INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	Srirupa Bhattacharyya
Roll Number	:	156106023
Programme of Study	:	Ph.D.

Thesis Title: Unfolding the Potential of Transmembrane-TNFα in Cancer Therapeutics

Name of Thesis Supervisor	:	Prof. Siddhartha Sankar Ghosh
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SHORT ABSTRACT

Tumor necrosis factor-alpha (TNFα), is involved in maintaining a plethora of immune responses in the human body. Although the anti-cancer potential of soluble TNFα was discovered more than a century back, its dual nature and tumor-promoting ability pose a major hindrance in its acceptance as an anti-cancer molecule. In contrast, the transmembrane TNFα (tmTNFα), the physiological precursor of soluble TNFα, holds the potential of tumor regression without initiating cell proliferation. In the **Introduction and Review of Literature** section, molecular aspects of soluble TNFα and tmTNFα have been mentioned. In this section, the objectives of the thesis have been framed by exploiting the ligand function of the transmembrane moiety and finally, the salient features of this thesis have been delineated. **Section 2** provides a description of the **materials** and **methods** used for the experiments in the current thesis. **Section 3** elaborates fabrication of a novel therapeutic module by coating chitosan nanoparticle core with engineered macrophage membrane-tethered TNFα. Cell viability assays on cancer cells revealed the innate anti-cell proliferative potential of these membrane coated nanoparticles. Translation of the therapeutic efficacy of the synthesized nanoassembly on tumor spheroids, further substantiated the biological relevance of the membrane-tethered protein. The subsequent endeavor was to develop tmTNFα in its purified form. For this, the full-length tmTNFα, was subcloned and expressed using a bacterial expression vector. The GST tagged tmTNFα was purified to homogeneity, and its structural integrity was assessed. The cell viability assays demonstrated significant antiproliferative effect. The final part of the thesis was to formulate a suitable delivery vehicle for the recombinant protein. This work was aimed to engineer a suitable cargo for stabilization and efficient delivery of functional tmTNFα *in vitro*. The synthesized microcarriers were characterized for the delivery of recombinant tmTNFα. Functionality of the protein-loaded microcarriers was assessed by cell viability studies. The results demonstrated the physical properties of the microparticles, efficient loading of the purified tmTNFα along with retention of its functional integrity and the cell viability assay results elucidated enhanced anti-cell proliferative potential of cargo immobilized tmTNFα. **Conclusion and Future prospects** summarises the key findings of this current thesis. The current work bestows a new lead towards formulating delivery platforms to achieve effective therapeutic efficacy of tmTNFα and provides future scope of testing efficacy of tmTNFα *in vivo* for its translational potential.

Srirupa Bhattacharyya