National Institute of Technology Rourkela

Defence Seminar

Seminar Title	: Prediction of repurposed drug to neutralise the effects of non-coding RNAs and their targets in Glioblastoma oncogenesis: A gene expression and molecular simulation approach
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Venue	: LS Seminar Room (qkq-ijyd-mip)
Date and Time	: 09 May 2024 (09.30 AM)
Abstract	: Glioblastoma multiforme (GBM), a prominent malignant brain tumour, is distinguished by its aggressive behaviour and emergence of resistance to treatments. Despite widespread usage, patients consistently develop resistance to Temozolomide (TMZ), resulting in tumour recurrence. Non-coding RNAs (ncRNAs), such as microRNAs (miRNAs) Piwi-interacting RNAs (piRNAs), and long ncRNAs, have emerged as significant factors in tumorigenesis and cancer drug resistance mechanisms. However, a comprehensive understanding of the role of these ncRNAs in GBM progression and chemoresistance remains elusive. Thus, this study aims to uncover pivotal ncRNAs influencing GBM progression and TMZ resistance. Utilising next-generation sequencing, we analysed the profiles of miRNAs, piRNAs, and genes in GBM cells, followed by various analyses, including target prediction, pathway enrichment, protein-protein interaction, co-expression studies, and qRT-PCR validations to elucidate their potential roles in malignancy. Notably, BRAF emerged as a target of two piRNAs, co-expressed with 19 sole targets of five miRNAs, including CCND1, collectively regulating cell proliferation in cancer. Further analysis indicated upregulated HRH1 and ATXN3 as common targets of both piRNAs and miRNAs, potentially inducing cell proliferation in GBM via G-protein-coupled receptor or Akt signalling pathways by downregulating respective small ncRNAs. Subsequently, we analysed the expression profiles of coding and non-coding RNAs in TMZ-resistant GBM samples compared to sensitive ones. We identified lncRNA-associated ceRNAs potentially regulating target genes involved in cancer pathways through miRNA sponging. Specifically, lncRNAs ARFRP1 and RUSC2 were found to regulate critical target genes associated with signalling pathways linked to TMZ resistance. We then predicted repurposed drugs that might counteract the effects of ncRNAs and enhance TMZ sensitivity in GBM. Molecular docking and simulation studies revealed BMS345541 as a promising candidate, showing superior binding affinity to its target protein FOXG1 with favourable pharmacokinetic properties. Furthermore, BMS345541 targets CCND1, suggesting its potential to enhance treatment outcomes for GBM patients, including those with TMZ resistance.