National Institute of Technology Rourkela

Departmental Seminar

Seminar Title	: The role of SETD2 in the molecular oncogenesis of glioma through m6A RNA modification
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Venue	: LS Seminar Hall
Date and Time	: 20 Nov 2024 (15:00 hrs)
Abstract	: Gliomas are classified as one of the most lethal cancers owing to their invasive and aggressive nature. Numerous genetic and epigenetic changes have been studied in the development and progression of GBM. Dysregulation of epigenetic function may bring about profound changes in gene expression to facilitate glioma formation and development. SETD2, a key epigenetic regulator is frequently mutated in various cancers; SETD2 regulates m6A mRNA methylation (epitranscriptome) via H3K36 trimethylation. The m6A RNA methylation modification regulates various biological functions like gene regulation, cell self–renewal and maintenance, cell differentiation, invasion, and tumorigenesis. The RNA modifications are executed by a set of complex proteins collectively known as writers, readers and erasers (RNA modifiers). These modifiers work along with the molecular cues laid down by SETD2 via H3K36 trimethylation. The positive correlation between SETD2 expression and m6A RNA modifiers highlights its direct involvement in epitranscriptomics. Glioma, a highly malignant grade IV brain tumor, is characterized by limited therapeutic options and poor clinical outcomes. However, the specific role of SETD2 in glioma and its impact on m6A RNA methylation remain inadequately defined. In this study, we investigated the expression of m6A RNA methylation regulators, the molecular pathways contributing to tumor progression, and the outcomes associated with SETD2-mediated m6A modifications in glioma. Our in vitro analyses demonstrated that knocking down SETD2 in glioma cell lines resulted in reduced oncogenic properties, such as decreased cell proliferation and invasiveness. This effect was accompanied by a global reduction in m6A methylation levels within the transcriptome, which was closely linked to the downregulation of key m6A writers, METTL3 and METTL14. These findings suggest that SETD2 plays a crucial role in maintaining m6A methylation, and its disruption can drive glioma progression through altered epitranscriptomic landscapes, offering new insights into molecular oncogenesis and potential therapeutic targets.