National Institute of Technology Rourkela

Progress Seminar

Seminar Title	: Lipid Raft Disruption and Epigenetic Remodelling: Investigating the Role of EGFR/FAK/ZRF1 Signaling in Oral Cancer Progression
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Venue	: LS Office Room
Date and Time	: 01 May 2025 (10:30 AM)
Abstract	: Mechanical forces may be generated within a cell due to tissue stiffness, cytoskeletal reorganization and the changes in the cell&rsquos physical surroundings. These changes of forces impose a mechanical tension within the intracellular protein network (both cytosolic and nuclear). Mechanosensitive proteins in the lipid raft of plasma membrane discern the physical forces and channel the information to the cell interior. In this study, methyl-&beta-cyclodextrin (MBCyD) treatment disrupted the lipid rafts, leading to actin cytoskeleton disorganization, downregulation of phosphorylated FAK (p-FAK), and reduced EGFR expression in FaDu and SCC9 cells. Inhibition of FAK using PF-573228 phenocopied these effects, confirming FAK&rsquos role in cytoskeletal regulation and executing mechanotransduction signaling. Both MBCyD and FAK inhibition significantly impaired EMT, along with attenuated migratory capacity of those cells. Overexpression of FAK restored EGFR/p-EGFR levels and mesenchymal markers. Mechanistically, we identified ZRF1 as a downstream effector of the EGFR/FAK axis, with its expression diminished upon FAK inhibition or lipid raft disruption and rescued by FAK overexpression. Importantly, FAK overexpression in ZRF1-depleted cells restored ZRF1 levels and EMT marker expression, reinforcing a regulatory loop. Furthermore, both MBCyD and PF-573228 reduced sphere and colony formation capacities, along with stemness marker expression, underscoring the role of EGFR/FAK/ZRF1 signaling in cancer stem cell maintenance. This effect was reversed by FAK overexpression and abrogated by ZRF1 silencing, with partial rescue upon co-expression. Collectively, our findings establish the EGFR/FAK/ZRF1 signaling axis as a critical regulator of EMT, epigenetic modulation, and stemness in oral cancer, offering novel therapeutic avenues for targeting cancer aggressiveness through mechanotransduction interference.