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

Students' Annual Seminar

Difference in Domain Interaction in Apolipoprotein E Isoforms Revealed by Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS)

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Apolipoprotein E (Apo-E), the major constituent of lipoproteins in the human body is responsible for the homeostasis of triglyceride and cholesterol. ApoE3 and ApoE4 differ by a single amino acid residue substitution but exhibit remarkable differences in functionality. Pathologically, ApoE4 is considered the strongest genetic risk factor of Alzheimer's disease whereas ApoE3 is normal and ApoE2 is protective. X-ray crystallography shows that structures of the N-terminal domains of the Apo-E isoforms are quite similar. Here we use Hydrogen-Deuterium exchange by Mass spectrometry (HDX-MS) to investigate the interactions between the N- and C-terminal domains. We find that under native conditions, ApoE4 exhibits enhanced domain-domain interaction than ApoE3. HDX kinetics of the N-terminal domain in the context of the intact protein and the isolated N-terminal fragments in ApoE4 are observed to be different. This indicates presence of domain interaction in apoE4. Peptide level (bottom-up) HDX-MS experiments identify the regions involved in domain interaction. Quantification of the domain interaction i.e., effect of C-terminal domain on the N-terminal domain was achieved considering intrinsic exchange behaviour as the reference.

Wednesday, Jul 24th 2024

14:30 Hrs (Tea / Coffee 14:15 Hrs)

Auditorium, TIFR-H