
Seminar Title	: An integrated study to identify microRNAs and their crosstalk with target genes modulating oncogenesis in Tongue Squamous Cell Carcinoma
Speaker	: Pooja Gupta (Rollno : 5191s1001)
Supervisor	: Prof. Bibekanand Mallick
Venue	: LS Seminar Hall
Date and Time	: 06 Jan 2025 (11.00 AM)
Abstract	: Tongue squamous cell carcinoma (TSCC) poses therapeutic challenges due to an incomplete understanding of molecular players and their crosstalk. This study investigates the molecular mechanisms underlying TSCC progression, focusing on microRNAs (miRNAs) and their crosstalk with other RNA transcripts as targets. Through small RNA sequencing, transcriptome sequencing, and microarray profiling of TSCC cells and tissues, we identified 269 dysregulated miRNAs and 2,094 genes. Target binding, pathway analysis, gene-gene interaction, and qRT-PCR revealed that miR-128-3p, downregulated miRNA, targets six genes, with MAP2K7 emerging as a key oncogene linked to critical cancer pathways, including epithelial-mesenchymal transition (EMT), apoptosis, and MAP kinase/JNK signaling. <i>In vitro</i> assays showed that miR-128-3p overexpression significantly inhibited TSCC cell viability, migration, and clonogenicity while inducing G0/G1 cell cycle arrest and apoptosis. Dual-luciferase assay and western blotting confirmed that miR-128-3p bind to 3'UTR of MAP2K7 and downregulated it at protein level, followed by suppressing JNK phosphorylation and influencing MAP kinase/JNK signaling. Moreover, miR-128-3p reduced the expression of EMT markers such as N-cadherin and MMPs, while simultaneously promoting the expression of E-cadherin. Further investigation showed that combined treatment with miR-128-3p and cisplatin (CIS) enhanced its sensitivity by decreasing ABC transporter expression within the JNK/c-Jun cascade and increasing intracellular CIS accumulation. Thus, miR-128-3p reduces c-Jun and ABC transporter gene expression, potentially decreasing drug efflux and enhancing CIS efficacy. We also identified other miRNAs regulating oncogenesis in TSCC through competing endogenous RNAs (ceRNAs). Integrated expression analysis of genes, lncRNAs, and miRNAs and ceRNA prediction revealed 23 lncRNAs forming networks with 75 miRNAs and 9 mRNAs. Among the lncRNAs, RAMP2-AS1, PWAR5, and LINC01527 emerged as key ceRNA candidates. Through survival analysis and expression validation by qRT-PCR, we hypothesize that high RAMP2-AS1 and PWAR5 expression promote TSCC progression by derepressing TNKS and PTPN11 via miR-1249-5p, miR-214-5p, and miR-4669 sponging, influencing apoptosis, EMT, and Wnt/ β -catenin pathways. Low LINC01527 expression in TSCC possibly fails to sequester miR-182-5p, resulting in GJB2 repression promoting TSCC growth. These findings highlight the MAP2K7/miR-128-3p axis and ceRNAs as critical regulators of TSCC oncogenesis, which lays the groundwork for developing RNA-based targeted therapies to improve patient prognosis and chemosensitivity.