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

Seminar

Mechanobiological Investigation of Epithelial Homeostasis during Epithelial Defence against Cancer

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TIFR, Hyderabad

Epithelial homeostasis is crucial for maintaining tissue integrity and function. Epithelium achieves biomechanical equilibrium by actively extruding unfit cells that may compromise epithelial barrier, through cell competition. Specifically, cell competition mediates non-cell autonomous removal of precancerous, transformed mutant cells expressing activating oncoprotein such as HRas V12, referred to as epithelial defense against cancer (EDAC). In particular, a biochemical crosstalk in conjunction with mechanical forces maintains the fidelity of this fundamental process. In this talk, I would discuss our work on the context of active Ras cells in the Epithelium, both cells in culture or in vivo in mice lung and gut, to explore the mechanobiological paradigms causal to Ras cell elimination through cell competition. I would elaborate on the subcellular modalities that bring about these features in play, to make competitive removal of transformed mutants robust. Specifically, I would show how non-proliferative cell competition is a unique feature of epithelial homeostasis during EDAC and is based upon the mechanical fragility of transformed mutant population in the face of active compression. I would introduce a novel mechanobiological technique called gel compression microscopy, which we developed to characterise compressibility in epithelial tissues and show mechanical fragility during transformation. Finally, I would elaborate on the subcellular load-bearing elements, the nucleus and cytoplasmic intermediate filaments Vimentin and Keratin, which power homeostatic cell competition against transformed epithelial cells. To this end, I would show nuclear deformation in transformed cells as a decisive factor towards successful EDAC. I would introduce Vimentin in the light of its unconventional role in epithelial cells during competition and argue towards its interplay with nuclear deformation in transformed mutants, ensuring efficient transformed mutant removal from Epithelia.

Tuesday, Jun 3rd 2025

11:30 Hrs (Tea / Coffee 11:15 Hrs)

Auditorium, TIFRH