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Development of Self-Assembling Nanoparticles for Drug Delivery Applications

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ABSTRACT

Bladder cancer is the ninth most common cancer in the world, and occurs in nearly four percent of all men. Although many cases are diagnosed as early stage cancer and the tumor can be removed by surgery, reoccurrence rates are high making treatment difficult and thus one of the most expensive cancers. To address this problem, drugs are injected intravesically after tumor removal to kill any residual cancer that may cause reoccurrence. While this was a significant improvement over surgery alone, high toxicity along with short residence times in the bladder limited its effectiveness. To combat these shortcomings, we will use short strands of DNA which cause an immune response to kill residual cancer. Unfortunately DNA is not readily taken up without first neutralizing the negative charge. In this study, nanoparticles were formed by neutralizing the DNA with varying positively charged polymers. Measurements were taken using Dynamic Light Scattering which determines size and dispersity of the nanoparticles. Stability was measured using heparin challenge and was run on agarose gel electrophoresis. After successful formulation of stable particles, a secondary coating of a modified fusion protein is planned to be used to confer enhanced stability as well as targeting. Chemical modification of the fusion protein via EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) coupling, was done along with purification, and characterization by SDS PAGE (Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis), and Mass Spectrometry. Following successful formation of nanoparticles, future studies will be aimed at cytotoxicity and uptake in bladder cancer cells.

KEYWORDS

Nanoparticle, Fusion Protein, Self-assembly