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

Seminar

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

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Epithelial cells sustain the tissue form and function by maintaining a tightly-regulated force equilibrium with the surroundings through an interplay of cell growth, proliferation, and death. Cell competition is one such established process that preferentially eliminates one cell population over another in an attempt to preserve tissue homeostasis. In epithelia, normal cells recognise and extrude out newly-emerged transformed cells by a process that is the most fundamental epithelial defence against cancer. Its occasional failure promotes oncogenesis. However, the factors that determine the outcome of this defence have largely remained elusive. In this talk, I will discuss our work that specifically explores the role of physical factors, such as cellular forces and tissue stiffness, in determining the dynamics of this defence. We discover that pathological stiffening of extracellular matrix attenuates the defence against $HRas^{V12}$ - transformed cells. We elucidate the molecular mechanism underlying this discovery, which involves stiffening-induced perinuclear sequestration of a cytoskeletal protein called filamin. Next, we highlight a mechanobiological signature of this process, i.e. extrusion of transformed cells requires a compression from the surrounding normal cells, and further explore the biophysical parameters influencing it. This work reveals how tissue mechanics function as a decisive factor in epithelial defence against cancer.

Wednesday, Mar 8th 2023

04:00 PM (Tea / Coffee 03.45 PM)

Auditorium, TIFR-H