Advances in Bone Tissue Engineering to Increase the Feasibility of Engineered Implants

Neelima Vidula
Northwestern University, USA

Jessy J. Mouannes
Northwestern University, USA

Nadia Halim
University of Illinois at Chicago, USA

Shadi F. Othman
University of Illinois at Chicago, USA

INTRODUCTION

Millions of patients experience bone loss as a result of degenerative disease, trauma, or surgery (Xu, Othman, Hong, Peptan, & Magin, 2005). Healthy bone tissue constantly regenerates itself and remodels its architecture to meet the mechanical demands imposed on it, as described by Wolff's "Law of Bone Remodeling" (Wolff, 1986). However, this capacity is severely limited when there is insufficient blood supply, mechanical instability, or competition with highly proliferating tissues (Pinheiro & Gerbei, 2006). Furthermore, severe bone losses can be detrimental to individuals, because they reduce the bone's ability to remodel, repair, and regenerate itself (Luo et al., 2005; Nordin & Franklin, 2001), ultimately resulting in the deterioration of a patient's health, and, in some instances, death (Luo et al., 2005).

Because the repercussions of bone loss are severe, it is important to replace lost bone in patients. The current *gold standard* for specific-site structural and functional bone defect repair is autologous bone grafts (Mauney, Volloch, & Kaplan, 2005) or autografts. While autografts do not present the problem of immune rejection, since the bone tissue is being transplanted from another region of the patient's own body (Rahaman & Mao, 2005), they present certain complications such as significant donor site morbidity (death of tissue remaining in the region from which the donor tissue was removed), infection, malformation, and subsequent loss of graft function (Mauney et al., 2005).

Another established and widely employed technique for the treatment of bone loss is the transplantation of allograft bone or bone tissue from a donor (Mauney et al., 2005). Although allograft bone is effective in treating bone loss, there are several common problems associated with it: first, a compatible donor must be found (Jones, Erhenfried, & Hench, 2006) in order to minimize the possibility of immune rejection by the patient; second, there is a risk of potential disease transmission from the donor to the patient; third, donor site morbidity can occur (Jones et al., 2006); and, finally, there is a limited supply of donor tissue (Mauney et al., 2005). Therefore, patients often experience long waiting periods before receiving the transplant, due to the scarcity of tissue donors, and this can exacerbate bone tissue loss (Jones et al., 2006).

The development of the field of bone tissue engineering has expanded the solutions available to the problem of bone tissue loss. Arguably, implants developed via tissue engineering applications may be a more viable solution to the problem of bone loss than conventional solutions. In contrast with transplants, such implants are not subject to patient-donor tissue biocompatibility issues, because donor tissue is unnecessary. Also, morbidity of the site of extracted tissue is not as great of a problem, since implants can be developed from less tissue. Additionally, implants are generally more

readily available to patients than transplants, which reduces the time for initiation of bone loss treatment (Jones et al., 2006). Therefore, bone tissue engineering may very well be the future gold standard treatment for bone loss.

BACKGROUND

One basic scheme of the bone tissue engineering process currently employed is illustrated in Figure 1. Briefly, mesenchymal stem cells are obtained from the patient, generally from the bone marrow (Stock & Vacanti, 2001). After a period of cellular expansion, the cells are seeded on biodegradable and biocompatible scaffolds (Stock & Vacanti, 2001). Poly-DL-lactic-co-glycolic acid (PLGA), gelatin, and collagen scaffolds are frequently employed as surfaces for bone tissue development (Wu, Shaw, Lin, Lee, & Yang, 2006; Xu et al., 2005; Zhang et al., 2006). These scaffolds are supplemented with bone differentiation promoting factors such as bone-morphogenic protein, dexamethasone, and ascorbate-2-phosphate that enable the stem cells to differentiate into osteoblasts (bone-forming cells) (Kim et al., 2005). After a substantial period of culturing, implantation of the scaffold into the patient occurs, leading to bone restoration (Xu et al., 2005).

Although this process has the potential to treat bone loss, it is far from optimal. Formation of engineered bone tissue currently takes several weeks (at least 3 to 4 weeks), resulting in extensive waiting periods for patients (Cartmell et al., 2005). Since time is of the essence for patients with bone loss, reducing the culture time of stem cells is necessary for implants to be effective. In addition, a portion of the engineered tissue is destroyed during invasive histological assessment conducted to confirm the formation of bone tissue. This form of assessment can further increase patient waiting periods, as the portion of engineered tissue used for testing is no longer available for implantation. A need exists for a bone tissue engineering process that overcomes these problems.

Reducing the culture time of stem cells is necessary to increase the effectiveness of engineered implants. The use of electrical and mechanical stimulation devices to accelerate stem cell differentiation into osteoblasts has been implicated.

Electric and electromagnetic fields may be effective in accelerating stem cell differentiation. Aaron, Ciombor, and Simon (2004) demonstrated that electric and electromagnetic fields can accelerate bone formation and healing, particularly in osteotomies and spine fusions, both *in vivo* and *in vitro*; osteotomy is a procedure in which bone is surgically cut to improve alignment (ASBA Glossary, 2005). Electric fields can be generated either invasively in bone, by placing electrodes directly into the healing site, or noninvasively, through capacitive or inductive coupling. Osteogenesis, or bone formation, is usually stimulated at the cathode (Aaron et al., 2004).

"Electrical Properties of Bone" by Lakes (2005) describes another type of stimulation that can be achieved by means of a piezoelectric actuator. It has been demonstrated by several researchers that bone is piezoelectric. The piezoelectric nature of bone indicates that any mechanical stress applied to bone can produce

Figure 1. A current process of bone tissue engineering is depicted