Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Seminar

Deciphering the isoform specific role of apolipoprotein E in Alzheimer's disease

Vinoth Kumar V

TIFR, Hyderabad

The e4 isoform of apolipoprotein E (ApoE4) is the major risk factor for Alzheimer's disease. In vivo, apoE4 is associated with higher amyloid aggregation of abeta and the tau protein. However, apoE4 has also been shown to exhibit cytotoxicity independent of its role in amyloid deposition. First, we explored the structural differences between the apoE isoforms and examined whether these differences can be responsible for the cytotoxicity of apoE. Our study using transgenic *Drosophila* models suggests that conformational instability and molten globule-like intermediates alone cannot explain the neurotoxic nature of ApoE4. Then, using an array of biophysical techniques, we examined whether and how apoE isoforms may influence the biomolecular condensates and subsequent liquid-to-solid transition of tau in vitro. Our study revealed that in the lipid-free form all three isoforms of ApoE accelerate the amyloid conversion of tau. However, when lipidated apoE was used only apoE4 accelerated the amyloid formation. This pathogenic property of apoE4 was correlated with accelerated delipidation of apoE4 in presence of the tau condensates. Taken together, our study suggests that improved lipidation of apoE4 as a potential therapeutic strategy for Alzheimer's disease.

Wednesday, Jul 16th 2025

14:30 Hrs (Tea / Coffee 14:15 Hrs)

Seminar Hall, TIFRH