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

Students' Annual Seminar

Investigating the structural and functional reorganisation of the nucleolus in response to DNA damage

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The nucleolus, a phase-separated sub-organelle within the eukaryotic cell nucleus, is emerging as an important sensor for cellular stress. In case of DNA damage, the nucleolus undergoes reorganisation of its tripartite structure to relocalise nucleolar proteins, ribosomal RNA (rRNA), and damaged DNA that aids in the downstream response. Using tools expansion microscopy, I will discuss my work on visualising the ultrastructure of nucleolus, structural reorganisation in response to global DSBs, its impact on rRNA synthesis and nucleolar proteins. Imaging these nucleoli under super resolution microscopy show that both the fibrillar and dense fibrillar centres show ring like organisation indicating a spatial ordering of nucleolar function that have not been adequately described till date. This pattern aids in efficient rRNA synthesis, but DNA damage actively leads to reorganisation of these compartments to the nucleolar periphery.

Additional challenges have to be overcome in repairing ribosomal DNA (rDNA) encoded and enclosed within the nucleolar domain because of its phase-separated and repetitive organisation. Double strand breaks (DSBs) caused within the nucleolus thus elicit a unique response involving reorganisation of both DNA damage response proteins, and nucleolar factors, but the dynamics and the purpose of such reorganisation remain elusive. We also aim to address how DSBs in rDNA affect the architecture and functional organisation of the nucleolus using laser-induced strand-breaks combined with tools of high-resolution microscopy. Localised laser irradiation within the nucleolus led to its expansion, and differential localisation of the repair factor Parp1 and the nucleolar compartment protein Nucleolin. Nucleolar expansion is found to be actin-dependent and may be regulated by chromatin remodellers. Probing this further will help us understand the roles of actin in early rDNA DSB responses within the cell.

Thursday, May 2nd 2024

14:30 Hrs (Tea / Coffee 14:15 Hrs)

Seminar Hall, TIFR-H