National Institute of Technology Rourkela

Departmental Seminar

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| Seminar Title | : Understanding role of MTP18-DRP1 fission signaling in mitochondrial proliferation and degradation |
| Speaker | : Prof. Sujit K Bhutia |
| Supervisor | : Santosh Kumar #2787 |
| Venue | : LS Seminar Hall |
| Date and Time | : 01 Jan 2025 (16:00 hrs) |
| Abstract | : MTP18, an inner mitochondrial membrane protein, plays a vital role in maintaining mitochondrial morphology. Furthermore, MTP18 induces mitochondrial fission with subsequent mitophagy, functioning as a mitophagy receptor that targets dysfunctional mitochondria into autophagosomes for elimination. Interestingly, MTP18 interacts with LC3 through its LC3 interacting region (LIR) to induce mitochondrial autophagy. Mutation in the LIR motif (mLIR) inhibits that interaction, thus suppressing mitophagy. Moreover, Parkin/PINK1 deficiency abrogates mitophagy in MTP18-overexpressing FaDu cells. Upon exposure to CCCP, MTP18[mLIR]-FaDu cells show decreased TOM20 expression without affecting COX IV expression. Conversely, loss of Parkin/PINK1 results in inhibition of TOM20 and COX IV degradation in MTP18[mLIR]-FaDu cells exposed to CCCP, establishing Parkin-mediated proteasomal degradation of outer mitochondrial membrane as essential for effective mitophagy. The MTP18-overexpressing FaDu cells transfected with p40phox were exposed to CCCP, stained for TOM20 and data showed that damaged mitochondria were concentrated in perinuclear clusters that were apposed to p40phoxPX–EGFP hotspots. Interestingly, loss of MTP18 expression in Drp1-overexpressing FaDu cells primes the loss of fission activity, resulting in hypermitochondrial fusion and loss of mitophagy, establishing MTP18-induced mitochondrial fission is essential for mitophagy. Further, PPA2, mitochondrial pyrophosphatase, promotes MTP18-mediated DRP1 activation and mitochondrial translocation to induce mitochondrial fission. |