Bioactive ceramics and glasses: reactivity, biological effects and tissue engineering use

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Introduction

In orthopaedic surgery, implant dentistry, and oral and maxillofacial surgery, there is a great need for bone tissue grafts and bone tissue augmentation materials. The approaches to these difficult bone repair problems include utilization of autografts or allografts. While the use of autograft material is the preferred technique, there are limitations such as donor site morbidity, limited donor bone supply, anatomical and structural problems, and elevated levels of resorption during healing. Allografts have the disadvantage of eliciting an immunological response due to genetic differences and the risk of inducing transmissible diseases. As a result, considerable attention has been directed towards the use of synthetic grafts, including hydroxyapatite (HA), tricalcium phosphate (TCP) and bioactive glass and glass ceramics (BG)[1].

Bioactive ceramics and glasses

HA, TCP and BG are usually described as bone bioactive ceramics. These are materials which, generally, bond to surrounding osseous tissue and enhance bone tissue formation. Since direct bone bonding to bioactive glasses was first observed[2], considerable progress has been made in understanding the basic mechanisms of the formation of a bone - biomaterial bond and its effect on bone tissue formation. This progress resulted mainly from two approaches. One focused on studying the bone - biomaterials interface that developed *in vivo*. The examination of the bonding zone revealed the consistent presence of an interfacial hydroxyapatite layer[2-3]. The other approach used *in vitro* immersions in simulated physiological fluids or cell containing media[4-5]. These analyses revealed that reactions occurred at the implant material surfaces such as dissolution, precipitation and ion exchange. These reactions were accompanied by adsorption and incorporation of biological molecules[6]. The combination of *in vivo* and *in vitro* studies led to a better understanding of surface reactions of bioactive ceramics in the body and their effects on bone formation and bone cell function.

Cellular effects

In vivo studies have clearly documented that bioactive ceramics affect cellular function. A series of experiments using porous hydroxyapatite and bone marrow cells showed that the osteoprogenitor nature of cells from bone marrow was activated more readily in heterotopic sites when they were cultured with porous, carbonated hydroxyapatite than when implanted by themselves. With these studies, Ohgushi et al.[7] were first to describe the idea of culturing cells capable of expressing the osteoblastic phenotype with the intent to synthesize artificial bone grafts. These authors focused primarily on issues related to stem cell preparation. When cultured on appropriate templates, the cell cultures produced extracellular matrix. Investigators from this laboratory also used periosteal-derived cells. It was shown that when the cells were combined with porous calcium-phosphate ceramics and implanted in a subcutaneous site in athymic mice, bone tissue was formed[8]. In these studies using marrow stroma-derived osteoprogenitor cells, it is important to realize that it is primarily the intrinsic capacity of the osteoprogenitor cells that produces the upregulation to cells of the osteoblast lineage. It was also demonstrated that stem cell differentiation to cells expressing the osteoblastic phenotype occurred in porous titanium[9]. However, the pattern of bone tissue formation was different. Whereas in porous hydroxyapatite it started at the ceramic surface, it started in the middle of the pore and was much slower in porous titanium. These data suggested that even though the intrinsic capability of pluripotential cells led to differentiation along the osteoblast pathway, the osteogenic potential of these cells was also stimulated by the bioactive material surface. Other data suggests that concentration of proteins which are naturally present in bone tissue repair sites or are added prior to surgery lead to a biologically very potent state of these molecules. These findings help to explain the major effect of bioactive ceramics on cell function and tissue formation[1].

Tissue Engineering

The use of *in vitro* synthesized bone tissue with marrow cells obtained from the patient is an appealing idea to avoid the profound limitations of biological and synthetic bone grafts. Porous, surface-modified bioactive ceramics integrate well with bone tissue in the healing of skeletal defects and resorb in concert with bone formation, which allows for improvement of the long bone's structural integrity over time. In fact, the osteogenic activity of tissue-engineered constructs in which osteoprogenitor cells were seeded onto scaffolds after culture and onset of expressing osteogenic markers, aids in restoring the mechanical behavior of bones.[10] Bone formation and the return of normal torsional properties were enhanced for the tissue-engineered constructs as compared to the scaffold alone.

References

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