Combination of PLGA/fibrin gel composite with MSCs and PEO-PLL/plasmid-TGF-β1 for cartilage repair

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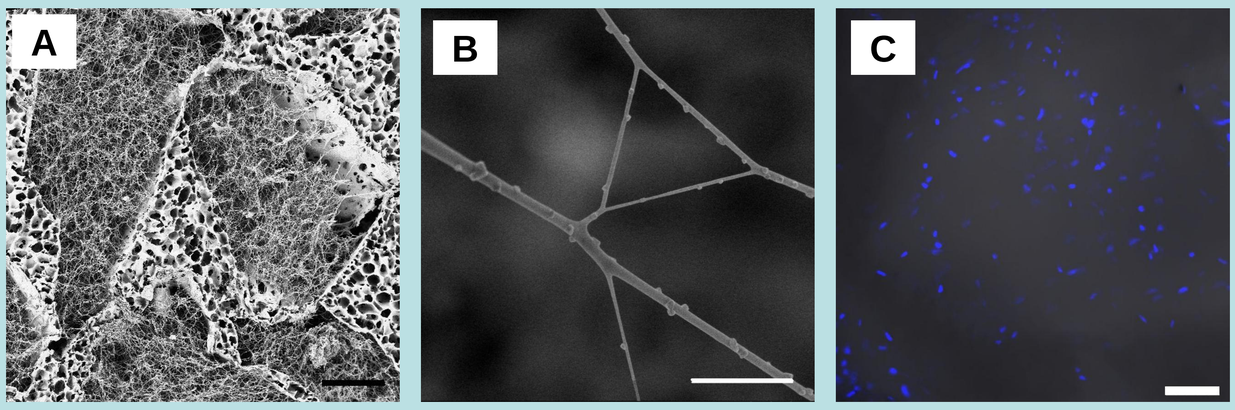
Introduction

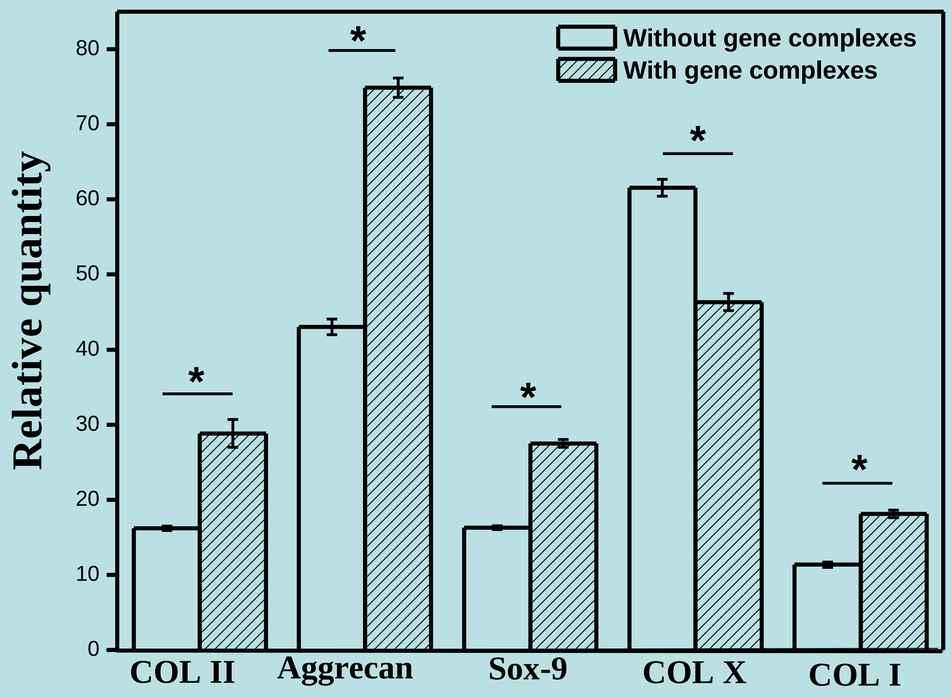
It is well known that damaged cartilage tissue is lack of self-healing ability. To overcome the dissatisfaction with current treantments outcomes, strategies following regenerative medicine concepts have been involved in the repair of cartilage for decades. Owing to their chondrogenesis potential and convenient manipulation, MSCs therapies are being studied intensively[1]. In this study a hybrid scaffold - PLGA/fibrin gel - was adopted to deliver MSCs into osteochondral defects in rabbit model. TGF-β1 plasmid was co-delivered for in situ production of TGF-β1 protein which was believed capable of promoting chondrogenesis of stem cells. Block copolymer PEO-PLL was employed to ensure effective transportation and transfection of plasmid DNA.

