

Optimized Allogeneic Decellularized Meniscus Scaffold Modified by Collagen - Affinity Stromal Cell-Derived Factor SDF1 α For Meniscus Regeneration: A 6- and 12-Week Animal Study in a Rabbit Model

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INTRODUCTION: Total meniscectomy for treating massive meniscus tears may lead to joint instability, cartilage degeneration, and even progressive osteoarthritis. The meniscal substitution strategies for advancing the reconstruction of meniscus deserve further investigation.

METHODS: We first modified decellularized meniscus scaffold (DMS) with collagen-affinity stromal cell-derived factor (C-SDF1 α) to fabricate a new meniscal graft (DMS-CBD). Secondly, we performed in-vitro studies to evaluate the release dynamics, biocompatibility, and differentiation inducibility (osteogenic, chondrogenic, and tenogenic differentiation) on human bone marrow mesenchymal stem cells (hBMSCs). Then in vivo studies, rabbits that received medial meniscectomy were subjected to a transplantation procedure to implement our meniscal graft. At postoperative week-6 and week-12, the meniscus regeneration outcomes and chondroprotective efficacy of the new meniscal graft were evaluated by macroscopical observation, histology, micromechanics, and immunohistochemistry tests.

RESULTS SECTION: In vitro studies, the optimized DMS-CBD graft showed notable biocompatibility, releasing efficient and chondrogenic inducibility. In vivo studies, the implanted DMS-CBD graft after total meniscectomy promoted the migration of cells and extracellular matrix deposition in transplant, and further facilitated meniscus regeneration and protected articular cartilage from degeneration.

DISCUSSION: Although treated with clinical surgical techniques, total meniscectomy treating massive meniscus tears often leads to joint instability, cartilage degeneration, or even progressive osteoarthritis. Considering the demands to fully mimic the anisotropic microstructure of native meniscus that artificial synthetic materials were difficult to meet, the meniscal substitution strategies for advancing the reconstruction of meniscus deserve further investigation. In our study, we presented a new meniscal graft by modifying decellularized meniscus scaffold (DMS) with collagen-affinity stromal cell-derived factor (C-SDF1 α). The optimized decellularized meniscus graft was found to be an ideal meniscus substitution, which was not studied before.

SIGNIFICANCE/CLINICAL RELEVANCE: (1-2 sentences): Allogeneic decellularized meniscus scaffold modified by collagen - affinity SDF1 α could promote whole meniscus regeneration and prevent articular cartilage from degeneration, which may serve as a potential meniscal substitution for clinical meniscectomy.

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IMAGES AND TABLES:

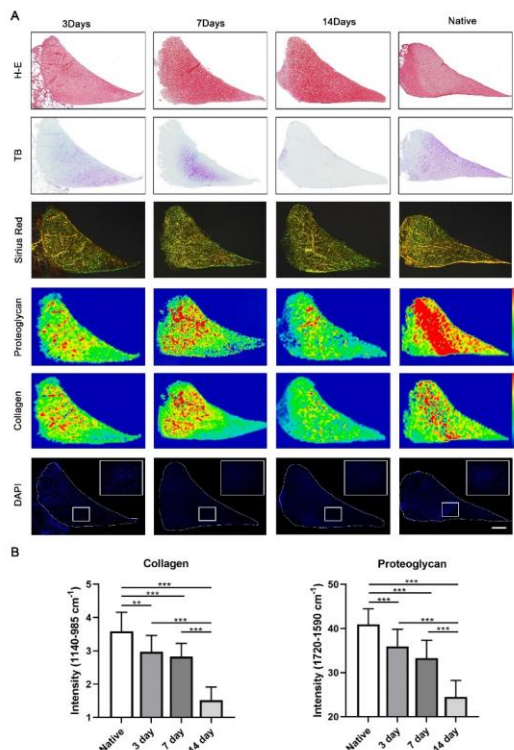


Figure 1. 7 days of decellularization could effectively remove meniscal cells and satisfactorily retained most ECM contents. (A) H&E and DAPI staining of the decellularized meniscus to reveal the overall structure change and residual cells with different decellularizing time points. (B) Toluidine Blue (TB) and Sirius Red (SR) staining show the preservation of meniscal proteoglycan and collagen left after different time groups. (C and D) SR-FTIR

mappings including proteoglycan and collagen distribution, of native or decellularized scaffolds in different time groups. Semi-quantitative analysis of proteoglycan (C) and collagen (D) contents of native or acellular scaffolds Scale bar: 100 μm . ** $P < 0.01$, *** $P < 0.001$.

