A Novel Approach to Targeted Oncologic Therapy - Co-culture Viability of Polymer Prodrug Conjugation to Mesenchymal Stem Cells

UMASS ABSTRACT

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ABSTRACT
<u>Background/Purpose</u>:
Conjugation of polymer prodrugs to tumor homing cells, such as Mesenchymal Stem Cells (MSCs), could provide a vehicle for actively targeted delivery of polymer prodrugs.

<u>Methods</u>:
Human Bone Marrow MSCs were conjugated to either a doxorubicin polymer prodrug or free doxorubicin and were co-cultured with T-cells. Viability was assessed through the use of a Vi-cell counter.

In Vivo Migration Analysis was performed NOD SCID mice implanted with subcutaneous MDA MB-231 breast cancer xenografts. Following tumor establishment, mice were injected via lateral tail vein injection with either saline or polymer loaded MSCs. Five days following stem cell injection, mice were euthanized, tumors were harvested and sections were analyzed using fluorescent microscopy and immuno-histochemical staining for cd105.

<u>Results</u>:
T-cell viability was reduced when co-cultured with MSCs conjugated to free doxorubicin although cells co-cultured with MSCs conjugated to doxorubicin polymer did not exhibit reduced viability. Polymer loaded MSCs displayed intact tumor homing migratory ability *in vivo* (Figure 1).

<u>Conclusion</u>:
MSCs conjugated to doxorubicin released the drug, resulting in reduced neighboring T-cells viability. MSCs loaded with polymer maintained their migratory capacity were able to migrate to tumors *in vivo*. MSCs therefore represent a potential vehicle for targeted

drug delivery. Future work will focus on developing methods for releasing the drug upon successful delivery to the target *in vivo*.