



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI  
SHORT ABSTRACT OF THESIS

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Thesis Title: : Targeting Triple Negative Breast Cancer Using Membrane-Derived Nanocarriers for Potential Therapeutic Applications  
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The current thesis focusses on targeting metastatic triple negative breast cancer via modulation of the tumor microenvironment by targeted delivery of inhibitors using a biologically derived nanosystem. Significant signaling pathways and the drug resistant potentiality of the TNBC cells were primarily targeted via the biologically derived nano-carriers which resulted in efficient suppression of metastatic breast cancer and development of an effective treatment module for targeting TNBC. Firstly, nano-vesicles were synthesised from the cell membranes of cancer cells and were evaluated for its homologous targeting efficiency with further loading of the nano-vesicles with an inhibitor. The use of cell membranes as biological nano-carrier, demonstrated impressive self-homing capabilities, thereby leading to the development of a potential nano-delivery system for cancer therapy *in vivo*, as they can be derived from the patient's own cells. In the subsequent endeavor, exosomes were employed for the modulation of tumor microenvironment and MDR dynamics of metastatic triple negative breast cancer cells. The exosomes from non-invasive breast cancer cells lead to the decrement in the expression of the ABC transporters, thereby making the metastatic TNBC cells more susceptible to chemotherapeutic drugs for effective anti-cancer activities. Taking into consideration, the advantages of the nano-vesicles and exosomes, a hybrid nanosystem was synthesised by fusing the nano-vesicles and exosomes. Significant signaling networks were targeted by loading an HDAC inhibitor into the fused nanosystem in combination with a tyrosine kinase inhibitor. The study showed that the targeted co-therapy resulted in an efficient subduing of metastatic TNBC that not only resulted in apoptosis of the MDA MB-231 cells, but also affected the regulatory pathways at the genetic and proteomic levels in a synergistic manner. Thus, the study showed that targeted co-therapy via the developed biomimetic hybrid nanocarriers played a very substantial role in the site specific delivery of the drugs for a more efficacious outcome. Thus the corroborations of this research might open up new horizons for the curtailment of metastatic TNBC with further validations in *in vivo* system.