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

# Students' Annual Webinar

## Connecting DNA damage responses to nuclear mechanics in living cells

## Shantam Yagnik

ATM (Ataxia Telangiectasia Mutated) and ATR (Ataxia telangiectasia and Rad3 related) are members of the family of phosphoinositide 3-kinase (PI3K) related kinases that catalyse phosphorylation of multiple proteins involved in the DNA damage response pathway. The recruitment of ATR and its downstream signalling in maintaining replication fork stability, coordinating cell cycle progression and mediating specific DNA damage responses (DDR) has been extensively studied. However, recent studies have focused ATR as a sensor of mechanical forces across the nucleus and also demonstrated the role of substrate stiffness on DDR. Converse experiments on how DDR affects nuclear mechanics remain to be done. I aim to ask how the nuclear envelope serves as a mechanotransducer in the context of DNA damage and how these changes bring about the recruitment of ATR and activate subsequent downstream signalling cascades.

In this talk, I will be discussing about the standardisation of a FRET based sensor to observe force changes across the nuclear envelope and work done so far to understand the interplay between mechanical forces and DDR. I will also describe other directions I have taken to investigate chromatin and nuclear organisation level changes that occur in living cells in response to DNA double strand breaks. I aim to use such methods to uncover how DDR and nuclear mechanics feedback on to each other.

***Friday, May 6th 2022***

***4:00 PM***