Chapter 21
Self-Assembled Biomimetic Scaffolds for Bone Tissue Engineering

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ABSTRACT

Cranial, maxillofacial, and oral fractures, as well as large bone defects, are currently being treated by auto- and allograft procedures. These techniques have limitations such as immune response, donor-site morbidity, and lack of availability. Therefore, the interest in tissue engineering applications as replacement for bone graft has been growing rapidly. Typical bone tissue engineering models require a cell-supporting scaffold in order to maintain a 3-dimensional substrate mimicking in vivo extracellular matrix for cells to attach, proliferate and function during the formation of bone tissue. Combining the understanding of molecular and structural biology with materials engineering and design will enable new strategies for developing biological tissue constructs with clinical relevance. Self-assembled biomimetic scaffolds are especially suitable as they provide spatial and temporal regulation. Specifically, self-assembling peptides capable of in situ gelation serve as attractive candidates for minimally invasive injectable therapies in bone tissue engineering applications.

INTRODUCTION

Among the six million fractures occurring every year annually, there are more than 1 million skeletal injuries that require bone graft procedures in EU and US (Greenwald et al., 2010; Salgado, Coutinho, & Reis, 2004a). Bone defects that were caused by primary and metastatic tumors or skeletal trauma, are currently being treated by using auto- and allograft procedures (Frohlich et al., 2008; Karaman et

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al., 2013). Autografts have been one of the most preferred bone grafts because autografts include the patient's own cells, extracellular matrix (ECM) and osteoinductive agents required for bone regeneration (I et al., 1999; Rose & Oreffo, 2002; Walmsley et al., 2015). However, these techniques have limitations in their clinical usage such as immune response, donor-site morbidity, and lack of availability (Kretlow, Young, Klouda, Wong, & Mikos, 2009; Scheller, Krebsbach, & Kohn, 2009). Therefore, the interests in tissue engineering applications for bone graft procedures have been growing rapidly. Currently, all kinds of biomaterials, including metals, ceramics and polymers have been studied for bone regeneration. However, none of these biomaterials, by themselves, can currently be used for full recovery of the patient due to the lack of biological cues on the biomaterials. In order to overcome this issue, engineered bone graft applications require a biomimetic 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).

Biomimetic bone tissue engineering scaffolds need to meet several criteria in order to be a successful candidate for bone graft procedures. An ideal scaffold should completely integrate with 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: (a) it should mimic the physical and chemical composition of the natural bone tissue, (b) it should be biocompatible, (c) it should be porous to allow bone tissue organization and vascular formation, (d) it should have appropriate surface chemistry and mechanical strength characteristics to support cellular attachment, proliferation, and differentiation, and (e) 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) and 30 wt% of organic matrix (mainly Type I collagen) (Pon-On et al., 2014). Mineralization of collagen nanofibers is a well-regulated process mediated by many extracellular matrix proteins, such as bone sialoprotein (BSP) and osteonectin (ON) (Fujisawa, Wada, Nodasaka, & Kuboki, 1996; Sarvestani, He, & Jabbari, 2008; Sarvestani, He, & Jabbari, 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). Therefore, engineered biomaterials which mimic the apatite-coated collagen fibers in bone tissue, provide temporary structural support to the regenerating region, initiate osteogenic differentiation, and degrade simultaneously with the production of extracellular matrix (ECM) have been gaining interest in recent years for bone tissue engineering applications.

Self-assembly has become an effective and promising approach to synthesize a wide range of novel nano-sized biomimetic scaffolds, which could potentially be used in bone tissue engineering applications. It is a type of process in which a disordered system of pre-existing components forms an organized structure or pattern as a consequence of specific, local interactions among the components themselves, without external direction. In this approach, building blocks of the structure organize themselves into functional units driven by the energetics of the system. It thereby will be an attractive candidate for producing engineered bone grafts. In this chapter, self-assembled biomimetic scaffolds development for bone tissue engineering will be reviewed.