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

Colloquium

Life, the Universe and Everything: Why we study 14-3-3 proteins

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14-3-3 proteins are conserved, dimeric, acidic proteins that regulate multiple cellular pathways by binding to proteins containing a phosphorylated Serine residue in one of three consensus motifs. Previous work from the laboratory has demonstrated that loss of either of two 14-3-3 paralogs, 14-3-3ε or 14-3-3γ, leads to centrosome amplification in multiple cell lines, due to the premature activation of cdk1. However, we find that while the knockout of 14-3-3ε leads to multi-polar mitoses, the knockout of 14-3-3γ results in centrosome clustering and pseudo-bipolar mitoses. 14-3-3γ knockouts demonstrate compromised desmosome function and a decrease in keratin levels, leading to decreased cell stiffness and an increase in centrosome clustering. Further, we have explored the contribution of two conserved acidic amino acids in the phospho-peptide binding groove to ligand binding using centrosome duplication as a model system. Our results indicate that 14-3-3γ prevents centriole duplication by inhibiting the function of NPM1, while 14-3-3ε inhibits centriole disengagement by inhibiting the activity of Plk1 and Separase. Our results indicate that 14-3-3 proteins regulate multiple pathways that regulate centrosome duplication and indicate that any phenotype observed upon loss of a specific 14-3-3 paralog might have contributions from multiple cellular pathways. Finally, I will focus on how another paralog, 14-3-3σ, regulates therapy resistance and tumour progression, and how the pathways activated or inhibited by 14-3-3σ lead to different outcomes in different cell types.

Monday, Feb 26th 2024

16:00 Hrs (Tea / Coffee 15.45 Hrs)

Auditorium, TIFR-H