National Institute of Technology Rourkela

Departmental Seminar

Seminar Title	: Lovastatin Suppresses Stemness and Induces Differentiation in Glioblastoma Stem Cells via DNMT1-Mediated Epigenetic Regulation of Caveolin-1.
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Venue	: LS Seminar Hall
Date and Time	: 24 Jan 2025 (10:30 AM)
Abstract	: Glioblastoma (GBM) stem cells exhibit elevated cholesterol biosynthesis and stemness markers, contributing to tumor aggressiveness and resistance to therapy. In this study, we generated GBM spheroids using the hanging drop method and found that cholesterol biosynthetic genes HMGCR, DHCR24, and caveolin-1, as well as stemness markers CD133, CD44, and Pax6, were significantly upregulated in spheroids compared to monolayer cultures of LN229 and U87MG cells. Additionally, increased expression of the TCA cycle gene IDH3A in spheroids indicated a metabolic reliance on mitochondrial respiration. Based on these findings, we hypothesized that elevated cholesterol biosynthesis supports the stemness of GBM cells and that targeting this pathway with lovastatin could disrupt these properties. Lovastatin treatment downregulated HMGCR, DHCR24, and caveolin-1, reduced stemness markers, and increased the differentiation marker S100B, alongside a decrease in IDH3A, suggesting a shift towards differentiation and metabolic exhaustion in glioma spheroids. To further elucidate the mechanism of lovastatin-mediated effects on GBM stemness, we focused on caveolin-1, a key regulator of cellular signaling enriched in spheroids. siRNA-mediated knockdown of caveolin-1 decreased stemness markers CD133, CD44, and Pax6 and increased expression of senescence markers p21 and p53, reinforcing caveolin-1's role in maintaining GBM stemness. Given evidence from the literature that DNMT1 can epigenetically regulate caveolin-1, we observed that DNMT1 expression was elevated in spheroids and further upregulated following lovastatin treatment. Methylation-specific PCR revealed increased promoter methylation of caveolin-1 upon lovastatin exposure, suggesting DNMT1-mediated transcriptional silencing of caveolin-1. In summary, lovastatin impairs GBM stemness through caveolin-1 downregulation mediated by DNMT1, promoting differentiation and metabolic exhaustion of glioma stem cells. These findings provide insights into targeting cholesterol metabolism as a therapeutic approach for GBM.