

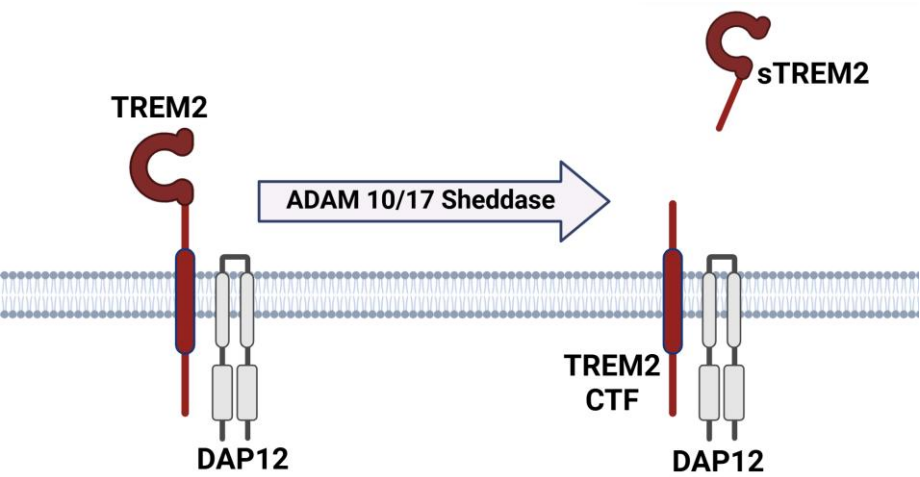
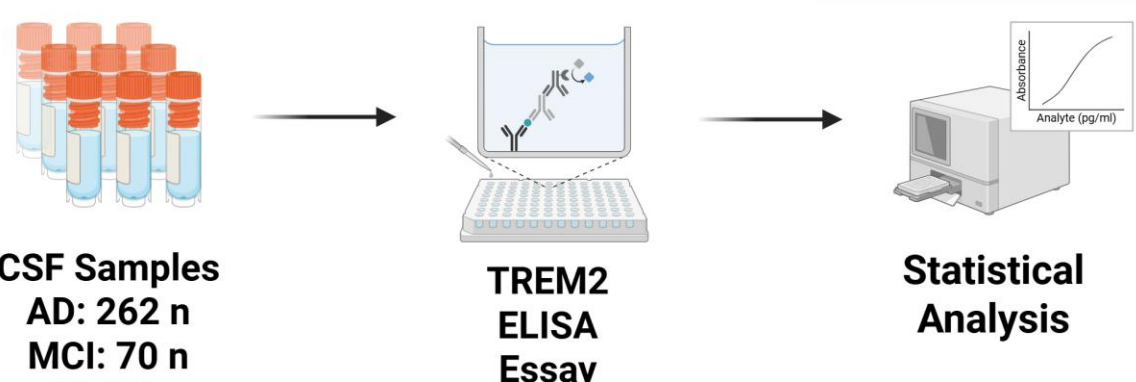
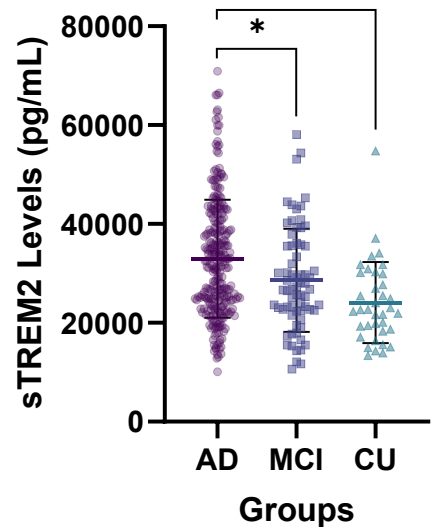
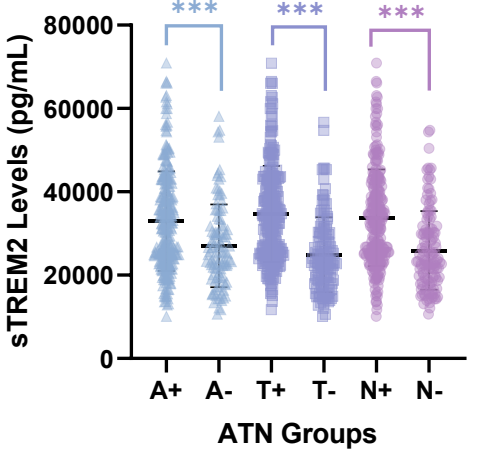
Cerebrospinal Fluid sTREM2 Levels Across The Alzheimer's Disease Clinical Spectrum And Relation To ATN In Turkish Cohort

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CSF sTREM2 is significantly elevated in AD and strongly linked to tau pathology; its early correlation with p-Tau181 during the MCI stage highlights its strong potential as an early diagnostic biomarker and reflects early microglial activation.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Cerebrospinal fluid (CSF) biomarkers play a crucial role in the diagnosis of Alzheimer's Disease (AD) [1]. Triggering receptor expressed on myeloid cells 2 (TREM2) is a transmembrane receptor expressed by microglia. Cleavage of TREM2 results in the formation of soluble TREM2 (sTREM2) (Fig 1.), which can be detected in the CSF [2]. This study aimed to elucidate the relation between CSF sTREM2 levels and AD pathology in clinically and AT(N) classified groups.  Fig 1. sTREM2 production	In this study, CSF samples of 262 Alzheimer's disease (AD) patients, 70 mild cognitive impairment (MCI) patients, and 37 cognitively unimpaired (CU) individuals were investigated (Fig 2.). Cases were diagnosed according to the NIA-AA 2011 criteria, and CSF core biomarkers (Amyloid β (1-42), Phospho-Tau (181P), Total-Tau) indicating AT(N) classification, and sTREM2 levels were determined by ELISA. Statistical analysis was performed using SPSS Version 31.0 [3].  Fig 2. Method steps	Analysis revealed a statistically significant difference ($p < 0.001$) in CSF sTREM2 levels among the AD, MCI, and CU groups (Fig.3). The highest CSF sTREM2 levels were observed in the AD group, compared to the MCI ($p = 0.019$) and CU ($p < 0.001$) groups. Furthermore, CSF sTREM2 levels were significantly higher ($p < 0.001$) in the A+, T+, and (N+) groups, compared to their negative counterparts, namely A-, T-, and N- groups (Fig 4.). The largest effect size was observed in the T+ vs T- comparison (Hedges' $g: 0.89$). In the MCI