Chapter 20
Mineralized Nanofibers for Bone Tissue Engineering

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ABSTRACT

The limitation of orthopedic fractures and large bone defects treatments has brought the focus on fabricating bone grafts that could enhance ostegenesis and vascularization in-vitro. Developing biomimetic materials such as mineralized nanofibers that can provide three-dimensional templates of the natural bone extracellular-matrix is one of the most promising alternative for bone regeneration. Understanding the interactions between the structure of the scaffolds and cells and therefore the control cellular pathways are critical for developing functional bone grafts. In order to enhance bone regeneration, the engineered scaffold needs to mimic the characteristics of composite bone ECM. This chapter reviews the fabrication of and fabrication techniques for fabricating biomimetic bone tissue engineering scaffolds. In addition, the chapter covers design criteria for developing the scaffolds and examples of enhanced osteogenic differentiation outcomes by fabricating biomimetic scaffolds.

INTRODUCTION

Bone defects, are currently being treated by using auto- and allograft procedures. These techniques have limitations in their clinical usage such as immune response, donor-site morbidity, and lack of availability (Damien & Parsons, 1991; Kretlow, Young, Klouda, Wong, & Mikos, 2009; Scheller, Krebsbach, & Kohn, 2009). Therefore, the interest in tissue engineering applications for bone graft procedures has been growing rapidly. Typical tissue engineering models for bone graft applications require a cell supporting scaffold in order to maintain a 3-dimensional substrate for cells to function during the formation of bone tissue (Burg, Porter, & Kellam, 2000; Frohlich et al., 2008). Among the 6 million fractures occurring every year in the United States, there are more than 0.5 million skeletal injuries that require bone graft procedures (Greenwald, Boden, & Barrack, 2010).

Biomimetic bone tissue engineering scaffolds need to meet several criteria in order to be a successful candidate for bone graft procedures. An ideal biomimetic scaffold should completely integrate with

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the surrounding bone tissue, exhibit sufficient mechanical strength, and function as a three dimensional framework for osteoprogenitor cells to fabricate bone matrix. In order to provide adequate 3D structure and allow for full integration into the site of the bone defect, a biomimetic scaffold should fulfill the following requirements:

1. It should mimic the physical and chemical composition of the natural bone tissue,
2. It should be biocompatible,
3. It should be porous to allow bone tissue organization and vascular formation,
4. It should have appropriate surface chemistry and mechanical strength characteristics to support cellular attachment, proliferation, and differentiation, and
5. It should degrade simultaneously with the newly grown bone tissue (Karageorgiou & Kaplan, 2005; (Stevens, Yang, MohandaS, Stucker, & Nguyen, 2008).

Bone tissue is a composite matrix mainly composed of approximately 70 wt% inorganic crystals (mainly hydroxyapatite) (NF) and 30 wt% of organic matrix (mainly Type I collagen) (Rho, Kuhn-Spearing, & Zioupos, 1998). Mineralization of collagen NF is a well-regulated process mediated by many extracellular matrix proteins, such as bone sialoprotein (BSP) and osteonectin (ON). These non-collagenous proteins contain a large amount of glutamic acid (Glu) residues, which act as frameworks for depositing apatite crystals on collagen fibers in natural bone (Fujisawa, Wada, Nodasaka, & Kuboki, 1996; Sarvestani, He, & Jabbari, 2008, 2007). The apatite crystals provide mechanical strength for bone formation (Fantner et al., 2004), while the collagen fibers provide structural support and locations for cell adhesion and regulate cell functions such as cell adhesion, proliferation, differentiation, and mineralization (Beachley & Wen, 2010). The simple fractures in bone tissue can be treated by standard conservative or surgical therapy. However, in some cases, such as extended bone defects due to trauma or cancerous resection, bone grafting procedures are being performed with engineered biomimetic materials (Farhadi et al., 2006; Logeart-Avramoglou, Anagnostou, Bizios, & Petite, 2005). Consequently, biomimetic bone scaffolds aim to mimic the hydroxyapatite/collagen nanofibrous structure observed in natural bone; in this chapter the structure of the materials and the fabrication techniques used to develop mineralized nanofibrous biomimetic scaffolds for bone tissue engineering will be reviewed.

FABRICATION OF NANOFIBERS BASED SCAFFOLDS FOR BONE TISSUE ENGINEERING

In order to mimic the 3D structure of natural bone, biomimetic scaffolds have to be fabricated using different methodologies to facilitate the cell distribution and to guide their growth into three-dimensional space. Collagen nanofibers in natural bone tissue have a fibrous structure with a diameter range of 50 nm to 500 nm (Elsdale & Bard, 1972; Ma, 2008). The ideal biomimetic scaffold fabrication techniques should allow for the accurate duplication of the nanofibrous structure of collagen in natural bone. Several methods have been developed to fabricate nanofibers, such as self-assembly (Hong, Legge, Zhang, & Chen, 2003), phase separation (Ma & Zhang, 1999), and electrospinning (Fang, Wang, Niu, Lin, & Wang, 2010; (Xue et al., 2009).