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

Students' Annual Seminar

Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS) reveals difference(s) in Dynamics and Domain Interaction in ApoE isoforms

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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)[1]. 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[2]. 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[3]. 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:

1. Weisgraber KH, Rall SC Jr, Mahley RW. Human E apoprotein heterogeneity. Cysteine-arginine interchanges in the amino acid sequence of the apo-E isoforms. J Biol Chem. 1981 Sep 10;256(17):9077-83
2. Strittmatter WJ, Roses AD. Apolipoprotein E and Alzheimer's disease. Annu Rev Neurosci. 1996;19:53-77. doi: 10.1146/annurev.ne.19.030196.000413.
3. Weisgraber KH. Apolipoprotein E: structure-function relationships. Adv Protein Chem. 1994;45:249-302. doi: 10.1016/s0065-3233(08)60642-7. PMID: 8154371.

Friday, Apr 28th 2023

5:00 PM (Tea / Coffee 4.45 PM)

Seminar Hall, TIFR-H