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

Students' Annual Webinar

Role of HP1 isoforms and Phase Separation in DNA Damage Responses in Heterochromatin

Darshika Bohra

Double strand breaks (DSBs) pose a severe threat to genomic stability and need immediate attention from the DNA damage response (DDR) machinery. DDR in heterochromatin has distinctive features owing to the nature of chromatin organisation. Heterochromatin Protein 1 (HP1) contributes significantly to the organisation, maintenance and function of heterochromatin. HP1 has three isoforms, α, β, and γ, which possess significant homology to each other yet have distinct functions and all three have been implicated in the context of DDR. In order to investigate DDR in heterochromatin, we focused on HP1 isoforms α and β, the first of which has recently been shown to mediate liquid-liquid phase separation in cells. Using the tool of fluorescence recovery after photobleaching or photodamage, live cell imaging and immunofluorescence, we observe that the dynamics of HP1α and HP1β differ at the site of laser induced DSBs. The expansion profiles of the damaged foci show a clear difference between the two isoforms, which may be controlled by nuclear actin. Cells overexpressing HP1 α or β isoform also show differential recruitment of repair proteins at the site of damage. We aim to probe the contribution of HP1α-mediated phase separation in affecting these damage repair outcomes. Further we aim to determine mechanistic interplay of these two isoforms, its impact on heterochromatin organisation, DDR and genomic integrity.

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5:00 PM