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

Colloquium

Energetic phosphates in cell signalling - *pyro*-phosphoinositol makes *pyro*-phosphoproteins

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Proteins undergo an array of posttranslational modifications that influence their abundance, activity and interaction with other proteins. Phosphorylation on Ser/Thr residues catalysed by protein kinases is one the most frequently occurring and best-studied posttranslational modifications. We have shown that a subset of phosphorylated Ser residues can undergo *pyro*phosphorylation by accepting an additional phosphate moiety. The phosphate donor in this case are inositol pyrophosphates – a class of energy-rich metabolites present in all eukaryotic cells that consist of an inositol ring substituted with mono- and di-phosphate groups. Serine (and in rare cases threonine) pyrophosphorylation is achieved by Mg^{2+}-dependent, but enzyme independent transfer of a β-phosphate moiety from an inositol pyrophosphate to a prephosphorylated serine residue located in an intrinsically disordered region of the protein, amidst acidic amino acid residues. We have demonstrated that serine pyrophosphorylation regulates diverse cellular processes, including rRNA synthesis, dynein-driven vesicle transport, protein stability and DNA repair. Our understanding of the molecular details of this phosphotransfer process from pyrophospho-inositol to generate pyrophospho-serine, is still nascent. Our current knowledge of the importance of protein pyrophosphorylation and recent advances in understanding the mechanism of this important yet under-appreciated posttranslational modification will be discussed.

Tuesday, Aug 22nd 2023

4:00 PM (Tea / Coffee 03.45 PM)

Auditorium, TIFR-H