INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Human Cripto-1 (CR-1) is an Oncofetal gene that promotes cell proliferation and differentiation in the fetus, but its aberrant expression in adults leads to aggressive and highly metastatic cancer. Solid tumours are known to have the ability to thrive in a hypoxic microenvironment and frequently develop resistance to multiple drugs. Hypoxia-Inducible Factor-1α (HIF-1α) is a crucial regulator of cellular processes triggered in hypoxic conditions, and Multidrug resistance protein -1(MDR-1) is involved in the emergence of resistance to a large number of drugs. In the present study, we explored the crosstalk between Cripto-1 (CR-1), Hypoxia-Inducible Factor-1α (HIF-1α), and Multidrug resistance protein -1(MDR-1).

To investigate this, we used different cellular models, i.e., Cripto-1 overexpression system, Chemical induction of hypoxia-like condition by using Cobalt chloride treatment, and 3D spheroid model. Our experimental data indicate a possible co-regulation of CR-1, HIF-1α, and MDR-1 in different experimental systems used in the study. We further investigated the proliferation behaviours and drug resistance of cells in the same models. Moreover, we examined the modulation of stem cell markers in our experimental system and observed possible co-regulation of common stemness molecules with the expression of Cripto-1. Further, we observed the modulation of canonical molecular signalling pathways, P-AKT and P-ERK pathways in our experimental system.

As a whole, our observations coming from multiple experiments shows that overexpression and oncogenic function of human Cripto-1 is part of an orchestrated modulation of molecular processes involving several key regulators for the genesis and progression of cancer.