Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

TIFR-UoH (Life Sciences) Seminar Series

Mitochondrial protein import components in redox regulation

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Modulation of the ubiquitously available Reactive Oxygen Species (ROS) is critical as low levels influence cellular signaling while higher levels are toxic. ROS has been implicated in several pathologies including Alzheimer's and Huntington diseases. Mitochondrial electron transport chain (ETC) is an important progenitor for most of cellular ROS. Any perturbation in ETC assembly and function can be deleterious as it affects cellular redox homeostasis and can lead to diseases.

Using mitochondria from yeast and mammalian cells, we have uncovered novel redox-mediated pathways that curiously involve two mitochondrial import components: a matrix localized Mge1/GrpE1 and an intermembrane space localized Mia40. Mge1 acts as a sensor for both oxidative and thermal stress. Single mutants Mge1 M155L and H167L confer resistance to oxidative and thermal stress respectively. However, Mge1 harbouring both the mutations (Mge1 DM) is highly sensitive to all abiotic stresses including oxidative and thermal stresses. Most importantly, Mge1 DM is compromised in its interaction with super-complexes of ETC that may adversely affect redox homeostasis.

The second narrative involves human Mia40 (CHCHD4), a soluble inter membrane space (IMS) import receptor of mitochondria that helps in the import, folding and retention of small IMS bound proteins. We have shown earlier that it has an essential role as a component of the mitochondrial Fe-S cluster export machinery. Our recent studies show that hMia40 undergoes post translational modification. Mutants of hMia40 defective for this modification affect ETC complex activities besides increasing ROS. Our studies shed new light on a hitherto unknown aspect in ETC regulation. During normal physiological conditions, hMia40 uses post-translational modification while Mge1/GrpE resorts to structural transitions during abiotic stress to fine tune and regulate ETC function that has important consequences on cellular homeostasis.

Wednesday, May 2nd 2018

11:30 AM (Tea/Coffee at 11:00 AM)

Auditorium, TIFR-H