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

Kaitlyn Wong  
*University of Massachusetts Amherst*

Nicholas Panzarino  
*University of Massachusetts Amherst*

Samantha McRae Page  
*University of Massachusetts Amherst*

*See next page for additional authors*

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Presenter Information
Kaitlyn Wong, Nicholas Panzarino, Samantha McRae Page, Richard Arenas, Sallie S. Schneider, and Todd S. Emrick

Comments
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ABSTRACT

Background/Purpose:
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.

Methods:
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.

Results:
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).

Conclusion:
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 therapy.
drug delivery. Future work will focus on developing methods for releasing the drug upon successful delivery to the target \textit{in vivo}.