National Institute of Technology Rourkela

Synopsis Seminar

Seminar Title	: Deciphering the Role of SOX2 in Lung Adenocarcinoma: Bioinformatics analyses, Epigenetic Modifications and Signaling Pathways
Speaker	: Niharika (Rollno : 519ls6015)
Supervisor	: Samir Kumar Patra
Venue	: LS Seminar Room
Date and Time	: 30 Jul 2025 (10:00AM)
Abstract	: Lung adenocarcinoma (LUAD), the most common histological subtype of non-small cell lung cancer (NSCLC), constitutes a major global health concern owing to its high mortality, pronounced molecular heterogeneity, and frequent resistance to therapy. Despite considerable progress in targeted and immune-based treatments, clinical outcomes remain suboptimal due to therapeutic failure and disease relapse. Compounding this challenge is the limited efficacy of current screening modalities, resulting in late-stage diagnoses and poor prognoses. Hence, the identification of robust early diagnostic biomarkers is a critical research priority. To address this, we performed a comprehensive meta-analysis of publicly available LUAD transcriptomic datasets to uncover key molecular drivers implicated in tumorigenesis. Bioinformatics analyses identified SOX2 as a potential early biomarker, acting with EZH2 as a cooperating oncogenic partner. Functional assays confirmed that silencing of SOX2 or EZH2 significantly impairs tumorigenic properties, as demonstrated by reduced cellular proliferation, migration, and invasiveness, highlighting their essential roles in LUAD progression. Additionally, we employed structure-based virtual screening to identify phytocompounds with potential epigenetic modulatory effects. Curcumin was identified as a non-nucleoside inhibitor of DNA methyltransferase 1 (DNMT1), and when used in combination with the nucleoside DNMT1 inhibitor 5-AZA-2&prime-deoxycytidine (5-AZA-CdR), it effectively downregulated SOX2 expression via modulation of DNA methylation. These findings reveal a critical regulatory link between DNMT1 and SOX2 in LUAD pathogenesis, suggesting that epigenetic reprogramming strategies could offer therapeutic benefit. Given the critical involvement of aberrant signaling pathways in cancer, we further explored the regulatory interplay between SOX2 and the Hedgehog (HH) signaling cascade. Our data demonstrate co-overexpression of SOX2, GLI1 (a key effector of HH signaling), and other pluripotency-associated factors in LUAD cells, establishing the functional relevance of the HH&ndashSOX2 axis in promoting tumor aggressiveness. Interestingly, similar co-activation of HH signaling and SOX2 was observed in androgen-independent prostate cancer, indicating a broader oncogenic role for this axis across multiple tumor types. Collectively, this study delineates a multifaceted oncogenic network involving transcriptional (SOX2), epigenetic (DNMT1/HDAC1/EZH2), and signaling (HH/GLI1) components that converge to drive LUAD progression. These findings underscore the importance of integrative approaches to unravel the epigenetic and signaling architecture governing tumor biology, which may facilitate the development of novel diagnostic and therapeutic strategies for advanced, therapy-resistant malignancies.