Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Students' Annual Seminar

Differences in Domain Interactions among Apolipoprotein E Isoforms

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Apolipoprotein E4 (apoE4) is the strongest risk factor in Alzheimer's disease while apoE3 is normal. Difference between ApoE3 and ApoE4 in primary structure is Cys/Arg mutation at 112 position. However structural differences between apoE3 and apoE4 are still unclear. Differences in the interactions between the N- and C-terminal domains have been proposed to cause functional differences between the isoforms. Our results show that the stability of the C-terminal domain is different between apoE3 and apoE4 indicating role of N-terminal domain on the stability of the C-terminal domain. Additionally, N-terminal domain in apoE4 but not in apoE3 is destabilized by the presence of the C-terminal domain. We have then performed systematic studies on the role of amino acid substitutions at position 112 on the domain-domain interactions. Hydrophobicity and size of amino acids at 112 position determine the stability and domain interactions in ApoE. We find that stability of the N-terminal domain of ApoE increases with increasing hydrophobicity of the amino acid at position 112. Domain-domain interactions measured by intra-molecular FRET between two domains of ApoE show that the domain-domain interactions are strongly altered with the mutations at 112 position of ApoE.

Friday, Mar 16th 2018

04:00 PM (Tea/Coffee at 03:30 PM)

Seminar Hall, TIFR-H