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# Development of a Smart Dual Acting Drug Delivery System (SDADDS)

BACKGROUND: The present-day challenge of delivering anti-cancer agents selectively to tumor cells to mitigate systemic toxicity has led to greater focus on drug delivery research using nanoscale carriers. Despite progress in preclinical studies, the therapeutic effects have not lived up to their expectations in the clinical setting. Though promising, these systems typically exploit passive delivery of a single therapeutic to the target tissue, for example, by the encapsulation of drugs in carrier systems followed by drug release under an external trigger. Our project addresses this issue through the design and synthesis of a Smart Dual Acting Drug Delivery System (SDADDS) consisting of monodisperse bifunctional nanocarriers capable of synergistic targeting of multiple drivers of cancer thereby overcoming current limitations to treating cancer. Triple negative breast cancer (TNBC), accounts for 10-15% of all breast cancers. TNBC is a multidriver disease that grows sporadically due to it having no selective actionable dominant target. This has caused no target therapy to be approved, thus making it an excellent model to explore the efficiency of SDADDS.

OBJECTIVES: This study aims to utilize two different modes of cellular targeting synergistically that would not only offer superior therapeutic *selectivity for tumor tissues*, but would also decrease chemotherapeutic toxicity due to *reduced drug dosage*. The SDADDS in theory should both target the overexpressed TAM receptors on tumor cells and deliver the therapeutic through nanomaterials to increase the bioavailability and decrease chemotherapeutic toxicity.

METHODS: The strategy for developing the proposed model is to first start by proving that the polyvalent targeting inhibitors on dendron A are efficiently able to attach to the overexpressed TAM receptors. In addition to efficiently attaching, they must be able to selectively bind to TAM(+) breast cancer cells over and TAM(-). Currently, we are synthesizing a fluorescent dendrimer to be functionalized with the TAM inhibitor for cellular binding and time lapse studies. We performed a two part synthesis, deprotection of the dendron with TFA followed by attachment of FITC dye to the deprotected dendron with TEA.

RESULTS: The fluorescent dendron was synthesized via a two-step process. First, the boc-protected terminal amines were deprotected using TFA and the product was confirmed by $^{1}$H NMR and MALDI-ToF. The deprotected intermediate product was then conjugated with the fluorescent dye, FITC. The reaction was monitored via MALDI-ToF and showed successful quantitative attachment of FITC to both arms of the deprotected dendron. Product purification was attempted using size exclusion but was unsuccessful with no product being isolated.

CONCLUSION:The synthesis of the modified TAM inhibitors is underway and will be attached to dendron A once completed. We are in the process of developing purification methods for the dye conjugated fluorescent dendron which will ultimately be attached to dendron A using click chemistry and subsequently used in cellular binding assays.The long term objective is to make the system customizable so that it can target varying pathways that occur in different cancer type, thus allowing for the creation of personalized treatment for late-stage cancer patients.