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

# Students' Annual Seminar

## Investigation of ApoE folding intermediates and their relation to neurodegeneration using *Drosophila*

## Vinoth Kumar V

Apolipoprotein E (ApoE) is the primary apolipoprotein in CNS and plays an important role in transporting lipids and cholesterol. There are three common isoforms namely ApoE2 (112 Cys,158 Cys), ApoE3 (112 Cys, 158 Arg) and ApoE4 (112 Arg,158 Arg). ApoE4 isoform is the strongest genetic risk factor gene for sporadic Alzheimer's disease in a dose-dependent manner (E4-4-fold & E4/E4-12-fold disease risk compared to E3/E3 individuals). However, the mechanism by which ApoE increases the risk and disease progression is not very clear. Although several in-vitro and in-vivo models consistently point to a detrimental effect upon ApoE4 expression compared to ApoE3, what structural property of ApoE4 differs from ApoE3 needs clear investigation. In our study, we have compared ApoE4 with other variants of ApoE with clinical/structural significance for their propensity to exhibit intermediate population and found a correlation between the population of intermediates and the stability of the protein. We further developed a transgenic *Drosophila* model to understand the association between the population of intermediates and neuronal toxicity. We also performed the functional study by comparing lipid transport ability of different ApoE variants in the retinal tissues. Overall, our results from fly model studies show a better correlation between a higher population of folding intermediates exhibited by ApoE4 and an increased toxicity.

***Friday, June 23rd 2023***

***2:00 PM (Tea / Coffee 1.45 PM)***

***Seminar Hall, TIFR-H***