Augmentation of Tendon-Bone Healing with the Utilization of Cell-Based Tissue Engineering in a Rat Supraspinatus Model
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INTRODUCTION: Rotator cuff pathology, a common cause of shoulder pain and disability, accounts for substantial health care costs. Despite advances in surgical management of rotator cuff tears, studies continue to find complications related to failure of tendon to bone healing. Cell-based tissue engineering offers exciting possibilities for improved rotator cuff outcomes through the use of autologous cells to improve tendon to bone healing. The objective of this study is to utilize these cells to amplify healing of a surgical defect in the rat supraspinatus tendon.

METHODS: Work was Institutional Animal Care and Use Committee approved. Soslowsky validated the rat for rotator cuff studies (1). Lewis rats were chosen as the animal model because they are inbred with great limited genetic variability and therefore have minimal potential for immunogenic response to cells transplanted between animals. Cells were harvested from the tendon-to-bone interface of one animal set, and expanded in monolayer. 5-bromo-2-deoxyuridine (BrdU), a synthetic nucleoside that is incorporated into cell DNA, was used to track cells in vivo. 150,000 BrdU-labeled cells were seeded into a 0.5 cm3 collagen sponge (Gelfoam, Upjohn) and implanted with sutures at the site of a critical rotator cuff defect (2). In treatment groups, the tendon was re-apposed to its anatomical insertion with monofilament suture (3) and passed through a bone tunnel created with a hand-powered drill. Experimental design utilized 5 groups of 13-14 week old rats: I, control without surgery; II, surgical defect in rotator cuff; III, surgical defect with suture repair; IV, surgical defect and repair with engrafted Gelfoam (without cells); V, surgical defect and repair with Gelfoam plus cells. Groups of rats were euthanized at 3, 6, or 12 weeks post-operatively. Each group contained 9 animals with 9 shoulders submitted for histology examination (sampling sizes based on sample size calculations). Decalcified, paraffin-embedded specimens were evaluated immunocytochemically and histologically for cellularity, inflammation, vascularity, and collagen disorganization. A semi-quantitative grading scale described by Soslowsky (1) was used to score each of these categories where “0” indicates normal, “1” indicates mild changes, “2” indicates moderate changes, and “3” indicates marked changes.

RESULTS: After three weeks, there was a significant increase in cellularity, inflammation, vascularity, and collagen disorganization in group V (surgical defect, repair with gelfoam and cells) compared to the other treatment groups. We found no major differences in any of these categories at 6 weeks. At 12 weeks, group V had significantly lower histology scores for collagen disorganization compared to the other treatment groups (Figure 1). Additionally, at 12 weeks, there was no difference in collagen disorganization histology scores between group I (control with no surgery) and group V (surgical defect, repair with gelfoam and cells). Masson Trichrome staining comparing these two groups at 12 weeks demonstrated similar patterns of collagen bundle longitudinal alignment (Figure 2). This increased collagen organization at 12 weeks was also seen surrounding the cells on immunocytochemical localization compared to the 3 week specimen (Figure 3).

DISCUSSION: Data presented here further the understanding of the functional capabilities of rotator cuff tendon-bone interface cells and support the utility of such cells in autologous cell-based therapy for rotator cuff injuries. The increased cellularity, inflammation, vascularity, and collagen disorganization at 3 weeks and the improved collagen organization at 12 weeks in the shoulders treated with cells suggest improved healing with autologous cells. Autologous cell-based therapy is a novel approach to improving healing in rotator cuff injuries.

REFERENCES:

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