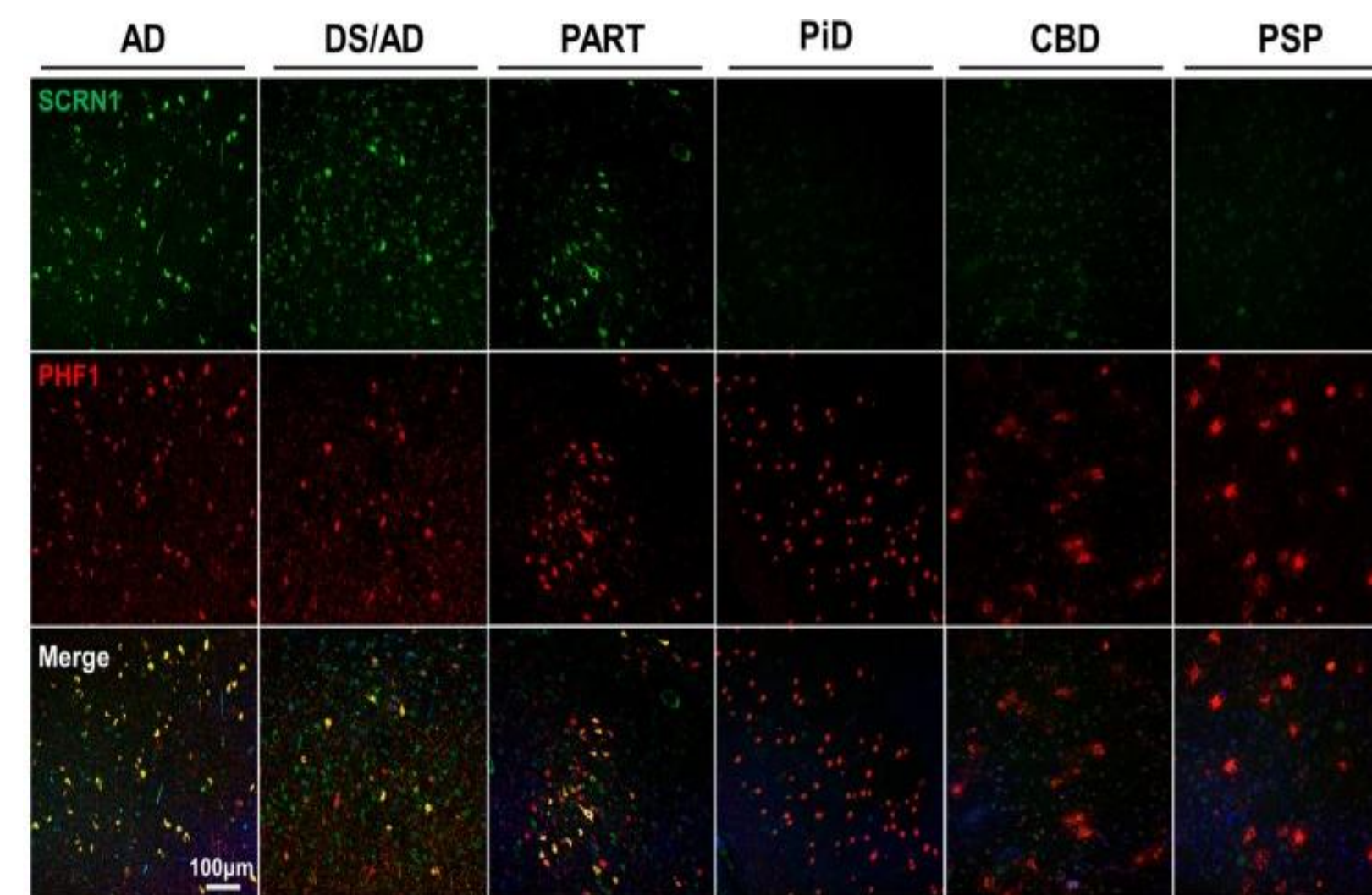
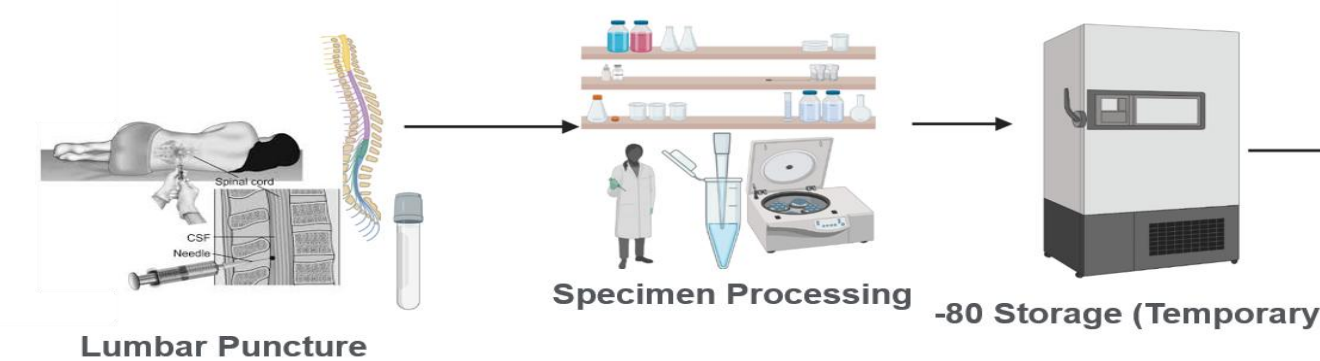


