Sustained Delivery of dbcAMP to the Transected Spinal Cord in the Presence of Schwann Cells and Mesenchymal Stem Cells

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Introduction

Re-establishment of functional connections after SCI requires injured axons to grow through the graft, enter normal tissue, find target cells, and establish synapses to complete a functional circuit. This study describes the use of oligo[(polyethylene glycol) fumarate] (OPF) hydrogel scaffolds as vehicles to deliver sustained dibutyryl cyclic adenosine monophosphate (dbcAMP) to the transected spinal cord. dbcAMP was encapsulated in polylactic-coglycolic acid (PLGA) microspheres, which were embedded within the scaffolds architecture.

Materials and Methods

Delivery of dbcAMP to the transected spinal cord was accomplished through incorporation of PLGA microspheres within OPF seven channel scaffolds, equal in diameter to the spinal cord. These channels were loaded with schwann cells or mesenchymal stem cells in a matrigel substrate. One month post transplantation, animals were perfused & spinal cords were transversely sectioned. Analysis included neurofilament axonal staining, vonWillebrand capillary staining and Gomori staining of collagen fibers infiltrating the injury.

Results

Our results showed that encapsulation of dbcAMP in microspheres lead to prolonged release and continued functionality in vitro. These microspheres were then successfully incorporated into OPF scaffolds and implanted in the transected thoracic spinal cord. Sustained delivery of dbcAMP inhibited axonal regeneration in the presence of SCs but rescued MSC-induced inhibition of axonal regeneration. dbcAMP was also shown to reduce capillary formation in the presence of MSCs, which was coupled with significant functional improvements.

Discussion and Conclusions

Our findings demonstrate the feasibility of incorporating PLGA microsphere technology for spinal cord transection studies. It represents a novel sustained delivery mechanism within the transected spinal cord and provides a platform for potential delivery of other therapeutic agents. Biological function of the encapsulated dbcAMP was demonstrated in both in vitro and in vivo environments, confirming the effectiveness of such a delivery platform.

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Disclosures

No conflict of interest exists.