Effect of topological structure of electrospun substrates on cell proliferation and morphology

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The topological structure of the substrate is of critical importance in tissue-engineered scaffolds. It has great effects not only on cell attachment and proliferation, but also on cell migration and differentiation. Studies on electrospun substrates have thus far focused on using non-beaded nanofibers because it has been assumed that they mimic the nature of the extracellular matrix (ECM) and improve cell growth, adhesion and proliferation [1]. In this study, the effect of electrospun substrates with various topological structures on fibroblast proliferation and morphology was investigated.

Beaded nanofibers (BN), less-beaded nanofibers (LBN), and non-beaded nanofibers (NBN) were fabricated by electrospinning poly(lactic-co-glycolic acid) (PLGA) at 10 wt.%, 15 wt.%, and 20 wt.%, respectively. As shown in Fig. 1A, B, and C, various topological structures are exhibited. MTT demonstrated that NBN had significantly improved cell proliferation at day 1, day 3, and day 7. The ECM expression of fibroblasts on NBN was increased as compared to that on BN and LBN. The morphology of fibroblasts on NBN was much better than that on BN and LBN as well (Fig. 1c). NBN with nanotopological structure might provide more topographical signals and cues to improve cell growth and the expression of ECM [2]. This work demonstrates that topological structures have great effects on cell growth and proliferation. Cell attachment, proliferation, migration and even differentiation can be controlled by manipulating the topological structure of the substrate.

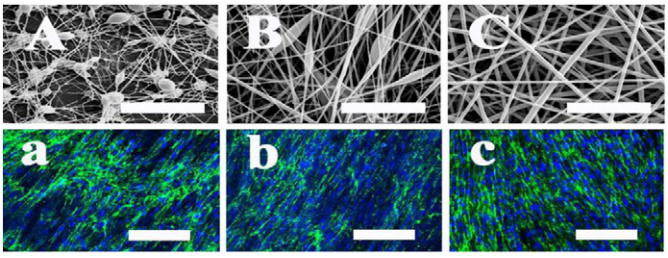

Fig. 1. SEM images of electrospun 10 wt.% (A), 15 wt.% (B), and 20 wt.% (C) PLGA nanofibers (bar scales: 10 μm). Confocal microscopic images of fibroblast on 10 wt.% (a), 15 wt.% (b), and 20 wt.% (c) PLGA (bar scales: 100 μm).

Keywords: Cell–biomaterial interactions, poly(lactide-co-glycolide), Electrospinning, Nanofibers

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Angiogenesis stimulated by adhesion peptide modified alginates, a mechanistic study

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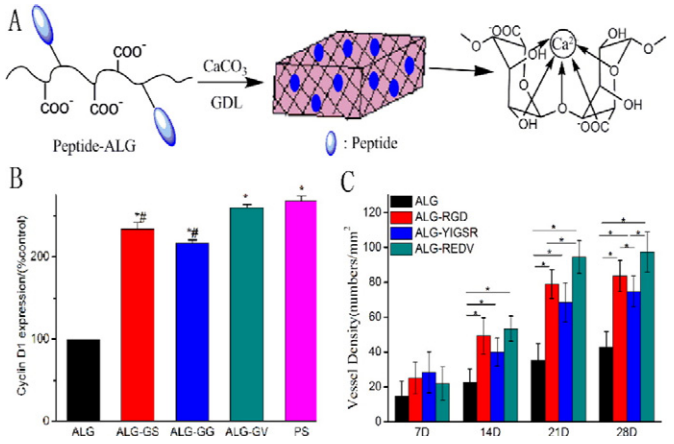
The supply of enough oxygen and nutrients to cells deep within the tissue is still a major obstacle to prepare successful scaffolds for thick tissue engineering. So, the optimal approach to induce and maintain vascularity within a biomaterial substrate should be identified in detail. Polymer hydrogels can closely mimic the hydrous environment and the nature of ECM when bioactive molecules such as the adhesive peptide RGD are introduced. These modified hydrogels are widely studied in tissue engineering to promote angiogenesis [1]. However, RGD can also interact with integrin $\alpha_v\beta_3$ on the surface of platelets, which increases the risk of blood coagulation. Therefore, the discovery of new bioactive molecules for promoting angiogenesis, instead of RGD, is very important.

In this work, another two adhesive peptides, YIGSR and REDV were selected to modify sodium alginate for preparing bioactive materials (YIGSR-ALG and REDV-ALG) (Scheme 1). The effects of the two peptide-ALGs on HUVEC adhesion, migration and proliferation were studied by cell assay and protein expression. The promotion of angiogenesis by the peptide-ALG hydrogels was evaluated *in vivo*. The result shows that REDV-ALG has the strongest effect on HUVEC proliferation, and the ELISA results reveal that the cells cultured on the REDV-ALG expressed the most cyclin D1 (2.6 fold verses ALG), which plays a key role in the cell proliferation. The *in vivo* angiogenesis results demonstrate that both peptides containing hydrogels effectively enhance the angiogenesis of the scaffolds, especially the REDV containing scaffold (83.7 vessels/mm^2 after implantation for 3 weeks). Due to the the fact that REDV-ALG shows the best effects on the HUVEC proliferation *in vitro* and angiogenesis *in vivo*, it has a good potential to be used for scaffolds in tissue engineering.



Scheme 1. (A) Schematic illustration of hydrogel formation (B) Cyclin D1 expression of HUVEC cultured on peptide-ALG surfaces (*P < 0.5 versus ALG, #P < 0.5 versus REDV-ALG, n = 3) (C) The average blood vessel density within different scaffolds after implantation for 1–4 weeks (*P < 0.5, n = 3).

Keywords: Angiogenesis, Sodium alginate hydrogel, REDV, Tissue engineering

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