Figure 4: Secernin-1 accumulates in pTau aggregates in AD, DS, and PART but not in PiD, CBD, and PSP. SCRN1 colocalization with PHF1 in AD, DS, and AD, PART, Pick's disease, CBD, and PSP. Representative images show SCRN1 staining in the hippocampus in AD, DS, and AD, PART, and Pick's disease, and of SCRN1 staining in the basal ganglia in CBD and PSP. SCRN1 (green) accumulated in neurofibrillary tangles and in dystrophic neurites in AD, Down syndrome, and PART but not in PHF1-positive aggregates (red) in PiD, CBD, or PSP.

Enrollment of Participants at NYU ADRC



We enrolled 139 patients at the NYU Alzheimer's Disease Research Center. CSF was collected from each patient following a minimum of 6 hours fast. The SCRN-1 levels were measured in the CSF of 101 patients using mass spectrometry.

Emerging AD Plasma Biomarkers using Single-Molecule Analysis (SIMOA) Technology



Detection and dosage of biomarkers in bio-fluid samples (pg/ml sensitivity)

Neurology 2 Plex BKit:

- Aβ40 (4.3 Kda)
- Aβ42 (4.5 Kda)
- GFAP (~50kDa)
- NfL (~70kDa)

Phospho-Tau Kit

- pTau 181 V2



- pTau 217 was analyzed using Lumipulse

Figure 5: Aβ40, Aβ42, GFAP, and NfL were measured using the Neurology 4 Plex E advantage Plus kit from Quantex. pTau181 was measured with pTau 181 V2 Kit (Quantex). pTau217 was measured with Lumipulse

Characterization of Secernin-1 by immunohistochemistry Secernin-1 distribution in the brain throughout the progression of AD

