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

Seminar

Reconstruction of Pathological Amyloid Polymorphs in vitro for Drug Design and Biomarker Discovery in Alzheimer's and Parkinson's Disease

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Amyloid diseases, such as Alzheimer's (AD), Parkinson's (PD), and systemic amyloidoses (Transthyretin Amyloidosis, ATTR; Serum Amyloid A Amyloidosis, SAA; Dialysis-Related Amyloidosis, DRA; Amyloid Light-chain Amyloidosis AL), result from the aggregation of proteins into insoluble fibrils with a cross-β-sheet structure. AD and PD affect ~55 million and ~10 million people globally, respectively, with costs projected to reach $2.8 trillion by 2030. In India, neurodegenerative conditions are often misdiagnosed due to limited awareness and healthcare access, especially in rural areas. PD is marked by α-synuclein (α-Syn) aggregation into polymorphic fibrils, influenced by pH and buffer composition. Cryo-EM studies have revealed new α-Syn polymorphs at pH 7.0, resembling those seen in juvenile-onset synucleinopathies. Amyloid formation occurs via nucleation, elongation, and secondary nucleation, the latter being the main driver of toxicity. The BRICHOS domain, derived from proSP-C, inhibits secondary nucleation by weakly binding to fibrils. Furthermore, Small molecules modelled on Aβ1-42 fibrils also reduce α-Syn and Aβ aggregation, offering a promising direction for personalised therapeutic development.

Wednesday, Aug 13th 2025

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Auditorium, TIFRH