CHAPTER 11

CLINICAL EFFICACY OF STEM CELL MEDIATED OSTEOGENESIS AND BIOCERAMICS FOR BONE TISSUE ENGINEERING

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Abstract: Lower back pain is a common disorder that often requires bony spinal fusion for long-term relief. Current arthrodesis procedures use bone grafts from autogenous bone, allogenic backed bone or synthetic materials. Autogenous bone grafts can result in donor site morbidity and pain at the donor site, while allogenic backed bone and synthetic materials have variable effectiveness. Given these limitations, researchers have focused on new treatments that will allow for safe and successful bone repair and regeneration. Mesenchymal stem cells (MSCs) have received attention for their ability to differentiate into osteoblasts, cells that synthesize the extracellular matrix and regulate matrix mineralization. Successful bone regeneration requires three elements: MSCs that serve as osteoblastic progenitors, osteoinductive growth factors and their pathways that promote development and differentiation of the cells as well as an osteoconductive scaffold that allows for the formation of a vascular network. Future treatments should strive to combine mesenchymal stem cells, cell-seeded scaffolds and gene therapy to optimize the efficiency and safety of tissue repair and bone regeneration.

INTRODUCTION

Disc degeneration is a common disorder in the lower spine. It remains a pervasive and intractable disease arising from a combination of aging and stress on the bony and
cartilaginous elements of the spinal column.\textsuperscript{1} As the discs in the spine dehydrate, they lose their ability to act as shock absorbers. At the same time, the bones and ligaments that make up the spine thicken and become less pliable. Some patients will have disease progression that, despite conservative and minimally invasive therapies, requires arthrodesis, or fusion, of particular spinal segments to directly treat the pathological pain. There are four stages to the deterioration; in the earlier stages patient discomforts include lack of stability, restricted movement, vision and mental problems, as well as muscle tingling and weakness. By the later stages, there are potential decreases in height, postural imbalances and nerve damage, along with permanent scar tissue and bone deformation. As spinal instrumentation has evolved over the last decade, the role that surgery plays in the treatment of degenerative spinal pathology has increased.

Treatment plans for patients are often tedious and complex, with the main goal of relieving the pressure on the nerve. Bony spinal fusion is often required for long-term durability and relief. In 2008, about 46,500 lumbar spinal arthrodesis procedures were performed in the United States, making it the second most common lumbar spine operation.\textsuperscript{2} Spinal fusion procedures employ several distinct surgical techniques to reduce or eliminate the motion between adjacent vertebrae at the culprit joint, bypassing the anomalies that cause the pain.\textsuperscript{3,4} While spinal fusion was initially developed as a method for treatment of scoliosis, spinal tuberculosis and small spinal fractures\textsuperscript{3} there has recently been a drastic and controversial expansion in the application of spinal fusion to treat pain degenerative morbidities. This broad category of disorders includes lower back pain without sciatica, spinal stenosis, degenerative disc disease and spinal deformity.\textsuperscript{3,5,6} Current procedures treat posterior, anterior and bilateral parts of the spine.

Arthodesis refers to the use of a bone graft matrix that is placed between roughened surfaces of opposing bones, eventually resulting in the fusion of two adjacent bone segments.\textsuperscript{3} Currently, bone grafts are obtained from autogenous bone, allogenic backed bone or synthetic materials. Autogenous bone grafts are harvested from a patient’s iliac crest via bone marrow aspiration or trephine biopsy and have several drawbacks including donor site morbidity, limited availability and pain at the donor site. While allogenic backed bone and synthetic materials carry a low risk of disease transmission and immunogenicity, their effectiveness varies.\textsuperscript{7,8} Furthermore, some synthetic bone materials can result in poor integration and adverse reactions leading to eventual bone resorption.\textsuperscript{7,10} The limitations of these available methods have caused researchers to focus on finding new treatments to safely and successfully promote bone repair and regeneration.

The success of the healing process at the desired site requires three elements: an osteogenic reservoir that provides an influx of cells to the newly forming bone, osteoinductive growth factors that promote development and differentiation of the cells and an osteoconductive scaffold that allows for vascularization and bone growth.\textsuperscript{6} Bone is a living and highly vascularized tissue. It depends on close connections with blood vessels to maintain its integrity.\textsuperscript{11} The vascular network transports oxygen and nutrients, as well as essential growth factors, chemokines and cytokines to the surrounding tissue. Therefore, angiogenesis is a prerequisite for large tissue reconstruction. A lack of blood vessels and the resulting hypoxia could threaten the success of tissue engineered implants.\textsuperscript{12} Prolonged hypoxic regions coupled with a lack of nutrients will ultimately lead to significant cell death.\textsuperscript{11,13} However, researchers also need to carefully control angiogenesis, both temporally and spatially, to prevent tumor formation.\textsuperscript{12,14} A strong blood supply is critical to the production and survival of new bone.