3D Bioprinting Novel Graphene Oxide Scaffold for improving Human Bone Marrow Mesenchymal Stem Cell Chondrogenic Differentiation

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Introduction

Articular cartilage repair and regeneration are a challenging problem worldwide due to the extremely weak inherent regenerative capacity of the tissue. Currently, the gold standard surgical procedures for treating chondral lesions are autologous cartilage transplantation or autologous chondrocyte implantation, etc. However, this approach is still not perfect due to limited resources of cartilage tissue. The goal of our study is to fabricate 3D graphene oxide (GO)-doped gelatin–based cartilage scaffold with hierarchical structures via our novel table-top stereolithography-based printer, and then investigate chondrogenic differentiation of human bone marrow mesenchymal stem cells (MSCs) in our designed scaffolds.

Overview and characterization

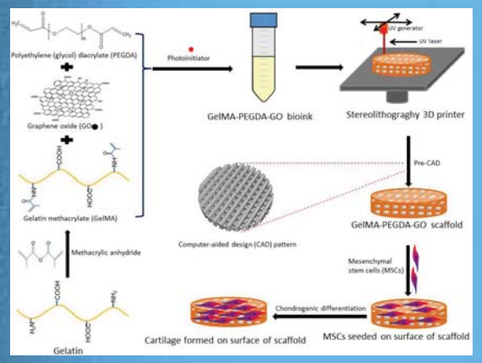

Figure 1. Schematic diagram of the research

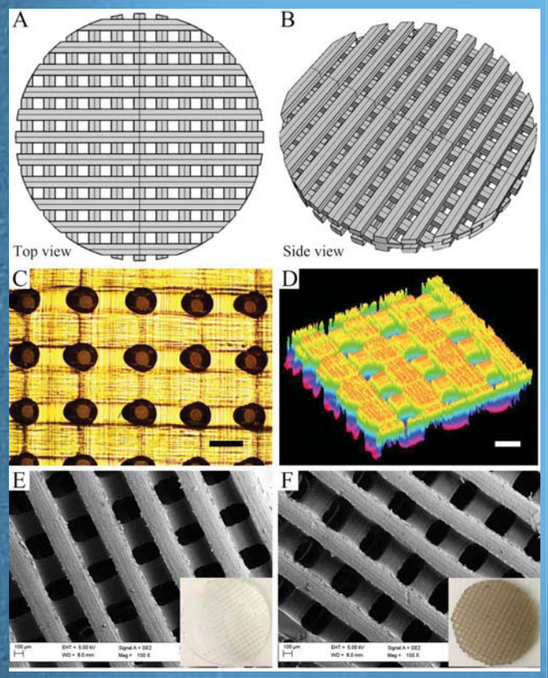

Figure 2. (A-B) CAD models of the 3D scaffold. (C) Microscope image, (D) surface plot, (E) SEM images of GelMA-PEGDA scaffold without GO and (F) with GO (0.1 mg/mL) . Scale bar= 200 μm in (C-D). The inset images are photographs of the corresponding scaffolds.

