Tissue Regeneration of Tendon-Bone Junction: Evaluation of the Role of TgfbR2 Expressing Progenitor Cells on Multiphase Resorbable Braided Scaffolds

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Introduction: Tendons and ligaments play an important role in transferring stresses and in maintaining the stability of joints. Tears in the joints have poor healing capacity and the lesions are associated with cartilage degeneration. Therefore, strategies are needed to promote repair and long-term regeneration of such joints.

The ultimate goal of this study is to develop a biodegradable scaffold for tendon-bone junction regeneration. As a first step to achieve this, polylactic acid (PLA) yarns were braided into tubular scaffolds and cultured with unique TGF-β Type II receptor-expressing joint progenitor cells under static conditions. The scaffolds were designed to mimic the natural mice tendon-bone junction in terms of its structure, mechanical and immunochemical properties.

Methods: Two types of PLA yarns were used to prepare the scaffolds. Those with round fibers had a 25μm diameter, while those fibers with a 4 deep grooved (4DG) cross-section had a thickness of 45μm. Three different tubular scaffolds measuring about 2 mm in diameter were braided on a Steeger 16-spindle braiding machine (Model K80/16-2008-SE) to mimic the tendon-bone junction by using these different yarns, changing the braiding angle and inserting an internal core which modulated the wall porosity and the different initial tensile modulus of the bone and tendon regions. The three scaffolds with different structures were: 1) PLA hollow tube using round fibers, 2) PLA hollow tube using grooved and round fibers (grooved fibers promote cell attachment and alignment), and 3) PLA multicomponent tube containing round fibers in the sheath and grooved core fibers inserted within the lumen. After braiding, the scaffolds were scoured, heat set and sterilized in ethylene oxide. The biological and mechanical performance of the three scaffolds were evaluated, including cell viability using an Alamar Blue assay, cell attachment and proliferation using a live/dead assay, laser scanning confocal microscopy (LSCM) and dynamic tensile strength and initial Young's modulus on an Instron mechanical tester.

Results: The Alamar Blue test on the TGF-β Type II receptor-expressing progenitor cells showed that the three scaffolds gave similar cell viability results and were superior to the control sample with no scaffold (Figure 1). The confocal microscope images demonstrated that the TGF-β Type II receptor-expressing progenitor cells were not only viable after 7 days, but their migration was also enhanced by including a central core within the braided structure to serve as a guidance component (Figure 2).

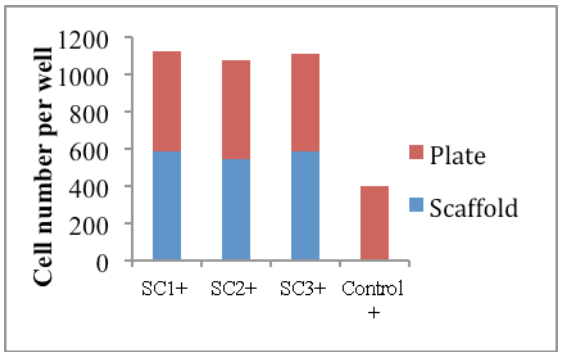

Figure 1: Alamar Blue results at Day 7 showing the relative proliferation of the presorted cells on the 3 prototype scaffolds and the no scaffold control sample.

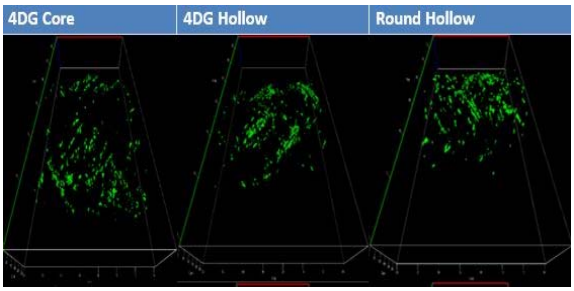

Figure 2: LSCM images of the live/dead (green/red) assay at Day 7 showing more extensive cell migration through the scaffold with the core component (left) compared to the hollow scaffold designs (center and right).

Regarding the tensile properties, the stiffest scaffold had a Young's modulus of 822MPa and contained the 4DG core yarn which mimicked the bone region. The Young's moduli of the round hollow and 4DG hollow PLA scaffolds were 290MPa and 342MPa respectively. This is in comparison to the Young's modulus of human tendon, which is about 250MPa. Thus a combination of these structures can provide a mechanically ideal scaffold for tendon bone junction regeneration.

Conclusion: The results of this study show that all three scaffolds exhibit good viability and cell attachment for the TGF-β Type II receptor-expressing progenitor cells. It also suggests that our approach to culturing these cells on specially designed scaffolds is promising. However, further study is required in order to demonstrate that a tendon/bone junction can be successfully cultured with its own unique interfacial tissue region.

References:

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