INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student : Deepanjalee Dutta

Roll Number : 136153007

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Name of Thesis Supervisor(s) : Prof. Siddhartha Sankar Ghosh and Prof. Arun Chattopadhyay

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SHORT ABSTRACT

Multifunctional nanomaterials have been a point of attraction in cancer research due to its breadth of applications in imaging, therapeutics and targeting. Apart from imparting targeted diagnosis and therapy, these systems render the advantages of combinatorial therapeutic regime in alleviation of cancer. Particularly, biopolymer based nanoparticle delivery systems have been developed for anticancer treatments, wound healing and hydrogel based injection modules. They can achieve efficient conjugation, entrapment, absorption and encapsulation of drugs or imaging probes and enable the delivery of the same to the desired regions. In addition, small chemical molecules also have been modified towards development of theranostic agents for enhancing therapeutic potential and cell permeability. Imaging techniques involved in field of theranostic is mostly dependent on various types of contrast agents out of which luminescence probes acquire special attention. Such luminescence based imaging probes can be used to monitor the accumulation of nanomaterials in tissues and to track their multivalent interactions in intracellular domain. This dissertation focusses on biopolymer as well as small molecule based multifunctional nanomaterials in achieving the combined goal of *in vitro* therapy and diagnostics in a single module. The **chapter 1** begins with an insight into the fascinating world of multifunctional nanomaterials. It traces back to the developmental junctures of theranostic nano-medicine and discusses the most recent progresses in the field. Some of the landmark findings have been highlighted to convey the importance of multifunctional nanomaterials in different arenas. **Chapter 2** deals with chitosan biopolymer mediated formation of bimetallic silver nanoparticle based luminescent gold

nanocluster composite nanoparticles for *in vitro* cancer theranostics. Herein, the composite nanoparticles deliver the combinatorial properties of both the metals present in different nanoscale domains and deliver both anticancer therapy and bioimaging of cervical cancer (HeLa) cells. The uptake of the composite nanoparticles was studied by time dependent sample analysis using TEM. The molecular events of cell death have been studied in detail by flow-cytometry based assays. Subsequently, **chapter 3** demonstrates cationic serum albumin based formation of composite nanoparticles embedded with luminescent bimetallic Au-Ag nanoclusters, which were applied for suicide gene therapy in HeLa cells followed by bioimaging. The combination therapy is achieved with cationic albumin based Au–Ag nanoclusters embedded composite nanoparticles loaded with a suicide gene (CD-UPRT). The suicide gene when successfully delivered into cells by the composite nanoparticles initiates a therapeutic response cascade by converting prodrug 5-FC to toxic 5-FU along with its metabolites. Additionally, the Au–Ag nanoclusters owing to their ultrasmall size generate reactive oxygen species, which further trigger apoptosis mediated cell death. Further, luminescence of Au–Ag nanoclusters serves to track the gene delivery into cells. The detailed mechanism of uptake and manner of cell death have been demonstrated to understand the combinatorial therapeutic efficacy of the composite system. In the **chapter 4**, a varied aspect of generation of reactive oxygen species for initiating apoptosis mediated cell death in HeLa cells was explored by implementing photodynamic therapy. Herein, a mucin protein based luminescent gold nanocluster embedded composite nanoparticle has been developed for the delivery of photosensitizer drug methylene blue with subsequent monitoring of drug delivery with the aid of luminescent Au nanoclusters in HeLa cancer cells. The mechanism of cell death and uptake was analysed by flow cytometry as well as confocal microscopy. The **chapter 5** reports phenylboronic acid mediated development of targeted luminescent gold nanoclusters for *in vitro* cancer theranostics. The gold nanocluster probe was applied for *in vitro* targeted bioimaging of HeLa and Hep G2 cancer cells. It successfully demonstrated specific therapeutic effects toward cancer cells as well as multicellular tumor spheroids. They exhibited pronounced effect toward HeLa cells as compared to other cell lines, and a pathway of cell death was established using flow-cytometry-based assays. The targeted phenylboronic acid gold nanoclusters were also applied for specific detection of a biomarker mucin *in vitro*, using a smartphone based device. In **chapter 6,** a rapid and easy method of synthesis of protein based gold nanoclusters have been reported for diagnostic applications. The gold nanoclusters were successfully applied towards protein expression studies of recombinant proteins GST and GST-hGMCSF using a custom developed bench top device.

In brief, this dissertation explores the various forms of cancer theranostic solutions employing multifunctional nanomaterials. Rapid and facile synthetic procedures for multifunctional nanomaterials using biopolymers as well as small molecules were developed. Applications for delivery of metal nanoparticles, suicide gene, photosensitizer as well as smartphone based diagnostics were reported.