INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE
2A&B, Raja S.C. Mullick Road, Jadavpur, Kolkata-700032, India

Seminar Notice

Org. by

Department of Spectroscopy

Title:	Prying into Prions: Deadly Conformational Switch of the Prion Protein
Speaker:	Samrat Mukhopadhyay, Centre for Protein Science, Design and Engineering, Department of Biological Sciences and Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER), Mohali, Punjab, India.
Date:	January 24, 2018 (Wednesday)
Time:	12:00 noon
Venue:	C V Raman Hall, IACS
Abstract:	Prion diseases are a family of fatal neurological disorders. The human prion diseases include Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker disorder and fatal familial insomnia, whereas, animal prion diseases are scrapie and bovine spongiform encephalopathy or 'mad cow' disease. The major causative agent of prion diseases is believed to be proteinaceous infectious particles comprising aggregates of a misfolded isoform of the prion protein (PrP), which is a GPI-anchored cell-surface protein. The key step in this pathogenesis is believed to be a profound conformational switch from a largely α-helical normal cellular form (PrP^{C}) to a predominantly β-sheet-rich protease-resistant scrapie form (PrP^{Sc}). A line of evidences indicates that the interaction of PrP with the anionic lipid head-groups of the membrane surface may play an important role in the conformational conversion of PrP^{C} to PrP^{Sc}. We have used a synthetic trans-conversion system comprising anionic surfactant that mimics the membrane environment and shares some key features of binding-induced misfolding of protein on biological membranes. Using a diverse array of spectroscopic and microscopic techniques coupled with the other biophysical, biochemical and cell biological tools, we have elucidated the mechanism of the deadly conformational conversion process that leads to the formation of cytotoxic amyloid-like aggregates from recombinantly expressed human PrP. Our results demonstrate that the *in vitro* generation of cytotoxic amyloids is mediated by the aggregation of a predominantly disordered intermediate of PrP. We have also been able to make a direct observation of PrP misfolding and oligomerization on the lipid membrane using picosecond time-resolved excitation energy migration. These studies provide a compelling evidence of membrane-induced misfolding and oligomerization of PrP. I will also discuss our unpublished results on the interaction of PrP with the distinct types of oligomers of amyloid-β that is linked to Alzheimer's disease.

All are cordially invited to attend the seminar