

## **Seminar**

### **Investigating the role of tissue mechanics in the regulation of epithelial defence against cancer**

**Phani Shilpa**

**TCIS, Hyderabad**

In epithelia, normal cells recognise and competitively extrude out newly transformed cells by a fundamental process known as epithelial defence against cancer. Its occasional failure has been shown to promote oncogenesis, however, the factors that determine the outcome of this defence have largely remained elusive. While previous studies have focused on biochemical signalling, we specifically explored the role of physical factors, such as cellular forces and tissue stiffness in determining the dynamics of this defence. We discovered that pathological stiffening of extracellular matrix abrogates the defence against activated HRAS oncogene - transformed cancerous cells. We further elucidated the molecular mechanism underlying this discovery, which involves stiffness-sensitive perinuclear sequestration of a cytoskeleton protein, filamin. Having shown that mechanical cues play critical roles in our defence against cancer, we further looked for a mechanobiological signature of this process. We established that the extrusion of transformed cells requires a compression from the surrounding normal cells. In this talk, I will highlight our findings that demonstrate the involvement of tissue mechanics in the initial phases of cancer progression.

***Wednesday, Jul 20<sup>th</sup> 2022***

***4:00 PM (Tea/Coffee at 03:45 PM)***

***Auditorium, TIFR-H***