

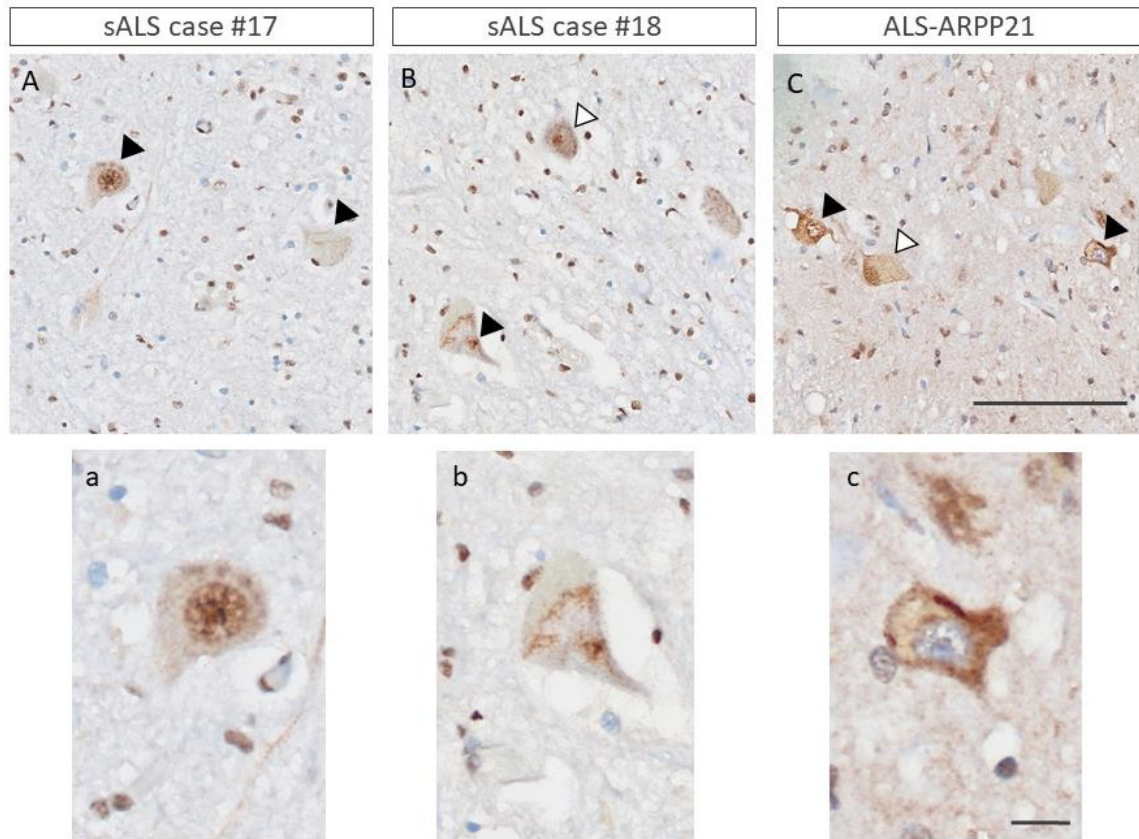


Figure S1. TDP-43 proteinopathy is present in an ALS carrier of c.1586C>T missense variant. Representative images of TDP-43 immunostaining of lumbar spinal cord tissue of two sporadic ALS cases (A-a, B-b) and one ALS carrier of familial c.1586C>T missense variant (C-c). Black arrows point to ventral horn motor neurons with TDP-43 deposits (diffuse or aggregates) and/or TDP-43 nuclear delocalization. White arrows point to motor neurons with the expected physiological TDP-43 pattern. Scale bar = 50µM.

