Porogen-induced Surface Modification of Nano-fibrous Poly(L-lactic acid) Scaffolds for Bone Tissue Engineering

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Introduction

Scaffolds that mimic extracellular matrix (ECM) have received considerable attention for tissue regeneration in recent years because they may provide optimal physiological environment for cells. Collagen-like nano-fibrous poly(L-lactic acid) (NF-PLLA) matrices have been fabricated using a novel thermally induced phase separation technique in our group. The nano-fibrous scaffolds have been shown to selectively enhance protein adsorption and promote osteoblastic cell adhesion. Here we further hypothesize that the incorporation of gelatin onto the surface of NF-PLLA scaffolds can mimic both the nano-fibrous structure and chemical composition of collagen, and this biomimetic scaffold may provide a better environment for cell function. In this study, a novel one-step process was developed to fabricate surface-modified NF-PLLA scaffolds. Gelatin molecules were entrapped onto the NF-PLLA scaffold surface during the phase separation process. The gelatin-modified NF-PLLA scaffolds were characterized and examined for cell adhesion and proliferation.

Methods

Gelatin spheres with smooth surface were prepared by non-surfactant emulsification, solvent extraction, and freeze-drying. A three-dimensional, NF-PLLA scaffold was then fabricated by using gelatin spheres as porogen. Gelatin molecules were immobilized onto the NF-PLLA scaffold surface during the phase separation process. The surface-modified NF-PLLA scaffolds were characterized by ATR-FTIR and XPS measurements.

Results and Discussion

In this one-step process, gelatin spheres acted as both porogen and surface-modification agent. As porogen, gelatin spheres controlled the pore size and shape of the scaffold. Collagen-like nano-fibrous structure was observed on the pore walls as a result of the desired phase separation. As a surface-modification agent, some gelatin molecules from gelatin spheres were entrapped onto the surface of the scaffold during the phase separation process. ATR-FTIR spectroscopy analysis indicated the existence of gelatin molecules on the surface of the scaffold (Figure 1). The appearance of nitrogen peak on the XPS spectra also demonstrated the success of immobilizing gelatin molecules on the NF-PLLA surface. The amount of gelatin on the scaffold surface increased with the ratio of solvent mixture of gelatin solution. The compressive modulus of scaffold prepared with gelatin spheres was more than 2 times higher than that prepared with the same size range of irregular gelatin particles.

The surface modification significantly improved initial cell adhesion and proliferation over 2-week culture. Cell numbers were significantly higher on the surface-modified scaffold than on the control 2 weeks after cell seeding (Figure 2). SEM images indicated that cells spread on the gelatin-entrapped scaffolds in contrast to spherical or spindle morphology on the control 1 day after cell seeding. Furthermore, more matrix secretion was observed on the surface-modified scaffolds than on the control after 2 weeks of in vitro cultivation.

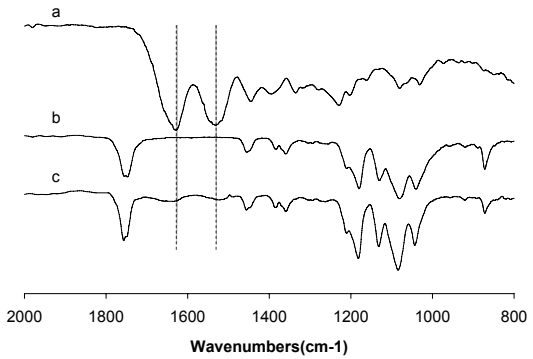

Figure 1. ATR-FTIR spectra of gelatin-modified NF-PLLA. (a) gelatin; (b) NF-PLLA virgin; (c) gelatin-modified NF-PLLA. The surface-modified NF-PLLA was rinsed in water at 40°C for 12 h.

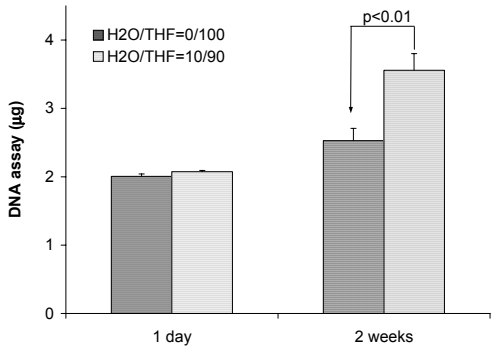

Figure 2. The attachment and proliferation of osteoblasts cultured on NF-PLLA scaffolds and surface-modified NF-PLLA scaffolds. 5×10^5 cells were seeded onto each scaffold.

Conclusions

This biomimetic approach provides a simple, one-step process to fabricate surface-modified NF-PLLA scaffold and has showed desired properties for bone tissue engineering.

References

[1] Ma, P.X. *Materials Today.* 7:30-40, (2004)
[2] Liu X., and Ma, P.X. *Ann Biomed Eng. 32*:477-486, (2004)