Transplantation of Rejuvenated Periosteum for Osteochondral Tissue Regeneration

INTRODUCTION
There are many potential autologous cell sources for chondral and osteochondral tissue regeneration. However, the optimal cell source for durable tissue regeneration has yet to be determined. Periosteum, the connective tissue that surrounds bones, contains multipotent mesenchymal stem cells capable of differentiating into chondrocytes, osteoblasts, adipocytes, and skeletal myocytes regardless of age [1]. Periosteum has been used clinically for joint resurfacing with the base of the defect with the cambium layer facing up into the joint. In a distal and spanning the entire width of the patellar groove prior to surgery. An osteochondral transverse defect, measuring 5 mm proximal to distal and spanning the entire width of the patellar groove was created. A rectangular graft of the periosteum corresponding to the size of the osteochondral defect was harvested, inverted, and placed in the base of the defect with the cambium layer facing up into the joint. After surgery rabbits were allowed unrestricted motion for 6 weeks. The rabbits were then sacrificed and the specimens were harvested. The repair sites and corresponding contralateral sites were cut in half longitudinally. Half of the samples were used for biomechanical testing followed by GAG and collagen typing analyses, while the other half from each limb was processed for histology, and scored by blinded observers, using a modified O’Driscoll histological and histochemical grading scale (max. cartilage score = 22; max. bone score = 8; max. total score = 30 [6]). The medial and lateral sides were evenly distributed between the outcome analyses to avoid potential bias.

RESULTS
The TGF-β1-injected periosteum was easier to elevate from the bone and it did not shrink noticeably after elevation, as does untreated periosteum. In addition, the TGF-β1-injected periosteum, was firmer while remaining flexible and was generally easier to handle during surgery. At six weeks post-op, gross analysis demonstrates complete filling of the defects with regenerated tissue in both the TGF-β1-injected and control groups with integration into the surrounding tissue and reformation of the original contours of the patellar groove (Fig. 1). The total histological score for the regenerated bone tissue in the TGF-β1-injected group (5.3 ± 0.27, n=7) was significantly higher (p<0.0001) than the non-injected control group (3.3 ± 0.95, n=7). This observation is also apparent in the histology samples shown in Fig. 1. Notably, all of the specimens from the TGF-β1-injected group had at least partial bone integration into the defect area and integration with the surrounding tissue compared to only 72% infiltration and 79% integration in the controls. Also, while greater than 80% of the specimens from the TGF-β1-injected group had a visible tidemark, only 40% of the samples from the control group had a tidemark present.

Neocartilage formation was observed in both groups (Fig. 1). The cartilage score in the TGF-β1-injected group (14.2 ± 1.8, n=7) was significantly higher (p<0.0001) than the non-injected control group (11.1 ± 2.4, n=7). Integration of the neocartilage was better in the TGF-β1-injected group with all of the specimens at least partially integrated, whereas 57% of the control samples were not integrated with the surrounding cartilage. Also, while surface regularity in 57% of the samples in the TGF-β1-injected group were scored as smooth and intact only 14% of the control samples received this highest score. The total histological score in the TGF-β1-injected group (19.5 ± 1.8, n=7) was also significantly higher (p<0.0001) than in the control group (14.4 ± 2.1, n=7). No significant differences in the equilibrium modulus were found between any of the groups, while GAG content and type II collagen % were significantly higher in the controls compared to the surgical groups (p<0.01 and p<0.05 respectively). It is important to note that the histological scores in both of the tissue regeneration groups were also significantly lower than the contralateral (i.e. intact) controls at 6 weeks post-op (p<0.05).

DISCUSSION
We previously reported that it is possible to rejuvenate periosteum using local TGF-β1 injection [4] and we now demonstrate that rejuvenated periosteum produces improved osteochondral defect repair at six weeks post-op compared to untreated periosteum. As expected, the tissue regeneration process is incomplete at 6 weeks post-op. Additional studies are currently being conducted to examine the outcome of this technique at 6 and 12 months post-op. These forthcoming results will provide insight into the maturation and durability of the regenerated tissue. If this simple approach to periosteal rejuvenation and transplantation can be translated to the clinic, the number of patients who could possibly benefit from the use of periosteum for tissue engineering or regeneration of cartilage would be greatly increased.

REFERENCES

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