Biotinylated PLGA nanoparticles as versatile targeting vehicles for anti-cancer drug delivery

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Introduction: Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. Current Treatments include surgery, radiation therapy, targeted therapy, chemotherapy, gene therapy, blood donations, and transfusions and more. Approximately 11.1 million Americans that were affected by cancer were alive as of January 2005. In 2009, 1,479,350 new cancer cases were diagnosed, of which 194,280 were breast cancer cases. In 2009, 40,610 people died of breast cancer which accounted for 7.22% of all the deaths due to cancer. The goal of this project is to create a nanoparticle that can target breast cancer tumor cells to deliver anti-cancer drugs locally, thus preventing the unwanted side effects from systemic delivery.

Materials: EZ-Link® TFPA-PEG_3-Biotin (Thermo Scientific), Dried Pellets of PLGA (Lakeshore Biomaterials), Bovine Serum Albumin (BSA) (Sigma Aldrich), 488-Streptavidin (Thermo Scientific).

Methods: The biotinylated PLGA was formulated by photoactivating the TFPA biotin and combining with the PLGA. The polymer was then formulated into nanoparticles using a double emulsion method. Particles were collected via centrifugation and dried prior to anaylsis. Particle size and morphology was assessed using SEM. To confirm that the biotin was attached to the PLGA, a biotin quantification kit was used (Fisher Scientific) as well as fluorescent tagging of the nanoparticles with 488-streptavidin. Release studies were performed using BSA as the model protein, at 37^0C in PBS. The BSA concentrations over time (and for encapsulation efficiency) were determined using a micro-BCA assay from Peirce Biotech.

Results: The biotin assay as well as the fluorescent imagaing of the 488-tagged nanoparticles confirms that the biotin is attached to the PLGA and available on the outside of the nanoparticle for avidin/streptavidin to bind. The size and morphology of the nanoparticles was confirmed to remain the same with or without the addition of the biotin using SEM (Shown in Figure 1).

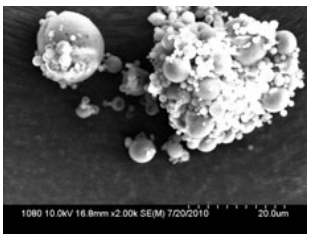

Figure 1. SEM of biotinylated nanoparticles

The encapsulation efficiency of the BSA was increased with the presence of the biotin and the release of the BSA over time was unaffected by the biotin (for up to 28 days, Figure 2).

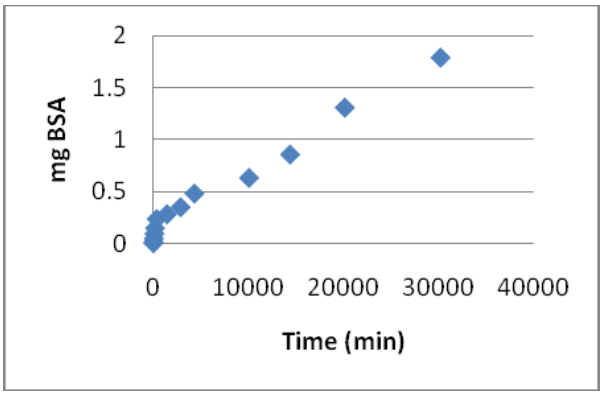

Figure 2: Average BSA release from biotin-PLGA particles over a 28 day period

Conclusion: It was found that biotin can be attached to the PLGA polymer and the protein BSA can be encapsulated with both the PLGA and the biotinylated PLGA. It was also found that the encapsulated BSA protein can be released from both the PLGA and biotinylated PLGA over a 28 day period. The encapsulation of BSA protein and release shows that a breast cancer drug can be encapsulated and released. In future trials, an actual cancer drug will be encapsulated and studied. Encapsulation efficiency must be increased to make the particle a viable drug delivery system with the continuation of release studies of the BSA to determine the full extent of release. The linkage of an avidin and monoclonal antibody to the surface of the optimized PLGA-Biotin particle will be analyzed. An MCF-7 breast cancer cell line will be cultured and the affects of drug release will be cultured.

References:

Kocbek, Petra, Natasa Obermajer, Mateja Cegnar, Janko Kos, and Julijana Kristl. "Targeting Cancer Cells Using PLGA Nanoparticles Surface Modified with Monoclonal Antibody." *Journal of Controlled Release* 120 (2007): 18-26. *Science Direct*. Web.