Constitution of the system



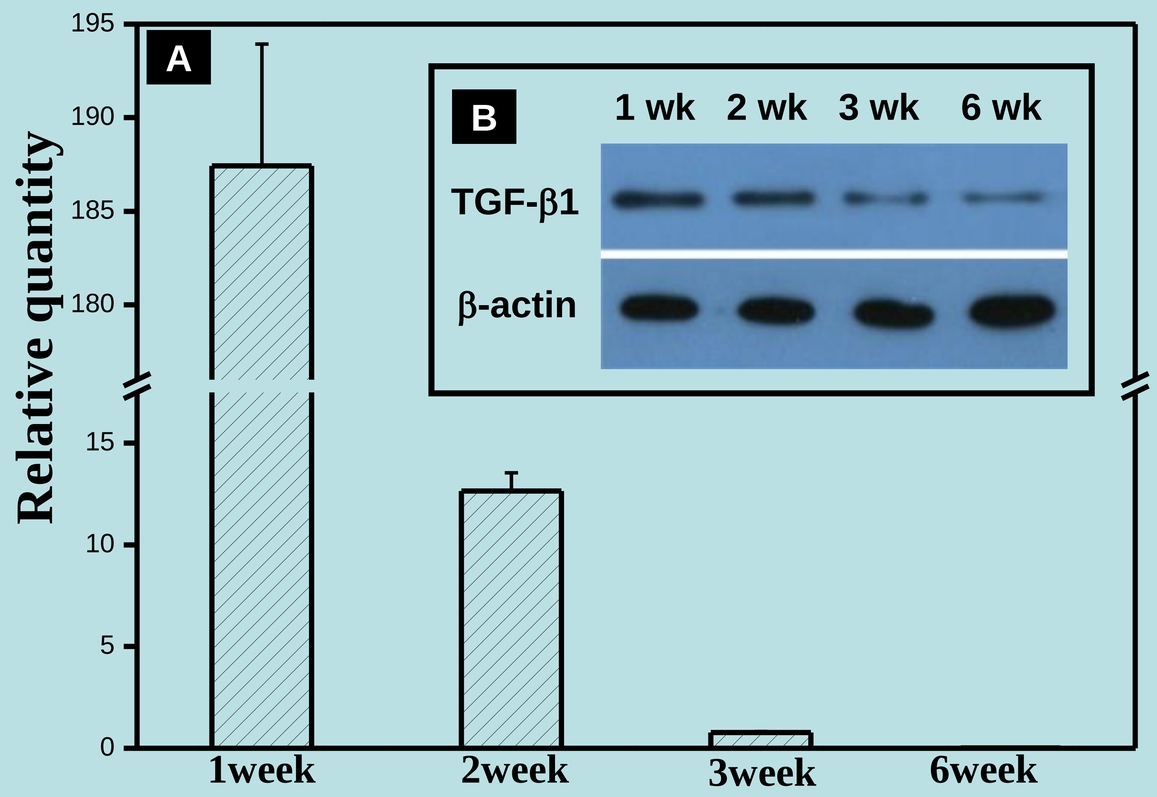
MSCs, PEO-PLL/plasmid-TGF-β1 complexes were mixed with fibrinogen solution, after which this mixture was introduced into PLGA sponges. Gelation was accomplished in thrombin to form the PLGA/fibrin gel composite loaded with gene complexes and cells. Nanofiber networks (Figure. A) with attached complexes particles (Figure. B) served as the support for MSCs which distributed evenly throughout the matrix (Figure. C).

