

Tau Seeding Activity in Alzheimer's Disease

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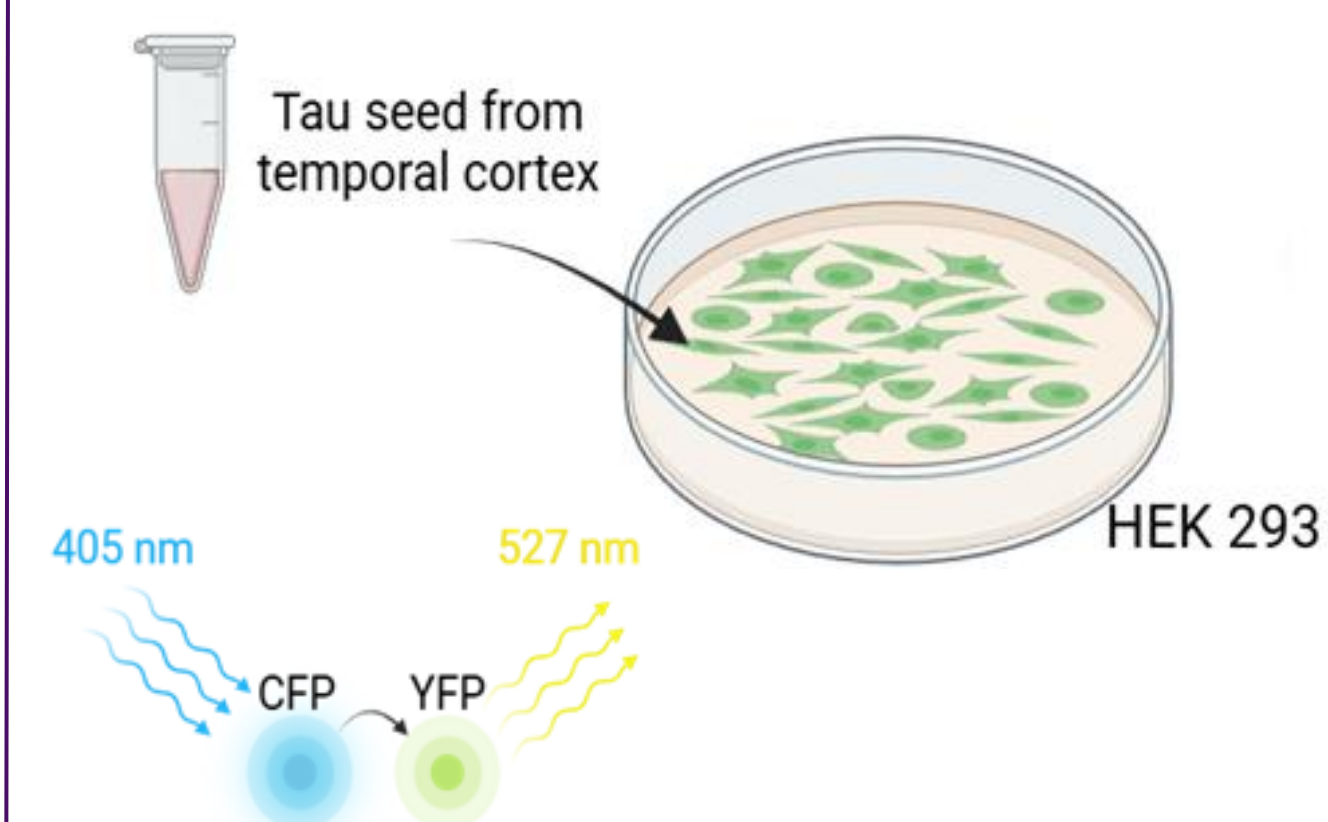
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INTRODUCTION

Tau protein is essential for maintaining synaptic integrity under physiological conditions but undergoes pathological changes in Alzheimer's disease (AD) that lead to synaptic dysfunction and degeneration. Even though neurofibrillary tangles are a hallmark of AD, there is growing evidence suggesting that soluble oligomeric forms of tau are the primary mediators of toxicity and disease propagation. Since tau pathology is believed to spread through synaptically connected networks, we investigated whether oligomeric tau drives seeding activity in sporadic Alzheimer's disease (SAD), autosomal dominant Alzheimer's disease (ADAD), Down syndrome (DS), DS with Alzheimer's disease (DSAD), and control, and whether oligomer-driven seeding is a shared mechanism across AD etiologies.