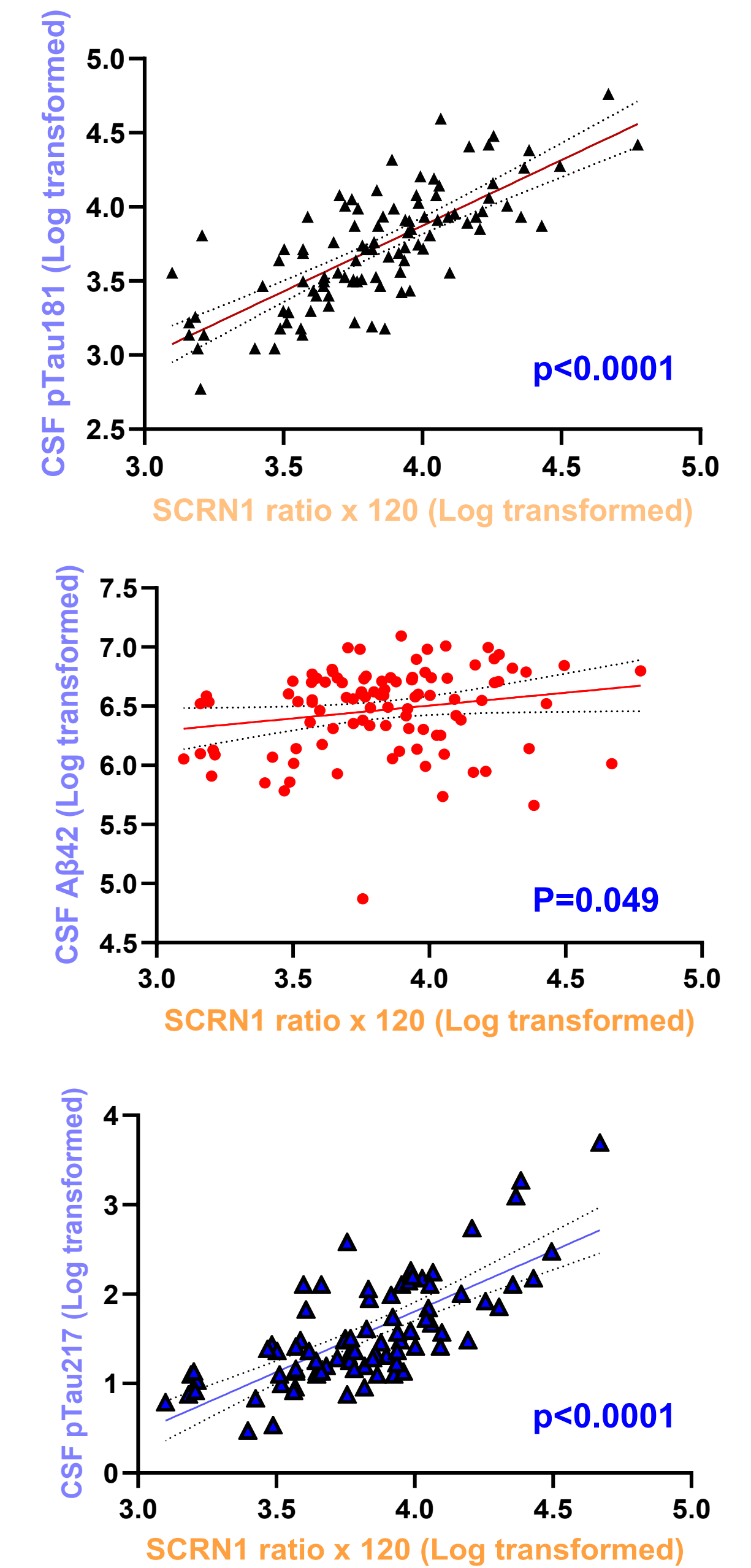


Figure 4: A) The analysis of 101 CSF samples from cognitively unimpaired participants (CDR= 0), showed a strong positive association between CSF SCRN1 and pTau181 levels ($p < 0.0001$), with an additional effect of age (estimate = -0.57, $p < 0.0001$). Together, these predictors explain approximately 63% of the variability in the outcome ($R^2 = 0.57$), and the robustness of their relationship. We are currently conducting further analysis with other biomarkers for AD. **B)** A positive association between SCRN1 and Aβ42, $p = 0.019$. **C)** A positive association was also observed with pTau 217, $p < 0.0001$

Emerging AD Plasma Biomarkers using Single-Molecule Analysis (SIMOA) Technology

- Strong correlation was detected between CSF SCRN1 and pTau181, and between CSF SCRN1 and pTau217.**
- A positive association between Secernin-1 and Aβ42**
- SCRN1 has the potential to become a key biomarker for identifying patients who meet criteria to participate in clinical trials for AD therapeutics.**

References

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