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Electrospun fibrous scaffolds with continuous gradations in mineral contents and biological cues for manipulating cellular behaviors

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ABSTRACT

Challenges remain in the generation of heterogeneous tissues and the repairing of interfacial tissue between soft and hard tissues. The development of tissue engineering scaffolds with gradients in composition, structure, mechanical and chemical properties is essential to modulate cellular behaviors in a graded way and potentially support the growth of functionally graded tissues. Integrated with the three-dimensional (3-D) nanofibrous skeletal structure of native extracellular matrix, electrospun fibers with gradients in amino groups were generated in the current study through an aminolysis process by using a microinfusion pump. Gelatin grafts were constructed to create fibrous scaffolds with gradients in hydroxyapatite (HA) contents, crystal size and mechanical properties through in situ mineralization. Plasmid DNA (pDNA) was included during the mineralization process, and gradations in pDNA loading contents were created on fibrous scaffolds on the basis of HA gradients. Obvious gradients in cell density, osteoblastic differentiation and collagen deposition were demonstrated along the long axis of fibrous mats after cell seeding. Gradients in the amount of pDNA released and the expression of target proteins were indicated on the fibrous mats, which offered a temporally and spatially controlled delivery of growth factors in scaffolds. The creation of gradient futures on 3-D fibrous scaffolds may provide physical, chemical and biological cues and result in efficient regeneration of tissues with spatial distributions of the cell proliferation, differentiation, and matrix secretion.

1. Introduction

Native tissues usually indicate complex spatial distributions of the composition, structure, and functionality, and many tissues are anatomically merged into neighboring tissues. often via a transit tissue. For example, the bone of diaphysis consists of cancellous bone covered with a shell of cortical bone. The microstructure of the bone tissue is a porous composite comprising mainly calcium phosphate and collagen, and the cortical and cancellous bones are a gradient system with respect to their structure and composition [1]. Another example is the bone–cartilage interface, where the concentrations and the orientations of the calcium phosphate mineral particles vary in the direction normal to the axis of the interface [2]. Meanwhile, the graded variations of extracellular matrix (ECM) and cell concentration at the tissue interface are nature's solution to match specific requirements of various tissues for optimal functions [3]. For example, the natural tendon-to-bone attachment relies on a gradient in structure and composition that translates into a spatial variation of mechanical stiffness [4].

Most of the tissue engineering scaffolds reported in the literature are porous solids of uniform composition and pore structure. For these reasons, generation of scaffolds with gradient in composition, structure, mechanical and chemical properties can modulate cellular behavior in a graded way and potentially be useful to support the growth of a heterogeneous tissue or an interface tissue. Scaffolds with gradients in pore size and porosity provided control over cell migration, which is restricted in the direction of decreasing pore sizes [5], or facilitated in the direction of increasing porosity [6]. Sherwood et al. indicated that scaffolds with gradients in material composition had less delamination at the transition region between tissues compared with biphasic designs [7]. DeLong et al. covalently immobilized growth factor gradient in photopolymerized hydrogels, which allowed guidance of engineered tissue formation and provided the opportunity to study detailed mechanisms of chemotaxis in vitro [8].

Many attempts have been made to construct gradients in material compositions and properties on various substrates. For example, microfluidic devices, lithography and computerized

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