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 rDNA damage

Sinjini Ghosh

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) affects the translational status of the cell immediately. Due to its phase-separated and repetitive organisation, repairing rDNA encoded and enclosed within the nucleolar domain has to overcome additional challenges. 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 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 motor proteins and chromatin remodellers. Probing the partitioning of nucleolar proteins under conditions of damage may provide insight into reorganisation of nucleolar function in response to strand breaks in rDNA. Further, using tools of expansion microscopy, and endonuclease mediated lesions in the context of nucleolar DSBs I seek to provide additional insight into structural reorganisation of the compartment in response to DSBs. I will discuss some of our efforts to this end. The roles of the nucleolus in general DSB-response will be subsequently investigated.

Friday, June 9th 2023

2:00 PM (Tea / Coffee 1.45 PM)

CR-1, TIFR-H