Cell proliferation

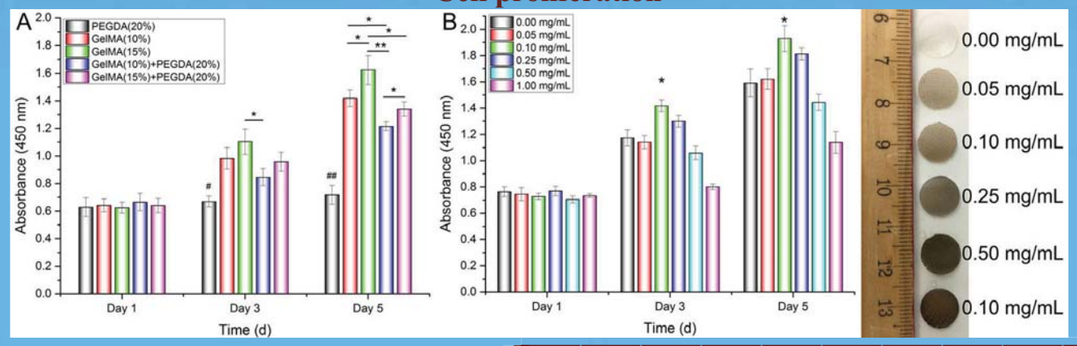

Figure 3. (A) Proliferation of MSCs cultured on 3D printed scaffolds with different components for 5 days. Data are mean ± standard error of the mean, n = 8. *p < 0.05, and **p < 0.01; #p < 0.05 and ##p < 0.01 when compared to others groups at respective days. (B) Proliferation of MSCs cultured on GelMA-PEGDA scaffolds incorporated different concentrations of GO in 5 days. The photographs are the corresponding scaffolds. Data are mean ± standard error of the mean, n = 8. *p < 0.05; when compared to others groups at respective days.

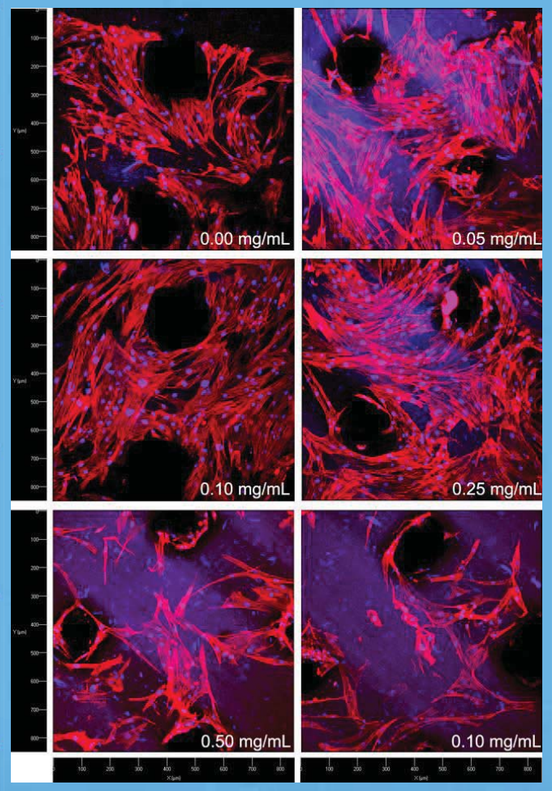

Figure 4. Confocal microscopy images of MSC proliferation on GelMA-PEGDA scaffolds incorporated different concentrations of GO in 5 days, respectively. The cytoskeleton and cell nuclei were stained by Texas Red®-X phalloidin (red) and DAPI (blue), respectively.

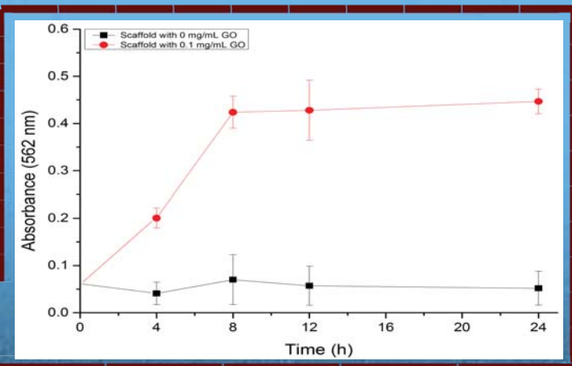

Figure 5. BSA adsorption profiles on GelMA-PEGDA scaffolds without and with GO (0.1 mg/mL) at different time, respectively. Data are mean ± standard error of the mean, n = 8.

