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

Students' Annual Seminar

Matrix stiffening promotes perinuclear clustering of mitochondria

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Mechanical cues from the tissue microenvironment, such as stiffness of the extracellular matrix, 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 and whether their form, function, and localisation change accordingly. Here, by performing an extensive quantitative characterisation of mitochondrial morphology, subcellular localisation, and dynamics on soft and stiff matrix, we show that while matrix stiffness affects all of these aspects, matrix stiffening most distinctively leads to an increased perinuclear clustering of mitochondria. Subsequently, we could identify the matrix stiffness-sensitive perinuclear localisation of Filamin A, an actin binding protein as the key factor dictating this perinuclear clustering. Photo-conversion labelling and fluorescent recovery after photobleaching experiments revealed that perinuclear and peripheral mitochondrial populations differed in their motility on soft matrix but surprisingly they did not show any difference on stiff matrix. Finally, 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 localisation on matrix stiffness, which possibly enables a cell to adapt to its microenvironment.

Friday, Mar 17th 2023

02:00 PM (Tea / Coffee 1.45 PM)

Seminar Hall, TIFR-H