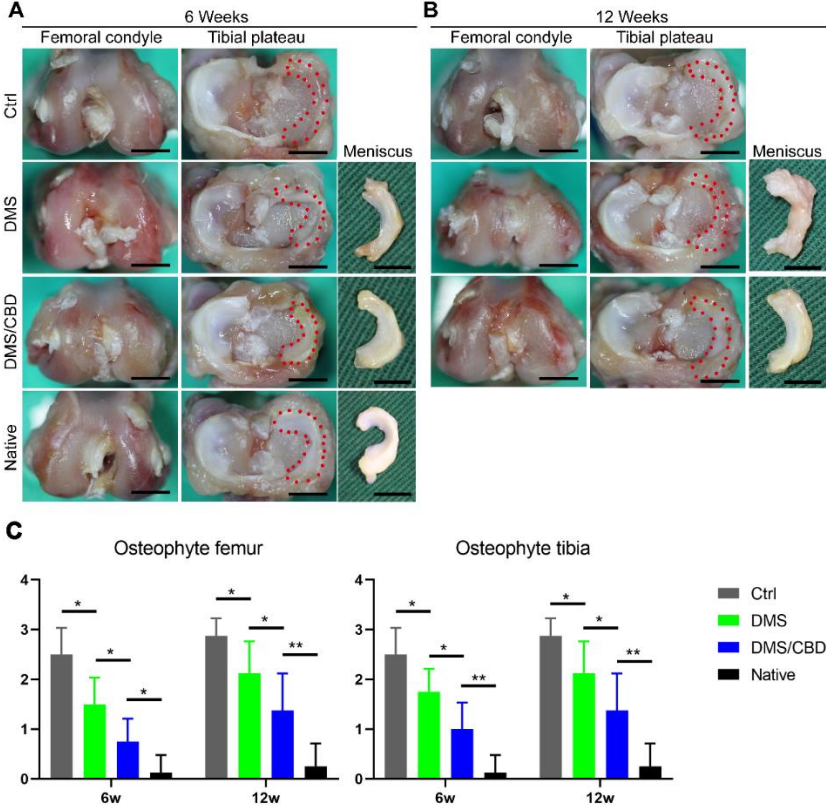


Figure 2. Macroscopical Evaluation of Implanted Grafts and Joint Cartilage Degeneration. Gross observation of tibial plateau, femur condyles, and meniscus at (A) 6 weeks and (B) 12 weeks after meniscal graft transplantation. (C) Osteophyte grading in the medial femur and tibia. Scale bar: 10 mm. * $P < 0.05$, ** $P < 0.01$

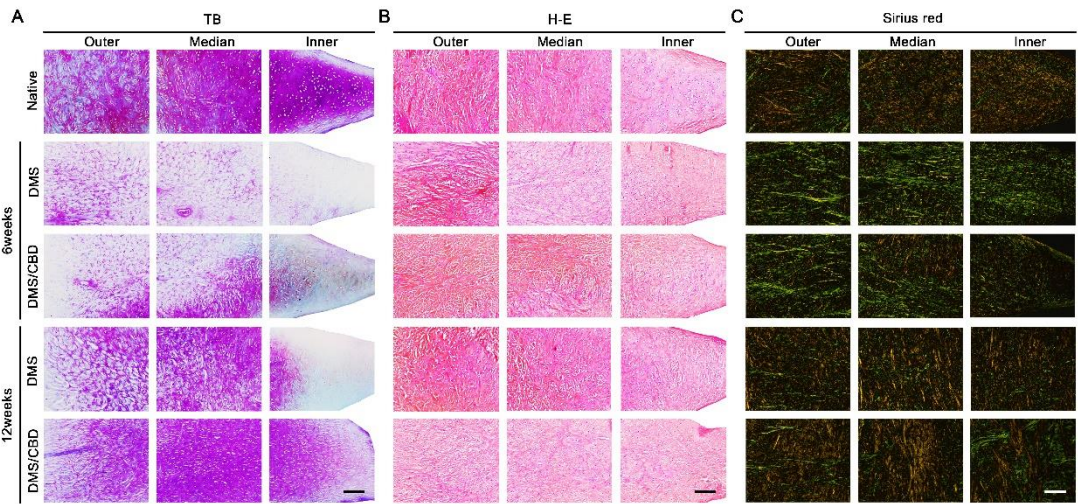


Figure 3. Histological Evaluation of Meniscal Graft Regeneration. Histological analysis of native meniscus and meniscal graft at postoperative weeks 6 and 12, including (A) toluidine blue/ fast green (TB&FG), (B) H&E, and (C) Sirius Red. Scale bar: 200 μm .