National Institute of Technology Rourkela

Departmental Seminar

Seminar Title	: Mechanotransduction Induced Chromatin Dynamics and Cancer Metastasis: Roles of KDM5A and MLL1/2 in Gene Expression and Epithelial to Mesenchymal Transition
Speaker	: Prof. Samir Kumar Patra
Supervisor	: Santosh Kumar #2787
Venue	: LS Seminar Hall
Date and Time	: 15 Apr 2024 (10:30 AM)
Abstract	: Differential expression of genes involved in cellular homeostasis is a collaborative outcome of coordination between molecular signal transduction, transcription factors and DNA and histone modification enzymes (Manna et al., 2023). Evidences are accumulating in favor of mechanotransduction induced chromatin modification and gene expression (Mishra et al., 2024). In response to specific signals, transcription factors and chromatin modifiers jointly dominate the expression/repression of genes. Tumor formation are induced by aberrant activation of developmental signaling and transcription factors, including SOX2, OCT4, NANOG for somatic cell reprogramming (Kar et al., 2023). Cancer progression (metastasis) is associated with the characteristic changes of epithelial cells undergoing transition to mesenchymal cells (EMT). Mixed lineage leukemia family (MLLs) and lysine demethylase family protein, KDM5A are functionally antagonistic enzymes. MLL1/2 enzymes act on histone 3 lysine 4 (H3K4) and trimethylates it to H3K4me3 facilitating gene expression, and H3K4me3 is in general depicted as active chromatin mark. KDM5A demethylates H3K4me3 to H3K4me1, which prevents gene expression. Herein, I shall present that, KDM5A may induce the process of EMT by two ways; in my laboratory, we have deciphered that when bound to epithelial marker, E-cadherin promoter, KDM5A acts as a classical repressor by demethylating H3K4me3, but on mesenchymal markers, it acts as a transcriptional activator Kirtana et al., 2023). Activation of transcription by KDM5A is due to inhibition of the activity of histone deacetylase (HDAC) and enrichment of H3K18ac. Ectopic expression of mutant KDM5A (enzymatic null mutant) implicated that while activating genes, H3K4me3 demethylase activity remain silent. Chromatin immunoprecipitation (ChIP) data implied that there is a co-occupancy of KDM5A with MLLs. We traced about the physical interactions between KDM5A and MLLs, and another component, WDR5, of the COMPASS complex. Our experimental data confirmed that, there is physical interaction between KDM5A, MLLs and WDR5.