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

Internal Webinar

Investigating the role of 9-1-1 complex in DNA damage sensing and ATR-mediated genomic stability

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Eukaryotic genomes are constantly threatened by external factors, such as radiation and carcinogens, as well as internal factors, including replication errors and reactive oxygen species, which can cause DNA lesions, including single- and double-strand breaks.

The DNA Damage Response (DDR) detects these threats, signals their presence, and coordinates repair. A key event is the generation of single-stranded DNA (ssDNA) during damage processing or replication stress, which triggers activation of the ATR kinase pathway.

ATR (Ataxia Telangiectasia and Rad3-related) is a central kinase in the DDR recruited to the DNA damage site. Central to this process is the 9-1-1 complex (Rad9-Rad1-Hus1), a clamp loaded onto the 5' junction of the damaged DNA by the Rad17-RFC complex and further recruits the ATR activators. The 9-1-1 clamp interacts with DDR proteins to facilitate ATR activation and subsequent CHK1 phosphorylation, ensuring cell cycle regulation and repair.

However, we still do not understand the contribution of the checkpoint clamp, 9-1-1, in mediating checkpoint activation and genome stability. In this seminar, I will be discussing the role of the 9-1-1 complex in ATR activation, its interactions with DNA substrates and DDR proteins, and its contribution to resolving replication stress and maintaining genomic stability.

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16:30 Hrs