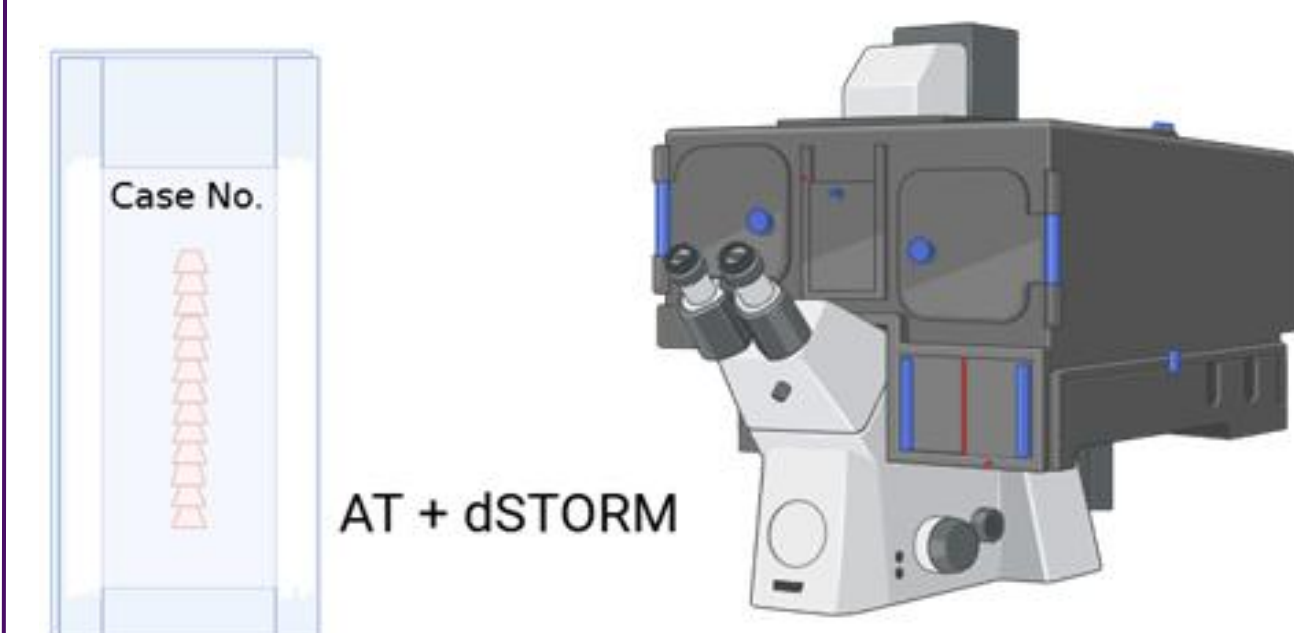
METHODS

1 Tau isolation and FRET seeding assay



2 Tau characterization by ELISA and WB

3 Super-resolution imaging to detect the presence of oligomers at the synapse



RESULTS

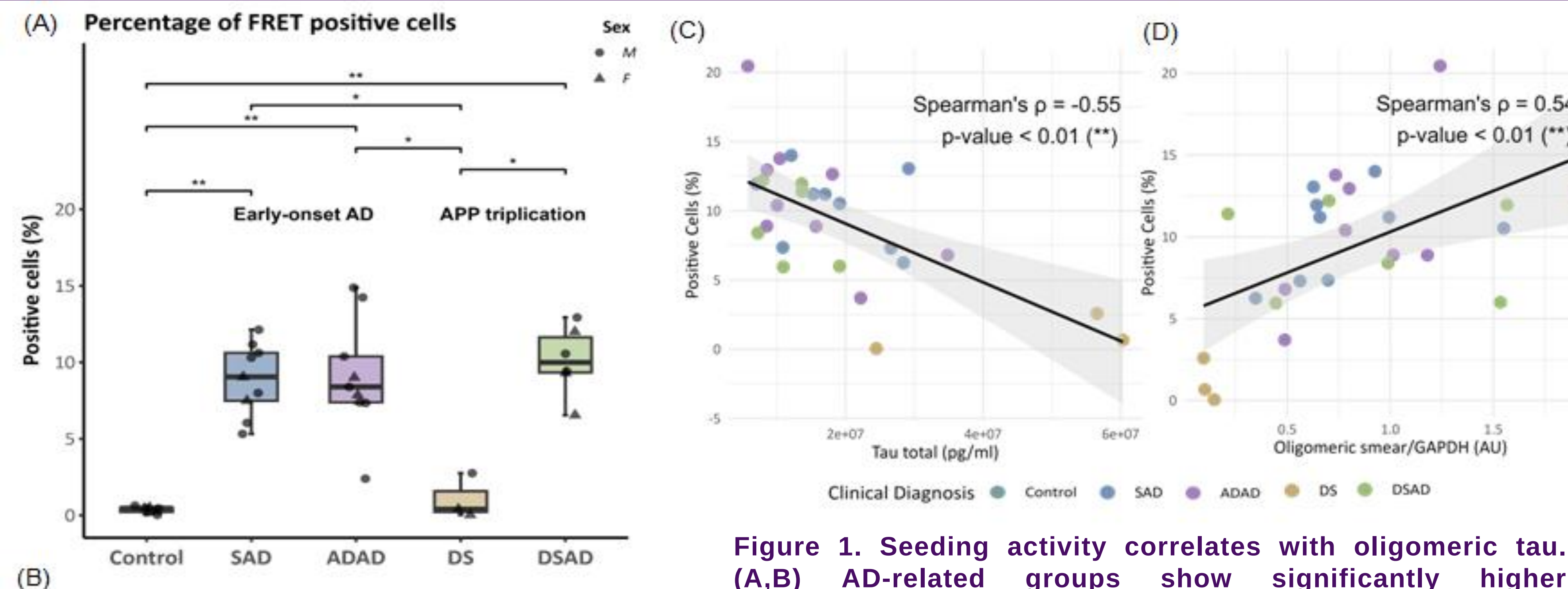


Figure 1. Seeding activity correlates with oligomeric tau. (A,B) AD-related groups show significantly higher percentages of FRET-positive cells than Control and DS. (C) Total tau levels in the isolated seed fraction do not explain the tau-induced FRET signal, whereas (D) oligomeric tau displays a significant positive correlation with the proportion of FRET-positive cells.

CONCLUSIONS

- Tau seeding activity is driven by oligomeric tau species rather than total tau levels.
- T22-positive oligomeric tau is localized in both presynaptic and postsynaptic compartments in genetic AD cases.
- These findings support the idea that synapses are key sites where pathogenic tau species accumulate and may facilitate disease spread.
- Future studies should determine how synaptic oligomeric tau contributes to the progression of tau pathology.

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Figure 2. Super-resolution images reveal the presence of T22-positive oligomeric tau (yellow) in both presynaptic (SYPH, magenta) and postsynaptic (PSD, cyan) compartments in genetic AD cases.