ABSTRACT

Statistical figures outline the five-year survival rate for all cancers diagnosed between 1996 and 2002 as 66%, which depicts a marked rise from the 51% that survived in 1975-1977[1]. However, cancer still remains the second leading cause of death in the United States, following heart disease. An American Cancer Society report estimated that in 2007, there will be over 1.4 million new cancer cases and over half a million cancer deaths in the United States[1]. Although significant oncology drug discoveries have been made during the past 30 years, conventional chemotherapeutic agents exhibit poor specificity in reaching the tumor site and are often restricted by toxicity factors. The lack of a uniform biodistribution leads to harmful side-effects to healthy tissues and the need for administration of a larger than necessary drug dosage with a higher repetitive rate so as to elicit a satisfactory pharmacological response.

Wide interest in cancer nanotherapy has led to the development of nanoparticle based "smart drugs" that have not only improved pharmacological and therapeutic properties of anticancer drugs, but also offer a less invasive alternative enhancing the patient's life expectancy and quality of life as well. Dendrimers, due to their unique architecture and macromolecular characteristics are currently used extensively in research of nanoparticles for targeted and controlled drug delivery. The research objective was to design, synthesize and characterize a novel nanoparticle based "PAINT-BRUSH" like multi-hydroxyl capped poly (ethylene glycol) (PEG) conjugate

(Figure 1) using the dendron – bishomotris that may have a potential use in targeted cancer nanotherapy.

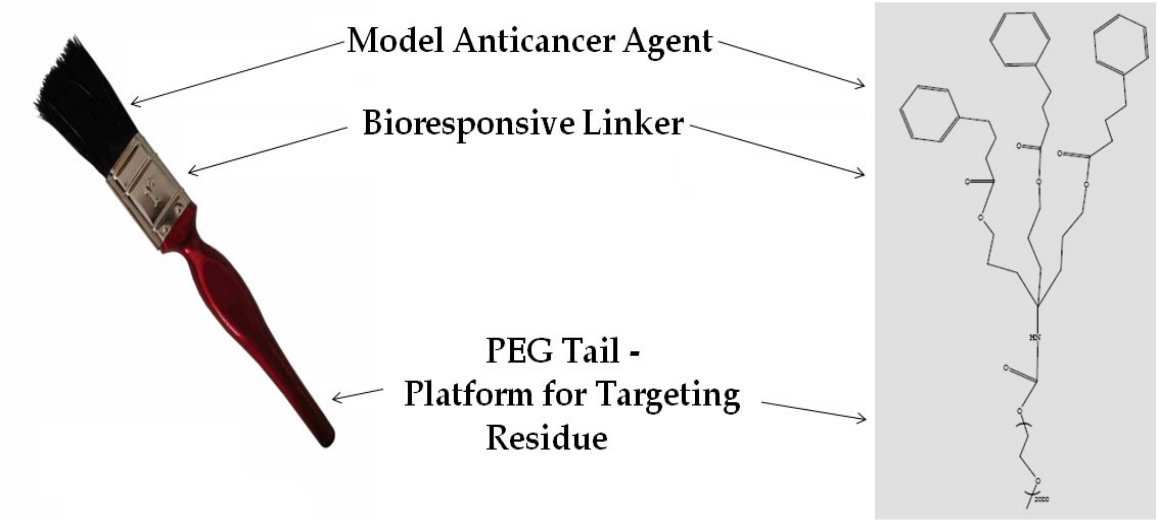
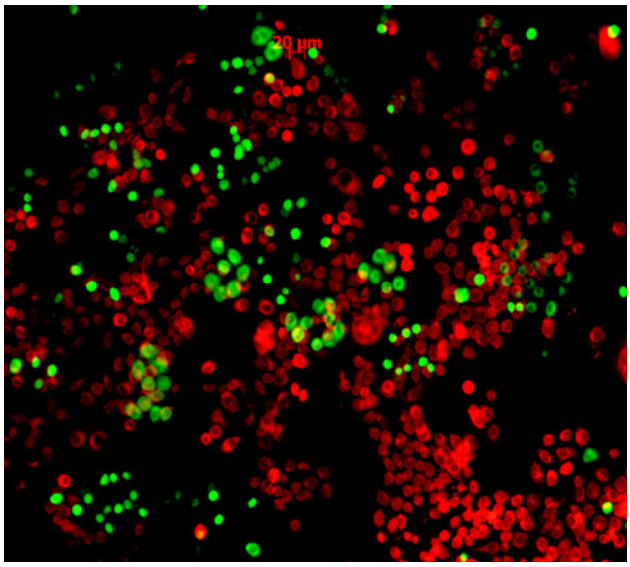
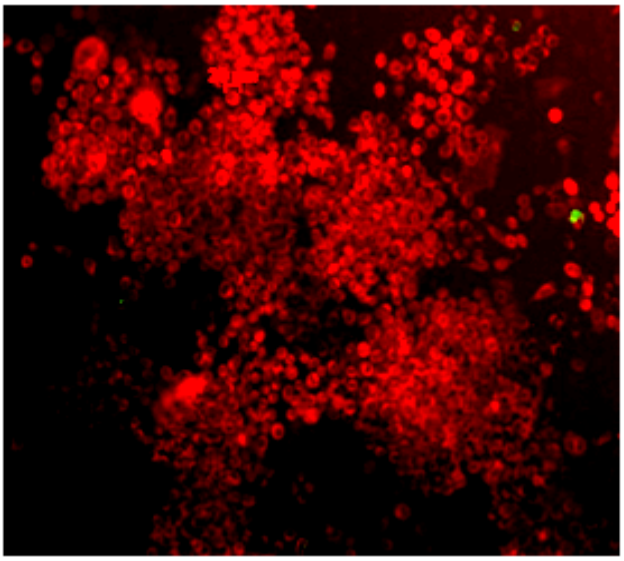


Figure 1) The "PAINT-BRUSH" Conjugate



(A)



(B)

Figure 2) 12 h fluorescence images of HeLa cells treated with BH (1mg/mL) – (A), PEG-BH (1mg/mL) – (B)

Characterization of the conjugates suggested that the synthesis was successful; resulting in the formation of nanoparticle "PAINT-BRUSH" conjugates. It was also found that these conjugates remain stable under normal physiological conditions but would activate in response to an acidic pH (*a characteristic trait of target cancer cells*) so as to release the anticancer drug. The research also presents the relative cell viability of the human epithelial carcinoma cell line (*HeLa S3*) with respect to *in-vitro* characterization of the conjugate to determine its suitability as a drug delivery vector. The study demonstrated that bishomotris was cytotoxic in nature evidently due to the interaction of positively charged amine group with the surface of HeLa cells. It was also evident that surface modification by PEGylation has led to a distinct reduction in toxicity levels thus laying foundations for further research to realize a promising new scaffold for cancer nanotherapy (Figure 2).

Reference:

1) *Cancer Facts and Figures 2007*, American Cancer Society, Atlanta, 2007