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

Students' Annual Seminar

ApoE Inhibits Elongation of Aβ42 Fibrils in an Isoform-Dependent Manner: A Single Fibril-Level Study

Sourav Das Adhikari

ApoE4 is the strongest genetic risk factor in late-onset Alzheimer's disease. Numerous in-vivo and epigenetic studies suggest a strong correlation between the apoE isoforms, viz., apoE4, apoE3, and apoE2 and the extracellular deposition of Amyloid-β in the brain. However, mechanistic details of how apoE affects the microscopic aggregation steps of Aβ42 have remained unknown. In this study, we used TIRF microscopy to examine the impact of the apoE isoforms on Aβ fibrilization with single fibril resolution. Our findings indicate that apoE2 and apoE3 are stronger inhibitors of the growth of the Aβ fibrils than apoE4. Furthermore, using array of single molecule fluorescence techniques, such as super resolution optical microscopy, viz., STORM and single molecule photo bleaching assay etc. we have established that apoE3 and apoE2 bind more strongly to the growing ends of the fibrils than apoE4. We hypothesise that the weaker affinity of apoE4 to the Aβ aggregates could lead to higher aggregation of Aβ in vivo. Moreover, weaker affinity of apoE4 to the Aβ fibrils may affect apoE-mediated clearance of the apoE-Aβ42 complexes, leading to increased amyloid burden in individuals with the apoE4 genotype.

Thursday, Jul 18th 2024

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

Auditorium, TIFR-H