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Repair of articular cartilage defect with layered chondrocyte sheets and cultured synovial cells

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ABSTRACT

In this study, we investigate the effects of treatment with layered chondrocyte sheets and synovial cell transplantation. An osteochondral defect was created of 48 Japanese white rabbits. In order to determine the effects of treatment, the following 6 groups were produced: (A) synovial cells (1.8×10^6 cells), (B) layered chondrocyte sheets (1.7×10^6 cells), (C) synovial cells (3.0×10^5 cells) + layered chondrocyte sheets, (D)synovial cells (6.0×10^5 cells) + layered chondrocyte sheets, (E)synovial cells (1.2×10^6 cells) + layered chondrocyte sheets, (F) osteochondral defect. Layered chondrocyte sheets and synovial cells were transplanted, sacrificed four and 12 weeks postoperatively. An incapacitance tester (Linton) was used to find trends in the weight distribution ratio of the damaged limbs after surgery. Sections were stained with Safranin-O. Repair sites were evaluated using ICRS grading system. In groups (A) to (E), the damaged limb weight distribution ratio had improved. The repair tissue stained positively with Safranin-O. Four and 12 weeks after surgery, groups (A) to (E) exhibited significantly higher scores than group (F), and groups (D) and (E) exhibited significantly higher scores than groups (A) and (B). This suggests the efficacy of combining layered chondrocyte sheets with synovial cells.

1. Introduction

Articular cartilage is avascular tissue nourished by synovial fluid. Articular cartilage shows limited capacity for regeneration after degeneration or injury [1],and leads to osteoarthritis ("OA"). As societies age, much attention is being focused on OA prevention and countermeasures. Treatments for osteochondral defects have included to date: micro fracturing [2–4], mosaicplasty [5–7] and endoprosthetic joint replacement. Beginning with the report by Brittberg et al [11] of autologous chondrocyte implantation (ACI), as a result of development in tissue engineering research a variety of cultured cell graft techniques [11–25] have become the subject of further enquiry. Microfracture surgery and drilling are techniques that encourage natural repair by filling osteochondral defects with marrow-derived repair cells. Normally, an osteochondral defect will induce the production of marrow-derived repair cells [8]. Osteochondral defects are generally thought to be ultimately replaced by subchondral bone after infiltration by blood vessels during endochondral ossification of chondrocytes from multipotent, marrow-derived MSC [9,10].Nagai et al. fabricated tissue-engineered cartilage without a scaffold and reported that chondrocyte plates were effective at repairing tissue in animal experiments [21,22]. The usefulness of temperature-responsive culture dishes was reported by Okano et al. [26,27]. Previously, myocardial, corneal and other types of cell sheets have been reported [28–30].

We are continuing to conduct animal experiments with the aim of developing clinical applications for articular cartilage treatment using cell sheets with adhesive properties that were obtained from temperature-responsive culture dishes. Kaneshiro et al. achieved good treatment outcomes by transplantation chondrocyte sheets into partial defect models [31]. Furthermore, Mitani et al. investigated chondrocyte sheets molecular-biologically and immunohistochemically, and examined the chondrocyte repair process [32].

Cartilage repair using synovial cell grafts has been carried out. Hunziker et al have reported synovial cells played an important role in the repair of the cartilage defects [43], and Koga et al have created osteochondral defects in rabbit knee joints and reported good results from grafts of synovium-derived mesenchymal stem cells used in conjunction with periosteum [44]. However, Ando et al investigated repair of articular cartilage using chondrocytes and

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