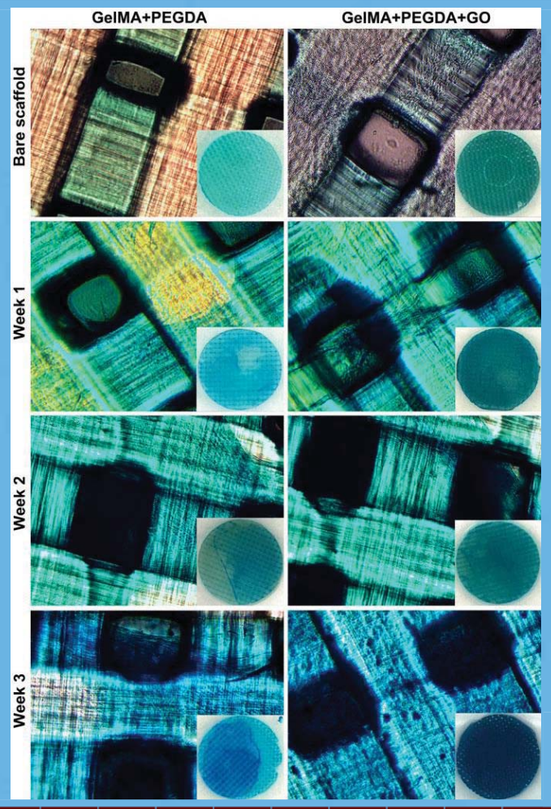

Figure 6. Alcian Blue staining images of MSC chondrogenic differentiation on GelMA-PEGDA scaffolds without and with GO in 3 weeks.

Chondrogenetic differentiation

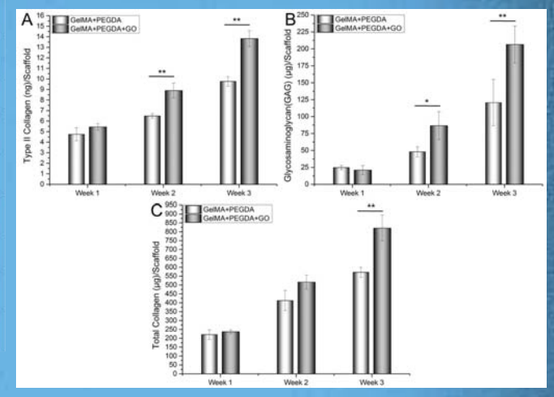

Figure 7. (A) Collagen II, (B) GAG and (C) total collagen secretion of MSCs in GelMA-PEGDA scaffolds without and with GO in 3 weeks. Data are mean ± standard error of the mean, n = 8. *p < 0.05 and **p < 0.01.

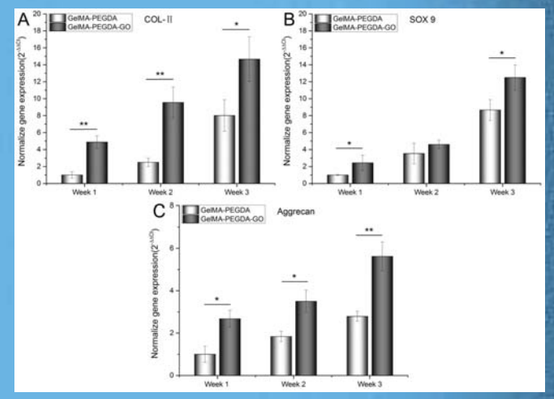

Figure 8. Chondrogenic gene expressions (Col-II, SOX 9 and Aggrecan) of MSCs in GelMA-PEGDA scaffolds without and with GO in 3 weeks. Data are mean ± standard error of the mean, n = 6. *p < 0.05 and **p < 0.01.

Conclusion

A customizable 3D printed GO-GelMA-PEGDA scaffold with hierarchical structure greatly promoted the GAG, total protein and collagen levels after GO induced chondrogenic differentiation of MSCs. In particular, the most significant improvement in chondrogenic gene expression of type II Collagen, SOX-9 and Aggrecan were observed on the GO-GelMA-PEGDA 3D scaffold. This study demonstrated that customizable 3D printed GO-GelMA-PEGDA scaffolds are excellent candidates for promoting chondrogenic differentiation of MSCs, thus promising for future cartilage regenerative medicine applications.

Acknowledgments

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