Public Abstract

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Title:Cubic and Spherical Nanoparticles for Detection and Therapy of Cancer

Cancer is the leading cause of high mortality rates. Cancer patients require advanced treatment due to lack of early prevention and diagnosis. Moreover, progression of the disease is unpredictable and personalized therapy options are being explored. Existing cancer therapy leads to drug resistance that worsens patient survival rates, and thus disease management is challenging. This necessitates the need to understand the underlying cause, early detection of possible biomarkers, monitor the disease state and develop effective therapeutics. Current innovations in cancer detection and therapy includes use of newer class of smart nanomaterials. These advances in nanoscale materials, due to their unique size, chemical and physical properties, make them ideal for nanomedicinal and nanoelectronic applications. The work performed in this thesis describes the design and the synthesis of cubic and spherical nanoparticles, and their subsequent applications toward energy interactions, biochemical interactions and cellular targeting. Details of receptor mediated endocytic mechanism, targeted capture of circulating tumor cells (CTC), athermal mechanism of controlled release of biomolecules from nanoparticles using femtosecond pulses, and targeted siRNA delivery using nanoparticles have been explained. Mechanistic studies showed that receptor targeting follows a clathrin mediated endocytic pathway. Receptor-targeted nanoparticles showed effective capture of EpCAM-negative CTCs. The cubic shaped nanoparticles were found to enhance the plasmon-photon coupling to efficiently release biomolecules. Spherical nanoparticle mediated siRNA delivery resensitized drug resistant NSCLC by downregulating two important oncogenes, AXL and FN14 as observed by both in vitro and in vivo studies. Additionally, the study highlights drug resensitization following the effective knockdown of AXL using CRISPR based gene editing. Overall, the results demonstrate the application of nanoparticles for advanced diagnostics and therapeutics.