National Institute of Technology Rourkela

Registration Seminar

Seminar Title	: Disruption of Lipid Rafts Restores IGFBP7 Expression in Breast Cancer Through Hedgehog-Mediated Repression of DNMT1 and EZH2 and Activation of MAPK Pathway
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Supervisor	: Samir Kumar Patra
Venue	: LS Seminar Room
Date and Time	: 22 Jul 2025 (10:30AM)
Abstract	: Breast cancer is driven by complex molecular mechanisms, including dysregulation of cellular signaling pathways and aberrant chromatin (DNA & Histones) modifications facilitating silencing of tumor suppressor genes and activation of oncogenes. This study explores the role of plasma membrane lipid rafts in modulating epigenetic regulators and signal transduction in breast cancer, with a focus on the tumor suppressor gene IGFBP7. Transcriptomic analysis of GEO datasets identified several genes among those UHRF1 acts as a key gene, whose function is associated with epigenetic DNA methylation. Functional studies in MDA-MB-231 cells demonstrated that disruption of lipid rafts using Methyl-&beta-cyclodextrin (MBCD) activated EGFR&ndashRAS&ndashMAPK signaling, downregulated DNMT1 and EZH2, and reactivated IGFBP expression. To confirm that, EGFR&ndashRAS&ndashMAPK signaling pathway is activating IGFBP7, we used RAS-MAPK specific inhibitors, and data confirms that IGFBP7 gene is regulated through this pathway. Protein&ndashprotein docking confirmed favourable interactions among UHRF1, DNMT1, and EZH2, indicating a coordinated repression complex. Notably, MBCD treatment upregulated GLI1, the effector of Hedgehog (Hh) signaling, which in turn suppressed DNMT1 and EZH2 while enhancing IGFBP7 expression. Inhibition of the Hedgehog pathway reversed this effect, implicating its role in repressing epigenetic silencers and promoting tumor suppressor reactivation. Functional assays showed that IGFBP7 reactivation reduced cell migration, colony formation, and stemness (as evidenced by downregulation of OCT4). These findings reveal a novel mechanistic axis linking lipid raft integrity, Hedgehog signaling, and epigenetic modulation, providing new therapeutic targets in breast cancer.