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

Webinar

Biophysical Characterization of Interactions between Apolipoprotein E and Amyloid-β

Shamasree Ghosh

TCIS, Hyderabad

Alzheimer's disease (AD) is one of the most prevalent forms of dementia among the elderly population in the world. It is characterized primarily by the deposition of Amyloid-β (Aβ) in the brain. However, the major genetic risk factor of AD is apolipoprotein E4. Apolipoprotein E (ApoE) is the major lipoprotein present in the human brain. It exists as three isoforms viz., apoE2 (Cys 112, Cys 158), apoE3 (Cys 112, Arg 158), and apoE4 (Arg 112, Arg 158). ApoE plays a critical role in the modulation of Aβ metabolism in an isoform-dependent manner. However, its interaction with Aβ, causing AD, remains poorly understood.

In this talk, first I will discuss the molecular mechanism of interaction between apoE and Aβ, by comparing the effects of different domains of apoE on the aggregation of Aβ. We find all the domains of apoE delay the kinetics of aggregation of Aβ in substoichiometric concentration. A competitive binding assay further shows that the binding affinity of the full-length apoE to Aβ is much higher compared to the individual domains. Taken together, we hypothesize that a high affinity of the apoE-Aβ interaction is achieved due to multivalent binding between oligomeric Aβ and full-length apoE. Further, we characterize the apoE-Aβ complexes using the Two-colour coincident detection (TCCD) method. We find the complexes formed are heterogeneous in nature Finally, I will discuss, how apoE affects various microscopic processes viz., primary nucleation, elongation, and secondary nucleation involved in the pathway of aggregation of Aβ42 using total internal reflection fluorescence microscopy (TIRFM). We find that all the isoforms of apoE inhibit the elongation and secondary nucleation of the fibrils.

Friday, Oct 8th 2021

4:00 PM