Endovascular Microcatheter Delivery of Neurotherapeutics in Mesenchymal Stem Cells: Compatibility and Viability

Visish M. Srinivasan MD; Joy Gumin BS; Kevin M Camstra MS; Frederick F. Lang MD; Peter Kan MD, MPH, FAANS, FRCSC

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Introduction

Based on preclinical studies, we have developed a tumor-selective oncolytic adenovirus (Delta-24-RGD) which has been shown to kill malignant gliomas. This virus can be loaded into a bone marrow human mesenchymal stem cell (BM-hMSC) as a tumor-tropic carrying vehicle. In preparation for clinical trials we sought to test the compatibility of several micro catheters with MSCs in vitro. We previously assessed and reported on microcatheter compatibility with the cells and testing injection parameters. For clinical application, we sought to establish hMSC-Delta-24 compatibility with endovascular medications and confirm post-injection tropic activity.

Methods

Delta-24-BM-hMSCs were prepared per our previous protocol. hMSC-Delta -24 cells were mixed with various combinations endovascular medications (heparin, verapamil, and Omnipaque) and assessed for cell count and viability. hMSC-Delta-24 solution was then injected via microcatheter and cells were collected from the distal end. hMSC-Delta-24 that were not passed through the catheter were used as a control. Separately, we took an identically prepared cell solution that had been passed through a microcatheter and injected into the carotid artery of a U87 mouse model. The murine brains

Results

BM-hMSC cell count was 1.12 x x 106 cells/mL (±0.069 x 106) with 98.7% viability prior to infusion. Mean concentration and viability for each medication mixture were: Heparin+Omnipaque, 1.35 x 106 cells/mL (±0.160 x 106) and 95.5%, Heparin+Verapamil, 1.16 x 106 cells/mL (±0.125 x 106), and Heparin+Verapamil+Omnipaque, 1.10 x 106 cells/mL (±0.176 x 106). None of these were significant differences. Cells were found to retain tropic activity to the tumor in the mouse model as identified by GFP staining.

Conclusions

Delta-24-hMSCs retain their tumor-tropic and tumor-lytic functions after microcatheter passage and appear to be compatible with endovascular medications. Endovascular microcatheter delivery of hMSC appears to be viable and practical.

Learning Objectives

1) Understand the background of mesenchymal stem cell use in neurosurgical pathologies

2) Appreciate the challenges and issues associated with endovascular delivery of mesenchymal stem cells

3) Understand the next steps involved in bringing endovascular MSC delivery to a clinical reality

References

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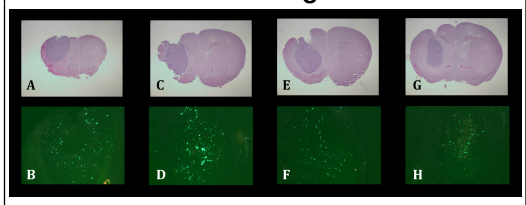
GFP Homing test



A/B, C/D, E/F, and G/H. Corresponding histology of murine brain tissues (axial) by hematoxylin and eosin (H&E) staining, and expression of reporter protein (GFP). The brain was injected with a U87 Glioma xenograft. The Delta-24-hMSCs were delivered via ipsilateral intra-carotid delivery after passing through a microcatheter.