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Microcatheter Delivery of Neurotherapeutics: Compatibility with Mesenchymal Stem Cells

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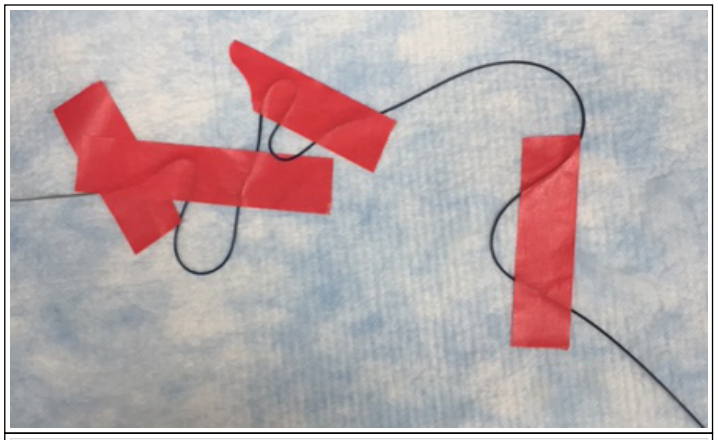
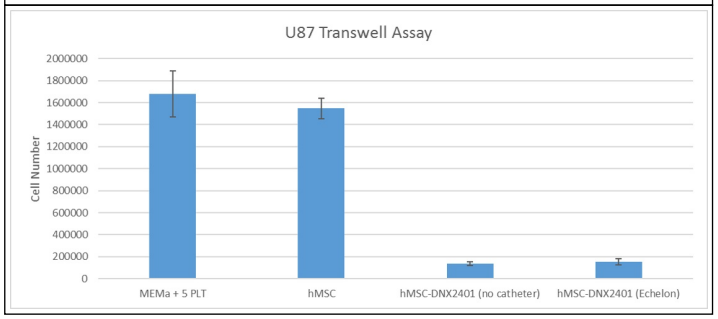
Introduction

Mesenchymal stem cells (MSCs) have been used for therapeutic clinical trials for the treatment of Multiple System Atrophy (MSA) and in ischemic/hemorrhagic stroke. A potentially major application of MSCs would be in the delivery of targeted therapeutic agents for the treatment of brain tumors such as malignant gliomas. One such agent, Delta-24-RGD, a tumor-selective oncolytic adenovirus that targets malignant glioma cells in vitro and in vivo, could be delivered in an MSC carrier, which could in turn be using neuroendovascular techniques. Further, bone marrow human MSCs (BM-hMSC) have been shown to have homing capability toward glioma xenografts. Before such endovascular delivery could be tested in an animal model, we sought to test the catheter compatibility with MSCs in vitro.

Methods

BM-hMSCs were cultured, transfected with Delta-24-RGD, and re-suspended in 1% HSA. Separately, U87 glioma cells were cultured and plated on a Transwell assay. The hMSC-Delta-24 solution was then injected via three different, microcatheters (Marathon, Echelon-14, and Marksman), all widely used neuroendovascular procedures. Cell count and viability was tested versus a baseline control in straight/tortuous configurations and with slow and fast injection. Transwell assay was performed with the injected cells to test the Delta-24-RGD activity against glioma cells.





Results

BM-hMSC cell count prior to infusion was 0.123 x 106 cells/mL, 98.7% viability. There was no significant difference in cell count after infused through any of the three catheters under standard conditions, with a mean concentration of 0.126 x 106 cells/mL and 97.9% (+/- 1.7%) viability. Injection velocity ranged from 1.01 cc/min to 73.17 cc/min, with no significant difference in cell count or viability. There was no significant difference in cell count or viability in the tortuous or straight configurations. Anti-glioma activity was maintained and did not vary significantly between the non-catheter-infused control and through each of the microcatheters.

Conclusions

BM-hMSCs are compatible with a wide variety of commonly used microcatheters. Stem cell viability and viral agent activity do not appear to be affected by catheter configuration or injection velocity. Endovascular stem cell delivery is a promising avenue for neurotherapeutics.

Learning Objectives

1) Describe the current applications of mesenchymal stem cells in neurotherapeutics and their potential in neuro-oncology

2) Describe the concerns with intra-arterial endovascular delivery of neurotherapeutics

3) Understand the wide variety of catheters that can be used in IA delivery of stem cells

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