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

Students' Annual Webinar

Hydrogen Deuterium Exchange Mass Spectrometry reveals difference(s) in dynamics in ApoE isoforms.

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Apolipoprotein E (ApoE), the major constituent of lipoprotein in human body is responsible for the maintenance of triglyceride and cholesterol homeostasis. 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 exhibits 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 N-terminal domain of ApoE suggested the isoforms of ApoE to be almost similar structurally[3]. Despite the similarity in structure, Hydrogen-Deuterium exchange followed by Mass spectrometry (HDX-MS) reveals that ApoE3 and ApoE4 differs in dynamics. ApoE4 indicates presence of intermediate state(s). The presence of domain interaction between N-terminal domain (NTD) and C-terminal domain (CTD) of ApoE was reflected in HDX-MS kinetics. We also explored the binding of several small molecules with ApoE that affects the HDX-MS kinetics of ApoE.

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.

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5:00 PM