REGENERATION OF ROTATOR CUFF TEAR BY USING A POLY-L-LACTIDE (PLLA) CELL FREE

SAFECODF IN A RABBIT MODEL

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Introduction
Various surgical procedures are available for the repair of massive rotator cuff tear, such as musculotendinous transfer and patch grafting using fascias or synthetic materials. Bioabsorbable scaffold has also been used as an optional patch material for rotator cuff regeneration due to its beneficial characteristics, which include a high affinity for living organisms, augmentation by newly formed extracellular matrices after degradation, and no threat of disease transmission. Several studies detailing rotator cuff regeneration using cultured cells, such as mesenchymal stem cells or fibroblasts, have been reported, however these methods require two step surgeries that firstly harvest the stem cells, and then transplant the cells. We hypothesized that certain forms of scaffold can induce stem cells from surrounding tissues, and repair massive rotator cuff tear without requiring harvesting, culture, and transplantation of stem cells. We prepared two types of bioabsorbable scaffolds from synthetic poly-L-lactide (PLLA) fibers and evaluated their use in the repair of massive rotator cuff tears in a rabbit model.

Methods
This investigation was approved by the Animal Research Committee of Kobe University Graduate School of Medicine. General anesthesia was administered to female Japanese white rabbits (2.7-3.5 kg), and two types of the scaffolds were implanted under the back skin in six rabbits. Two types of scaffolds were woven from PLLA fibers; type A scaffold has a smooth surface on both sides, and type B scaffold has a smooth surface on one side and a rough surface on the other side. Each scaffold was superimposed in double layers by keeping the smooth surface outside and the rough surface outside, and both edges of the double layered scaffolds were bonded by thermocompression. Thus, the inside of the type B scaffold was rough to allow the surrounding cells to migrate and remain in it. The scaffolds were evaluated at 3 weeks after surgery histologically and the total DNA amount was measured. Next Type B scaffolds were implanted in the rotator cuff defects. To create a rotator cuff defect, the infraspinatus tendon (5 mm in width and 5 mm in length) was resected from the greater tuberosity, and the mid-substance of the tendon was cut through in a posterosuperior approach. To repair this defect, type B scaffolds were transplanted. Histological examinations were conducted at 4, 8 weeks postoperatively. The specimens were fixed in 4% PFA, decalcified with 0.25 mol/L ethylenediaminetetraacetic acid, and embedded in paraffin wax. Sagittal sections (7 µm thick) were cut and stained with hematoxylin and eosin. Immunostaining of type I and type III collagen were also performed. Serial sections were obtained from each specimen and examined microscopically.

Results
In the back skin scaffolds, some spindle shaped cells adhered to the outer surface of the scaffold in the type A scaffold, however there were few cells inside the scaffold histologically. On the other hand, the type B scaffold had fibrous tissue and many fibroblasts internally (Fig.1). The average total DNA amount was 685ng/mg in the type A scaffold, and 741ng/mg in the type B scaffold. In the rotator cuff repair study, macroscopically, all the defects with the implanted PLLA type B scaffolds were covered with a smooth scar tissue that appeared healed. Microscopically, at 4 weeks postoperatively, the type B scaffold persisted in the regenerated tissue, and the fibroblasts and macrophages were observed around the PLLA fibers. Crimp patterns with some alignment of collagen fibers could be seen at the interface of the bone and the scaffold (Fig. 2). Immunohistochemically, type III collagen was mainly detected in the regenerated fibers of the scaffold.

Discussion
A combination of scaffolds, cells, and growth factors has been used in successful tissue regeneration. Scaffolds which have a single layer structure were used in many studies. We hypothesized that an appropriate scaffold can induce stem cells from the surrounding tissues without using growth factors or cultured cells. We produced two types of tubular scaffold, which fibroblast could migrate into both scaffold. Type B scaffold, which has three layer structures, had more cell migration. Type B scaffold could prevent adhesion on its smooth surface and incorporate surrounding cells internally because of its rough structure. In the rotator cuff repair study, the type B scaffolds could introduce surrounding fibroblasts which include stem cells to the scaffold’s structure and culture within the scaffold. The regenerated tissue in the implanted scaffold showed crimp patterns with some alignment of collagen fibers, however some inflammatory findings were also seen. Thus, this technique might enable tissue engineering of a massive rotator cuff tear via a single surgery, which would involve grafting a rotator cuff tear with a new PLLA bioabsorbable scaffold without the use of cultured cells.

Figure1. 3weeks after implantation under the back skin (A; type A scaffold, B; type B scaffold)

Figure2. 8weeks after implantation to the shoulder

Reference