National Institute of Technology Rourkela

Synopsis Seminar

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| Seminar Title | : Understanding the role of MTP18 in regulating fission mediated mitochondrial architecture and its significance in oral squamous cell carcinoma |
| Speaker | : Bishnu Prasad Behera ( Rollno : 519ls1003) |
| Supervisor | : Prof. Sujit Kumar Bhutia |
| Venue | : LS Seminar Room |
| Date and Time | : 19 Dec 2024 (11.00 AM) |
| Abstract | : MTP18, a nuclear-encoded inner mitochondrial membrane protein, is crucial for mitochondrial integrity. MTP18 is a downstream target of the phosphatidylinositol 3-kinase (PIK3CA) regulated transcriptionally by mTOR. MTP18 is known to promote mitochondrial fission and supports cancerous outcomes. However, there are limited studies on the mechanistic role of MTP18 contributing to mitochondrial fission associated oncogenesis. In the current study, we found that MTP18 regulates the DRP1-MFF-FIS1 signaling axis to promote mitochondrial fission. Interestingly, MTP18 overexpression elevated mitochondrial DNA content and upregulated the symmetric mitochondrial fission by modulating DRP1 and MFF, a DRP1 receptor. Additionally, MTP18 was found responsible for the activation i.e., phosphorylation of DRP1 at Ser616, and the translocation of DRP1 to mitochondria to initiate fission. The knockdown of MTP18 resulted in the suppression of DRP1 and MFF activity resulting in hyper elongation of mitochondria. In addition to this, MTP18 was also found to stabilize MFF which in turn participates in symmetric mitochondrial fission. In MTP18 knockdown condition, MFF was found to undergo degradation through ubiquitination. MTP18 was also found to mitigate various mitochondrial stress like proteotoxic stress, respiratory stress and to inhibit apoptosis during CDDP treatment. MTP18 was able to do so by the activation of stress response pathways involving Hsp60, CHOP, FIS1 mediated asymmetric mitochondrial fission and by the inhibition of pro-apoptotic signaling molecules like BAX, PARP, and CytC. In this connection, the therapeutic modulation of MTP18 mediated mitochondrial fission and mitochondrial stress management during the early onset of cancer can be employed. For this, we have used a MTP18 activating natural molecule butein to check the transition of precancerous stage to a cancerous one linked with mitochondrial dysfunction. We showed that various early mitochondrial aberration parameters like increase in ROS production, decrease in mitochondrial membrane potential and mitochondrial hyperfusion were countered by butein treatment to have a healthy and functional repertoire of mitochondria. |