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

Students' Annual Seminar

Dissecting the molecular mechanisms of mammalian DNA replication regulation in the context of oncogene-induced replication stress

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Faithful replication of DNA is essential to preserve genetic information of a cell. In preparation for DNA replication, certain proteins bind to multiple sites on the genome called origins – a step called origin licensing – during the G1 phase of the cell cycle and DNA replication initiates during the S phase from only a small fraction of the licensed origins. The mechanism behind this origin selection is not well understood. On the other hand, modalities such as DNA damages, non-B DNA structures, transcription collision etc. can cause replication stress, which can lead to genomic instability, if unresolved. Oncogene-induced replication stress has been phenotypically linked to de-regulated origin firing, over-replication, under-replication, dysregulation of cell cycle etc., without any mechanistic details. Since oncogenes perturb the replication dynamics, causing replication stress to provide proliferation advantages to transformed cells, and two-thirds of the pathological driver mutations in cancer are known to stem from replication errors, we are trying to understand the differences in replication patterns between wildtype and viral-oncogene induction model systems, both in absence or presence of external stressors, to eventually unfurl the control of the mammalian replication pattern. We are also trying to study the differences between active and dormant origin proteomes, which might give us cues to extract mechanistic details of origin firing regulation in mammalian DNA replication. In this talk, I will discuss the models we have established and results obtained so far.

Friday, Nov 22nd 2024

14:00 Hrs (Tea / Coffee 13:45 Hrs)

Seminar Hall, TIFR-H