Tata Institute of Fundamental Research
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Webinar

On Cell Cycle-Dependent DNA Damage Responses and Gene Expression as Assayed from Microscopic Image Analysis

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Cell cycle encapsulates all the processes that go on inside a cell to ensure a faithful transmittance of genetic information to the next generation. This makes the cell cycle an important regulator of most processes inside a cell and particularly those dealing with genome stability. Many of the existing methods to study cell cycle-dependent regulation of cellular processes do not yield information about subcellular localization and cell-to-cell heterogeneity of such processes. In this presentation I describe a novel microscopy-based method of cell cycle staging which addresses some of these shortcomings. I further use the technique in combination with DNA FISH*, single molecule RNA FISH (smFISH) and immunofluorescence for Cyclin A2 gene to investigate links between nuclear architecture and cell cycle-dependent gene expression. Finally I use these methods to study DNA damage responses in the context of the cell cycle. I show that the peak in γH2AX, a general DNA damage marker, in the S phase cells after UV irradiation corresponds to the active replication sites at the time of UV irradiation and not to the extent of actual DNA damage. The Thesis proposes that it is DNA damage response and not DNA damage itself which is cell cycle-dependent. Moreover, it discusses the central role of the cell cycle in the regulation of DNA damage repair and gene expression and presents a high-throughput, high-resolution, imaging-based technique to study these processes at a single-cell resolution.

* FISH: Fluorescence in situ Hybridization

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