THE EFFICACY OF MAGNETIC TARGET DRUG DELIVERY TO TREAT SKIN CANCER

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STATEMENT OF PURPOSE: There is high prevalence of skin cancers worldwide and it can be life threatening. Current application of therapeutic agents to treat skin cancer defuses to the rest of the body and does not release the therapeutic agent in a consistent manner; thus many treatments are required with dramatic swings in concentration. A method of preventing therapeutic agent from diffusing to the rest of the body, with a constant release of the therapeutic agent is desirable. This study is to evaluate the feasibility and efficacy of a targeted magnetic drug delivery using a mouse model.

METHODS: A drug delivery system (DDS) was produced by oil in oil emulsion process. The DDS consisted of 500 nm nanospheres with 5 constituents: 34.5% poly(lactic-*co*-glycolic acid) (PLGA), 34.5% Albumin, 20% Fluorouracil (5-Fu), 10% magnetic nanoparticles and 1% 1,6-Diphenyl-1,3,5-hexatriene (DPH). The emulsion process was dispersed at a rate of 10,000 rpms for one and a half hours. The DDS was centrifuged and washed 6 times with hexane to remove any residue oil. The DDS was then vacuum-filtered with 200 nm filter paper. The DDS was allowed to sit in a vacuum for three days to remove any excess solvent.

All the surgical procedures on mice have been approved by the Institutional Animal Care and Use Committee. 20 athymic nude mice were subcutaneously inoculated with squamous cell carcinoma (SCC) cells on the left and right lower back regions, and the tumors were allowed to grow until distinguishable (>5mm in size). The mice were split into 4 groups of 5 mice each (n=5). The 1st group was negative control with no treatment. The 2nd group was given subcutaneous injections of the DDS around the left tumors, and the mice in group 3 received both DDS injections and a local magnet glued to skin of the tumor surface. The 4th group was positive control receiving 5-Fu peri-tumor injections instead of the DDS. The mice were injected four times every 2 days, except one injection that was done 3 days after the previous injection.

To monitor the tumor growth, the tumors were assumed to be in the shape of a rectangle. Thus, the area of the tumor was characterized by measuring the longest width of the tumor and the perpendicular direction from the measured length in the middle of tumor. The two measurements were taken every Monday, Tuesday and Friday for 19 days after the first injection.

RESULTS: The left side tumor growth of the three batches showed exponential growth: no treatment control (R^2 = 0.97), DDS (R^2 = 0.97) and DDS + Magnet (R^2 = 0.92). The best fit for the 5-Fu (R^2 = 0.95) injection is that of a polynomial fit. The three batches showing exponential growths displayed drastically different exponential exponents. The largest of the exponential exponents is the control (0.091x), then the DDS (0.059x). The lowest exponent is of the DDS + Magnet (0.0336x). The 5-Fu positive controls showed a much more erratic growth, and 9 days after the last injection showed a clear exponential growth mimicking that of the control.

The right tumors all displayed exponential growth: control (R^2 = 0.92), DDS (R^2 = 0.95), DDS + Magnet (R^2 = 0.71) and the 5-Fu injection (R^2 = 0.92). The exponential exponent for the growth of the right side tumor displayed similar results: Control (0.085), DDS (0.089), DDS + Magnet (0.0714) and 5-Fu (0.086).

DISCUSSION: Comparing the right tumor to the left tumor it was seen that treatments to the left side tumor had little effect on the right side tumor in all the groups. The left side tumors of control group displayed an exponential growth with a high exponent compared to the other groups, thus the three treatments was successful in reducing the growth of the tumors. From Figure 1, it can be seen that the treatment of the DDS has reduced the growth of the tumor compared to the control. The tumor growth of the DDS + magnet has further reduced the growth. This suggests that magnetic targeting DDS has improved the efficacy of the treatment by preventing diffusion of the DDS throughout the body. The pure 5-Fu injections have shown a similar response to growth rates as the DDS + magnet, however after 9 days from the injections the tumor growth displayed a more exponential growth reflecting that of the control. Further study is currently carrying on for histological assessment and molecular analyses. Nevertheless, the data suggests that DDS + Magnet improve the efficacy of local chemotherapy for skin cancers.

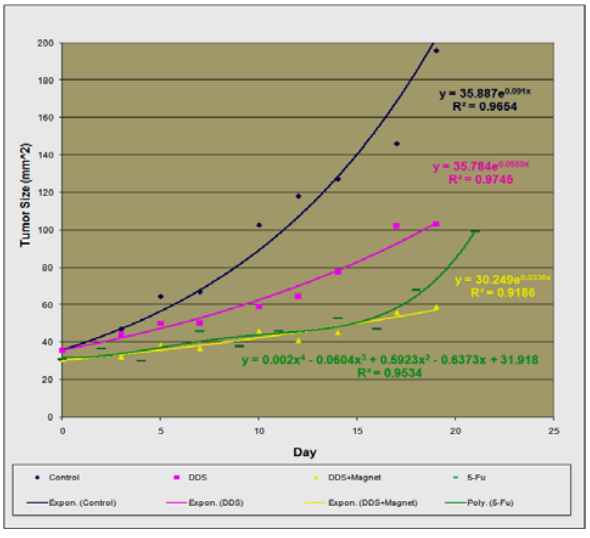

Figure 1: The left side tumor area vs. days after injection among the groups.