ABSTRACT: This manuscript focuses on bone repair/regeneration using tissue engineering strategies, and highlights nanobiotechnology developments leading to novel nanocomposite systems. About 6.5 million fractures occur annually in USA, and about 550,000 of these individual cases required the application of a bone graft. Autogenous and allogeneic bone have been most widely used for bone graft based therapies; however, there are significant problems such as donor shortage and risk of infection. Alternatives using synthetic and natural biomaterials have been developed, and some are commercially available for clinical applications requiring bone grafts. However, it remains a great challenge to design an ideal synthetic graft that very closely mimics the bone tissue structurally, and can modulate the desired function in osteoblast and progenitor cell populations. Nanobiomaterials, specifically nanocomposites composed of hydroxyapatite (HA) and/or collagen are extremely promising graft substitutes. The biocomposites can be fabricated to mimic the material composition of native bone tissue, and additionally, when using nano-HA (reduced grain size), one mimics the structural arrangement of native bone. A good understanding of bone biology and structure is critical to development of bone mimicking graft substitutes. HA and collagen exhibit excellent osteoconductive properties which can further modulate the regenerative/healing process following fracture injury. Combining with other polymeric biomaterials will reinforce the mechanical properties thus making the novel nano-HA based composites comparable to human bone. We report on recent studies using nanocomposites that have been fabricated as particles and nanofibers for regeneration of segmental bone defects. The research in nanocomposites, highlight a pivotal role in the future development of an ideal orthopaedic implant device, however further significant advancements are necessary to achieve clinical use.

KEYWORDS: bone graft substitute, nanocomposite, hydroxyapatite, collagen, nanofiber, biomimetic, nanobiomaterial, osteogenic, segmental defect, tibia defect

1 Introduction

Bones are a type of dense connective tissue that comprises the rigid organs that form part of the skeletal system in most vertebrates. Physically, bone functions to support the body, act as a lever system during movement, and protect the internal organs from shock and injury. Its physiologically functions include hematopoiesis, the formation of blood cells, source of progenitor population, and mineral
homeostasis’s, as a reservoir for calcium, phosphate, sodium, potassium, zinc and magnesium. In addition, bone matrix maintains storage of growth factors and fatty acids, buffers against excessive pH changes in the blood, and is involved in endocrine signaling. Bone is a very dynamic organ that constantly undergoes self-remodeling and has within itself the unique ability to repair/regenerate to a certain extent following injury. About 6.5 million fractures occur annually in the United States of America, and more than 500,000 of these individual cases require application of a bone graft material [1–2]. Fractures of the hip, ankle, tibia, and fibula occur most frequently, and in general men experience more fractures than women. The total number of hip replacements increased 33% to 152,000 cases in the year 2000 as compared to the year 1990 in USA alone, and it is expected to increase to about 272,000 by the year 2030 [3]. Thus, there is a large need for synthetic grafts for fracture repair, and there are significant opportunities to improve the existing graft material. A market survey conducted by Medtech Insight reported that biomaterial sales for orthopaedic use was found to exceed 980 million dollars in 2001 in the USA, and was 1.16 billion dollars in 2002 [4]. Sales of bone graft and bone graft substitutes in US alone were 1.5 billion dollars in 2009 [5]. The number of bone graft procedures has increased worldwide, and in 2000, 15% of all bone graft surgeries conducted in the world used synthetic bone grafts.

2 Bone grafts

As illustrated above, the repair and replacement of damaged or lost bone due to trauma, pathological degeneration, or congenital deformity of the tissue is a major clinical problem in the United States and around the world. This number will continue to grow as life expectancy and the population increase in the United States [6]. Although bone itself can help restore and repair minor fractures, the regenerative capacity is limited especially in the case of fracture non-unions (up to 10% of the fractures) and a large mass bone loss associated with osteoporosis, osteosarcoma, and revision total joint replacements [7]. The patients will experience major dysfunction and severe pain if no treatments are undertaken.

2.1 Autografts

Autografts, allografts and a variety of bone graft substitutes are used for surgical treatments [8–10]. Autografts which constitute ~58% of the bone substitutes are typically tissues harvested from the patient’s own iliac crest. They are considered the gold standard for bone repair, since they possess all the properties necessary for new bone growth. Upon implantation, the grafts are able to support the attachment and migration of new osteoblasts and osteoprogenitor cells (osteocconductivity), in situ mineralization of the collagen matrix produced by osteoblasts to form new bone (osteogenicity), the recruitment and differentiation of stem cells or osteoprogenitor cells into osteoblasts (osteointuctivity), and formation of intimate bonding between the newly formed mineralized tissue and host bone tissue (osteointegrativity). However, they are limited in availability and often associated with donor-site morbidity and increased operative blood loss particularly when a large graft is required [11].

2.2 Allografts

Allografts are tissues obtained from banked freeze-dried bones of human cadavers and represent about ~34% of the bone substitutes. They are osteoconductive and have fewer limitations on supply [8]. However, allografts are usually not osteoinductive or osteogenic and are associated with risks of immunological reaction or disease transmission. Furthermore they possess insufficient mechanical properties for load-bearing bone applications. Studies have shown the failure rate of allografts is between 25% and 35% [12–13].

2.3 Bone graft substitutes

As alternatives to the autografts and allografts, a variety of bone graft substitutes have been developed and account for ~8% of bone graft use [8]. On a basis of material composition, they can be classified as allograft-based, factor-based, cell-based, ceramic-based, and polymer-based bone graft substitutes [8]. They have been developed for repair due to unlimited supply, ease of sterilization and storage. However, each suffers from a number of disadvantages. Human derived allograft-based bone graft substitutes can be potentially associated with immunogenicity and disease transmission. Factor- and cell-based bone graft substitutes often need additional structural support. Ceramic-based bone graft substitutes are brittle and possess inappropriate mechanical properties for use in load-bearing sites. In addition, some of the ceramic-based bone graft substitutes do not remodel over time.

To overcome the limitations associated with the current