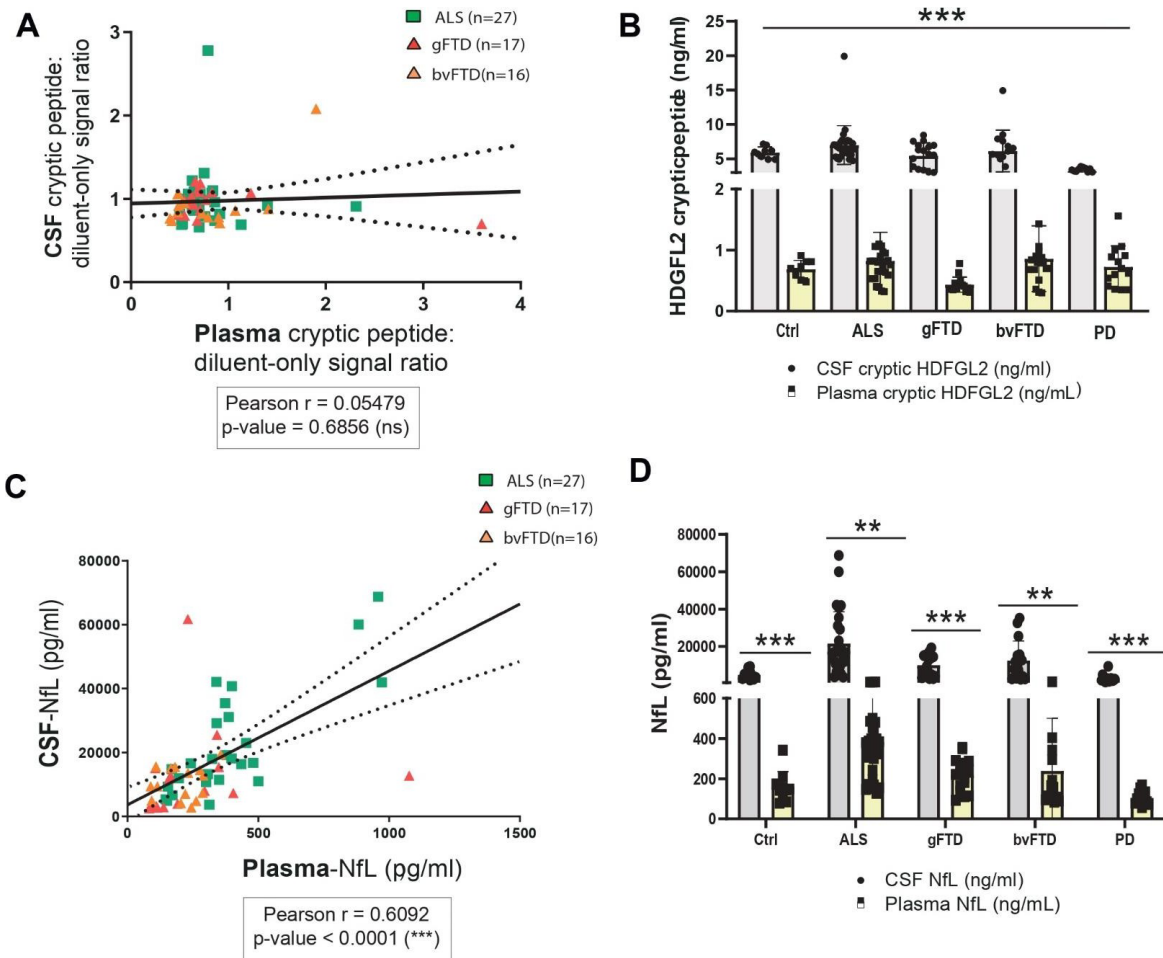


Figure S2. Correlation of HDGFL2 cryptic peptide signal and NfL (pg/ml) in CSF and plasma samples. Pearson correlation two-tailed analysis to assess the linear relationship between cryptic HDGFL2 (A) and NfL (C) in both biofluids, including ALS (n=27), genetic FTD (gFTD, n=17) and behavioral variant FTD (bvFTD, n=16) cases. The correlation coefficient (r) indicates the strength and direction of association. Concentration of HDGFL2 cryptic peptide (ng/ml) (B) and NfL (pg/ml) (D) found in CSF and plasma samples. Statistical analysis was performed by Mann-Whitney U test for categorical variables; **p<0.01, ***p<0.001 vs CSF concentration for each disease group.