Apolipoprotein E (ApoE), the major constituent of lipoproteins in the human body is responsible for the homeostasis of triglyceride and cholesterol. This 299 residue long protein has three common isoforms viz. ApoE2 (Cys 112, Cys 158), ApoE3 (Cys 112, Arg 158) and ApoE4 (Arg 112, Arg 158). ApoE3 and ApoE4 differ by a single amino acid residue substitution but exhibit remarkable differences in functionality. ApoE4 is considered to be the strongest genetic risk factor of Alzheimer’s disease whereas ApoE3 is normal and ApoE2 protective. Several biophysical studies and the X-ray crystallography structure of the N-terminal domain of ApoE suggest that the structure of isoforms of ApoE are almost identical. Despite the similarity in structure, Hydrogen-Deuterium exchange followed by Mass spectrometry (HDX-MS) reveals that ApoE3 and ApoE4 differ in dynamics. ApoE4 indicates presence of intermediate state(s). The presence of domain interactions between N-terminal domain (NTD) and C-terminal domain (CTD) of ApoE was reflected in HDX-MS kinetics. Peptide level HDX-MS experiments identify the regions involved in domain interaction.

References:

Friday, Apr 28th 2023
5:00 PM (Tea / Coffee 4.45 PM)
Seminar Hall, TIFR-H