Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Internal Seminar

Investigation of ApoE-lipid interaction using anisotropy and fluorescence studies

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Apolipoprotein E4 (apoE4) is a major risk factor in late-onset Alzheimer's disease relative to the common ApoE3 isoform. Difference between ApoE3 and ApoE4 in primary structure is Cys/Arg mutation at 112 position. Hydrophobicity and size of amino acids at 112 position determine the stability and domain interactions in ApoE. Here we have performed systematic studies on the role of amino acid substitutions at position 112 on the domain-domain interactions using biophysical methods including fluorescence anisotropy, spectrofluorometer and size exclusion chromatography. For the same we expressed and purified 112 mutants by substituting 112R with Ala, Val, Leu, Ile, Met and Thr.

Our results show that the stability of the C-terminal domain and N-terminal domain is different between different 112 mutants. Measurements of urea dependent Forster Resonance Energy Transfer (FRET) shows that the stability of the domains are changing drastically due to the 112 mutation. Moreover, the FRET studies in the presence and absence of liposomes shows significant difference at the structural and conformational level of ApoE. Taken together our data indicate that the ApoE unfolding happens in different stage with first unfolding the C-terminal domain and then the N-terminal domain.

Friday, Aug 23rd 2019

2:30 PM (Tea/Coffee at 2:00 PM)

Seminar Hall, TIFR-H