Antibody-functionalized Carbon Nanotubes in Cancer Therapy

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Executive Summary

As breast cancer is the second leading cancer in women today with a projected 1.6 million victims in the US, we want to develop a treatment to attach monoclonal antibodies to single-walled carbon nanotubes (SWNT) to selectively target breast cancer cells and then use near-infrared (NIR) radiation to eradicate the tumors. Carbon nanotubes were selected as the delivery vehicle due to its small size and unique properties (most notably, its strong adsorption of NIR). This treatment has already shown success on the laboratory scale. As a minimally invasive alternative to traditional breast cancer treatments, such as chemotherapy or surgery, this treatment offers increased cancer cell death and minimal side effects to normal tissues.

We developed mathematical models to predict the initial dosage for intravenous injection, emitting time for the NIR radiation as a function of the tumor volume. Tissue disposition of the drug was also modeled based on the Physiologically-based pharmacokinetics (PBPK) model including the two-pore model and the subcompartment model. Using MathCad software enabled us to find the optimal time to begin irradiation – when the drug concentration in the surrounding cells is at a minimum. The numbers of the SWNTs were determined by generating the random number and the initial dose of SWNTs were calculated based on the tumor contents of the mAb. In order to predict the required time for tumor damage and temperature gradient during NIR irradiation, the finite difference equations were developed and MATLAB software were used to plot the temperature contour to find the death rate of the cancer cells and the core temperature of the tumor.

The maximum required initial dose of the SWNTs to treat the tumor volume of 25 ml is 6×10^{-9} M. The tumor content is 3.02%. The optimal emitting time for the NIR radiation is 15 hours after injecting the initial dose. The required time to kill the tumor is three minutes. The death rate of the tumor after emitting the NIR is about 70%. The interval time between the first NIR radiation and the second in order to prevent the overheating of the tumor is about 10 min if we assume that the tumor volume is reduced by the maximum death rate ratio after the first NIR treatment.

Graphs of the concentrations of mAb-SWNT for the tumors and surrounding tissue were generated based on the PBPK model. The point where the concentration of the mAb-SWNT is at a minimum for the normal cells is the optimal place to begin NIR irradiation.

Based on the simulation of the temperature gradient of the tumor, the damage to the surrounding normal tissue will be minimal due to the small amount of energy emitted from the NIR laser. Assuming that the critical temperature is 57°C, three minutes of irradiation is sufficient to kill most of the tumors while curtailing negative effects to the surrounding tissue. The mAb-SWNT uptake by the normal cells due to its lower expression of HER2 and IGF1R recptors is assumed to be very small compared to the uptake by cancer cells. Additionally, the NIR laser is intended to only target the tumor area, so as to further minimize any damage to adjacent normal cells.

The large-scale production of the drug treatment includes cultivation of the monoclonal antibodies, as well as their conjugation to the SWNTs. The total capital investment was estimated to be $128 million. The total product cost for the drug is $760 per gram.