In vitro differentiation



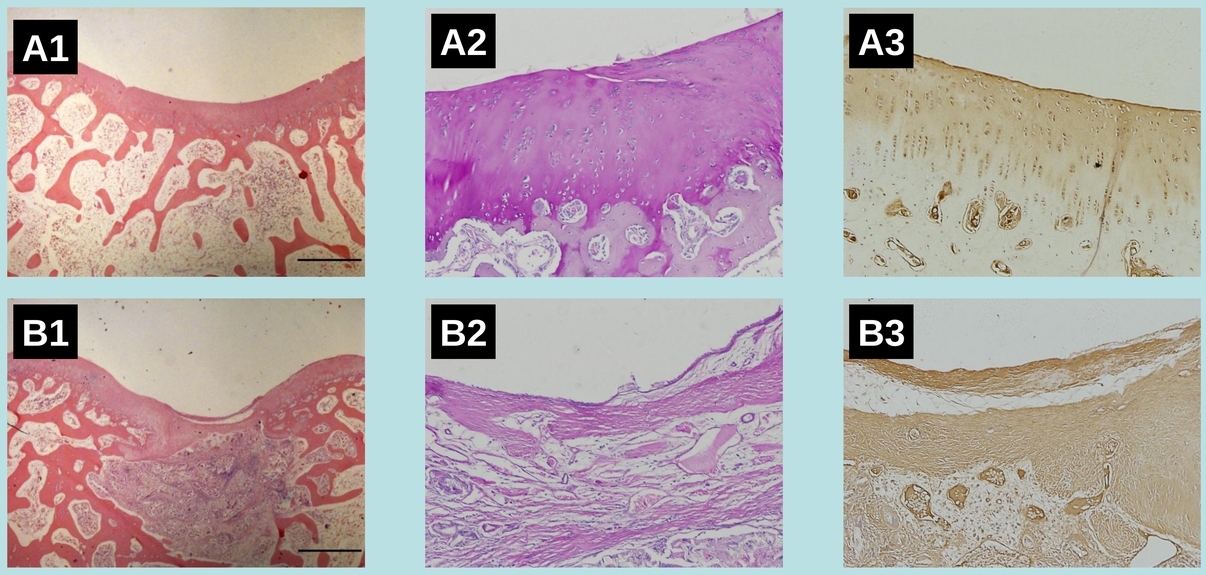
After 21 days culture in vitro, chondrocyte-marker gene expressions of MSCs were analyzed by qRT-PCR. mRNA levels of those marker genes were significantly elevated by the addition of gene complexes suggesting the chondrogenesis of MSCs.

In vivo TGF-β1 production



Variation of TGF-β1 expression with time in the osteochondral defects was monitored by PCR (Figure. A) and western blotting (Figure. B). Both results showed the decline of the target along with time.

Repair outcomes at 12 weeks



At 12 weeks postoperatively, tissues were retrieved for histological examination. HE staining of sections (Figure. A1) repaired by PLGA/fibrin gel/MSCs/(PEO-PLL/plasmid- TGF-β1 complexes) showed a well integrated neo-tissue which had similar color, thickness, and cell morphology with host cartilage. Accumulation of GAGs and COL II in the neo-tissue was indicted by PAS (A2) and immunohistochemistry (A3), respectively.

Conclusion

PLGA/fibrin gel composites were utilized to deliver MSCs and PEO-PLL/plasmid- TGF-β1 complexes into the osteochondral defects. This system was proved to be able to promote chondrogenesis in vitro and contribute to the cartilage repair in vivo.

[1] Wang W, Li B, Li Y, Jiang Y, Ouyang H, Gao C. Biomaterials 2010; 31(23): 5953-65.

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