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

Seminar

Topoisome: A new player in cancer and DNA damage response

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The dynamic interplay between the proto-oncogene MYC and the repair engine p53 dictates cellular fate by balancing tumorigenesis and the DNA damage response (DDR). While MYC drives rapid proliferation through hyper-transcription for tumour progression, p53 safeguards genomic integrity. However, excessive MYC or p53 activity induces severe DNA supercoiling, leading to topological stress across the genome. To resolve this, both MYC and p53 assemble a novel complex, the 'topoisome,' which recruits and superactivates Topoisomerase I (TOP1) and Topoisomerase II (TOP2). The topoisome functions as a critical regulator of genome dynamics, maintaining equilibrium between MYC-driven oncogenesis and p53-mediated DNA repair. This study aims to understand the functional dynamics of the topoisome while exploring its therapeutic potential in Colorectal Cancer (CRC). My research goal is threefold; first, I will (1) Regulate MYC-topoisome formation by exploring MYC Structural Dynamics and post-translational modifications that modulate its interactions and oncogenic potential. (2) characterize topoisome-driven oncogenesis by a) defining the structural organisation and functional diversity of topoisome complexes, investigating the role of topoisome in colorectal cancer (CRC) progression, b) Target the topoisome in CRC using Tyrosyl-DNA-phosphodiesterase (TDP) inhibitors, Bivalent inhibitors, or AI/ML-enabled therapeutic drug designing and discovery pipelines and c) Translational and in-vivo validation in PDO/PDX models. (3) study Telomere Supercoiling and Telomerase Engagement Atlas (TeSEA) mapping: Mechanochemical Control of Chromosome-End Maintenance by MYC-topoisome. Understanding the MYC-p53-topoisome axis will provide novel critical insights into oncogenesis, DNA topology regulation, aging and tumour adaptation, paving the way for novel therapies.

Tuesday, Nov 11th 2025

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Auditorium, TIFRH