Tata Institute of Fundamental Research
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Seminar

Investigating the role of matrix stiffness in mitochondrial morphodynamics and function

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Mechanical cues from the tissue microenvironment, such as stiffness of the extracellular matrix (ECM), modulate cellular forms and functions. As numerous studies have shown, this modulation depends on the stiffness-dependent remodelling of cytoskeletal elements and cell-matrix adhesions. In contrast, very little is known about how the intracellular organelles such as mitochondria respond to matrix stiffness. To this end, we show that mechanical signals arising from the stiffness of ECM alter mitochondrial morphology, localisation, and motility, which we collectively refer to as morphodynamics. By performing an extensive quantitative characterisation of mitochondrial morphology, subcellular localisation, and dynamics on soft and stiff matrix, we show that upon matrix stiffening, mitochondria undergo a transition from a uniformly distributed, filamentous, and highly networked topology to a fragmented and less networked topology showing perinuclear clustering. We further show Drp1 GTPase activity and perinuclear aggregation of filamin as key mechano-players driving the stiffness-sensitive alterations in mitochondrial morphology and localisation respectively. Mitochondria in highly mechanosensitive stem cells and highly metabolic hepatocytes also respond to mechanical cues from the extracellular matrix, extending the generality of our findings. In particular, perinuclear mitochondrial clustering appeared to be crucial for priming human mesenchymal stem cells towards an osteogenic fate on a stiff matrix. Taken together, our results elucidate a dependence of mitochondrial morphodynamics and function on matrix stiffness, which possibly enables a cell to adapt to its microenvironment.

Friday, Jul 14th 2023

11:30 AM (Tea / Coffee 11.15 AM)

Auditorium, TIFR-H