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Introduction

According to the National Cancer Institute, there are several hundred drugs that have been developed with anti-cancer abilities. However, cancer is still the second leading cause of death in the United States according to the CDC. The effectiveness of most anti-cancer drugs is not limited by its potency but instead by its non-targeted delivery and unwanted side effects. Many cancer treatments such as chemotherapy can effectively kill cancer cells, but lack the selectivity and specificity to avoid wreaking havoc on the rest of the body. Thus, gold nanoparticles (AuNP) have been employed in an effort to overcome some of the downsides of current chemotherapy options. AuNPs have the potential ability to heat upon exposure to near infrared irradiation and their nanometer sized dimensions aid in their selective delivery to solid tumors. Using AuNPs as a platform, the ability to selectively deliver two different anti-cancer therapeutics via heat sensitive conjugations was investigated. Two DNA strands of different melting temperatures were developed separately as potential temperature-sensitive tethers for drug attachment to AuNPs. Fluorophores were utilized to tag DNA strands during simulation of drug release and track attachment to the AuNP platform. Single-stranded DNA tethers were successfully conjugated to AuNPs by gold-thiol bond formation using a 5’ thiol DNA modifier, but synthesizing the full AuNP platform proved to be more challenging. After attempting several attachment sequences and methods, there were no visible indications of successful attachment of dsDNA tethers to the AuNP platform. Future work will consist of identifying what is preventing the full dsDNA tethers from attaching or if its attachment is being masked. Finally, efforts will turn to synthesizing AuNPs with both DNA tethers attached which are able to denature independently at different temperatures to achieve a timed and temperature-dependent dual-drug release.

General Structure of AuNP Targeting Platform

DNA Tether Sequences

Two complementary sequences with TYE665 attached at opposite ends were developed in order to investigate the effect of fluorescent quenching. Two complementary sequences with TYE665 attached at opposite ends were developed in order to investigate the effect of fluorescent quenching.

FAM and TYE665 Emission/Excitation Spectra

Conjugation and Hybridization of DNA-AuNPs

Two approaches were implemented to form the DNA-AuNP platform: 1) Complementary thiolated and fluorescent ssDNA strands were hybridized together and then conjugated to the AuNP by a gold-thiol bond; and 2) The thiolated ssDNA strand was conjugated to the AuNP first, followed by hybridization of its complementary fluorescent ssDNA strand.

Conclusions and Ongoing Research

AuNP platforms were successfully synthesized and conjugated with each of the designed dsDNA strands. However, lack of fluorescence on the AuNP platform indicated that either hybridization and conjugation of either fluorescent dsDNA tether was unsuccessful or was being masked by fluorescent quenching. Fluorescence and SERS data suggest the possibility of successful DNA tether attachment at a concentration below the fluorometer detection limit. Further experimentation will be focused on the following:

- Exploration of different DNA tether attachment techniques
- Achieving full AuNP delivery platform assembly with both DNA tethers and stabilizing PEG
- Quantification and analysis of timed temperature-sensitive DNA release
- Loading the AuNP platform with anticancer drugs and optimizing payload delivery in living organisms to increase selectivity and efficacy of cancer treatment

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