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

Seminar

Stress induced spatial and temporal reorganisation of the nucleolus and its role in DNA damage response

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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. Nucleoli are major sites of ribosome biogenesis, and damage to the ribosomal DNA (rDNA) can affect both transcriptional and translational status of the cell. Additional challenges have to be overcome in repairing rDNA encoded and enclosed within the nucleolar domain because of its phase-separated and repetitive organisation. We aim to understand the structural and functional reorganisation of the nucleolus upon cellular stress. In this talk, I will discuss how we have spatially resolved the tripartite structure of the nucleolus to understand partitioning of nucleolar proteins under conditions of damage using methods of expansion microscopy and in situ RNA detection. We show that the nucleolar reorganisation upon DNA damage or inhibition of RNA Polymerase I scales with nascent rRNA levels, and such modulation of nucleolar function may merge naturally from the physical chemistry of the sub-organelle. We further discuss the changes in the dynamics of the resident protein, a possible proxy for the condensate properties, which get altered upon cellular stress. We then study the temporal reorganisation of the nucleolus in the initial stages upon targeted rDNA damage. We observe that 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 the buffering of both G-actin and F-actin within the nucleus.

Tuesday, Jul 15th 2025

10:00 Hrs (Tea / Coffee 09:45 Hrs)

Seminar Hall, TIFRH