Axonal Regeneration Supported by Schwann Cells and Mesenchymal Stem Cells through Hydrogel Scaffolds in the Transected Rat Spinal Cord

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Introduction

Traumatic spinal cord injury results in complete tissue destruction and loss of neurologic function below the level of the lesion in 40% of patients in Ireland. Tissue engineering, using biodegradable polymer scaffolds loaded with different cell types, offers potential to rebuild neural tissue through the glial scar and to reestablish functional connections. In this study we compare the capacity of Mesenchymal Stem Cells (MSCs), Schwann Cells (SCs) to support axonal regeneration in a thoracic spinal cord transection model in rats over 4 weeks.

Materials and Methods

Multichannel polymer scaffolds were made from positively charged oligo [polyethylene glycol] fumarate (OPF+) hydrogel by mold injection cast over 7 parallel wires of 290 um diameter followed by UV polymerization. MSCs are derived from GFP rats (GFP-rMSC), and SCs from wild type pup sciatic nerve. The cells are fully characterized for surface marker expression and differentiation potential prior to implantation. Rats received cell loaded OPF+ scaffolds into a complete T9 spinal cord transection. Cells were loaded at a density of 50,000 cells per ul of Matrigel, 0.26 ul of culture per scaffold. Animals were sacrificed for analysis at 4 weeks. Neurofilament-stained axons were counted 1/4, 1/2, and 3/4 of the way through the scaffold. Immunohistochemistry was done to determine the cellular constituents of the channel tissue.

Results

Differentiation of GFP-rMSC to adipose lineage, and osteocyte lineage was shown. FACS analysis characterized a homogeneous CD90+ population of GFP-rMSC, and a mixed population of CD73+ cells. No marker expression is seen for Leukocyte (CD45) or Macrophage (CD11b/c) cell types. Functional improvements by BBB scoring were not statistically significant at 4 weeks. Scaffold channels convey tissue cables that extend between cord ends within the soft, translucent hydrogel (below, left). GFP-rMSC remain viable within channels in high numbers at 4 weeks post implantation (right).

Discussion and Conclusions

GFP-rMSCs seeded into OPF+ scaffold channels survive implantation but do not support axonal regeneration compared to Matrigel™ alone and Schwann cell seeded scaffolds. We are now extending these studies to determine if the number of regenerating axons can be increased or rescued using genetically-modified cells. Stable MSC and SC lines secreting neurotrophin-3, bone-derived neurotrophic or glial cell-derived growth factor at physiologic levels have been characterized and implanted in the transected cord within OPF+ scaffolds.

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Table 1. Mean of total axon counts seen at sections ¼, ½, and ¾ the scaffold length. [n=6 rats per group] * p<0.05 compared to Control (Matrigel™ only) and Schwann Cells.