ABSTRACT

The most dynamic and diverse class of macromolecules, proteins come armed with an array of opportunities in the field of therapeutics. Their delicate and complex structure is essential to perform multifaceted functions. However, their structure is prone to degradation, which posses a major challenge in harnessing their therapeutic remuneration. Amid numerous formulations, maneuvering nanomaterials provide ample scope for judicious designing of application based nanostructures.

Given the importance of a curative protein in the field of healthcare, the current thesis work focuses on characterizing and evaluating the anti-proliferative efficacy of the two isoforms, PTEN and PTEN-Long, alone and in combination with anti-cancer drugs. The **introduction** section describes in details the role of aberrant signaling in cancer and the panorama of recombinant protein therapy, which is consolidated by presenting literature reports on the subject in the **literature review** section. The **material and methods** section describes in details the materials required and the methodologies of the experimental procedures. The **results and discussion** section begins with the cloning and purification of PTEN and its transcriptional variant PTEN-Long. The cell based studies establishes the anti-proliferative and anti-invasive role of the membrane-permeable recombinant PTEN-Long protein in primary glioblastoma cell line. To investigate the therapeutic benefit of PTEN, silica nanoparticles were successfully employed to mediate stabilization of the GST tagged PTEN protein. Silica nanoparticles mediated cellular delivery resulted in reduced proliferation of drug resistant glioblastoma. Further, amalgamation of delivery and tracking of therapeutically relevant recombinant PTEN on a single platform was made possible by utilizing luminescent silver nanoclusters. The PTEN-nanocluster ensemble was then coated with PEG to formulate spherical nanocomposites. Evaluation of the PTEN-nanocomposite on monolayer culture and spheroid model of U-87 MG and MCF7 demonstrated modulation of cellular signaling culminating into reduced proliferation, opening up promising avenues for PTEN based therapy. Additionally, successful combination therapy of recombinant proteins with small molecule drugs strengthens the foundation for commercial application of the co-therapy strategies in future. The **conclusion and future prospects** section summarizes the findings of the work with potential biomedical application of the recombinant proteins.