group, sTREM2 levels showed positive correlation with CSF Aβ ($p = 0.004$), P-tau181 ($p < 0.001$), and T-tau ($p < 0.001$) levels (Fig 5.). Within the AD group, the correlation between sTREM2 and Aβ was not statistically significant ($p = 0.063$). However, T-tau and p-tau181 exhibited significant positive correlations ($p < 0.001$).  Fig 3. Comparison of CSF sTREM2 levels across diagnostic groups.	Our findings support previous studies and demonstrate that CSF sTREM2 levels are significantly increased in AD pathology [2,4,5]. Furthermore, the correlation between sTREM and pTau (181) is not only in AD but also in non-AD MCI groups, but not in CU, which might indicate an early event for AD-type pathology in MCI. This might increase the potential of sTREM2 to serve as a biomarker. It also supports the relationship between AD, microglial activation, and neurofibrillary tangle formation. This research was supported by TUBITAK (Project ID: 22AG017)  Fig 4. CSF sTREM2 levels stratified by ATN biomarker status.	1. Jack, Clifford R Jr et al. "NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease." <i>Alzheimer's & dementia : the journal of the Alzheimer's Association</i> vol. 14,4 (2018): 535-562. 2. Suárez-Calvet, Marc et al. "sTREM2 cerebrospinal fluid levels are a potential biomarker for microglia activity in early-stage Alzheimer's disease and associate with neuronal injury markers." <i>EMBO molecular medicine</i> vol. 8,5 466-76. 2 May. 2016 3. İlhan, Nazlıcan et al. "The CSF Levels of Mitochondrial Phosphoenolpyruvate Carboxykinase 2 as a Novel Biomarker in Alzheimer's Disease." <i>Molecular neurobiology</i> vol. 63,1 98. 20 Nov. 2025 4. Knapskog, Anne-Brita et al. "Cerebrospinal fluid sTREM2 in Alzheimer's disease: comparisons between clinical presentation and AT classification." <i>Scientific reports</i> vol. 10,1 15886. 28 Sep. 2020, doi:10.1038/s41598-020-72878-8 5. Zhou, Wenchuan et al. "Association between Cerebrospinal Fluid Soluble TREM2, Alzheimer's Disease and Other Neurodegenerative Diseases." <i>Journal of clinical medicine</i> vol. 12,10 3589. 22 May. 2023
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