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Characterization and *In Vitro* Cyto-compatibility of Hydroxy-apatite Bio Ceramics

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Introduction

The three-dimensional-printed BC-Exo scaffolds, exhibiting a predefined structure and persistent release of exospores, displayed distinct immune modulatory effects and improved ontogenesis/angiogenesis. The BC-Exos in the printed scaffolds modulated macrophage polarization and the expression of chemokine's for the recruitment of bone marrow mesenchyme stem cells (BMSCs) and endothelial cells. Scaffolds with BC-Exos from macrophages with a mixed phenotype significantly enhanced the estrogenic differentiation and immunosuppression of BMSCs and improved the antigenic activity of human umbilical vein endothelial cells *in vitro*. For the potential mechanism, β-TCP bio ceramics have an important effect on the immunomodulation of macrophages by regulating gene expression, increasing exospore production, and altering exosomal mRNA cargos, thereby affecting the paracrine effects of BC-Exos on immunomodulation and ontogenesis/angiogenesis. This study suggests that 3D printing of bio ceramic-induced macrophage exospores may be a useful strategy for tissue engineering and regenerative medicine.

Description

Our skeletal system that plays a key role in our lives, supporting our bodies and enabling us to have mobility. Since in the early days of Hippocrates in ancient Greece, it has been recognized that bones are very dynamic tissue with unique capacities to heal and remodel under appropriate conditions without leaving a wound. This set of properties are associated with its capacity to withstand load bearing makes bone a very complex system to be substituted using synthetic materials. Thus, it is the great challenge for all of the bone functions when it is damaged or injured through accidents and by diseases. This regeneration of bone tissue using the body's own self-healing mechanisms is the ideal approach for the bone repair which is a major goal of tissue engineering, restoring diseased or impaired tissue to its original states and functions, reducing the need for transplants and replacements. However, when an area of damaged bone is excessively large for self-repair healing, the injured site must be repaired using alternative materials, such as auto grafts, Allografts and by the artificial materials. Additionally, an increasing clinical demand for synthetic and artificial bone substitutes has been observed due to the rapidly aging population worldwide.

Currently, in the order to address the problem, there are several classes for synthetic bone grafting biomaterials for the in vivo applications, such as- natural coral-derived materials, bovine demineralized bone, human demineralized bone matrix, bioactive glasses, glass-ceramics, alumina-based ceramic, hybrids and calcium orthophosphates (CaP). All of the biomaterials need to be biocompatible and osteo conductive for the cell proliferation and guiding the bone tissue growth leading to its tissue repair and remodeling. For the reason, over that last four decades, bioactive ceramic materials have gained highest attention for the scientific community and professionals because of the extraordinary potential use as a suitable bone substitutes. Commonly, bio ceramics are considered ceramics that are designed to induce specific biological activity for the repairing damaged organs. Since from the discovery of Biogas, many researchers has developed numerous types of bioactive ceramics, such as hydroxyapatite (Ca_{10} $(PO_4)_6(OH)_2$) and glass-ceramic.

Despite the fact that materials science technology has resulted in unquestionable advances in the field of bone replacement medicine and no totally satisfactory bone substitute, which fulfills all the requirements, have been developed yet. Hence, the development of the bioactive materials that is showing not only bioactivity but also the mechanical properties similar to the living bone is still much needed. Among several alternatives of the Ceramic-based materials for the bone replacements and repairs bioceramics made of calcium phosphates (CaPs) appears very promisingly due to both excellent biocompatibility and their abilities to bond to live bone in the body, which is the intrinsically related to the abundance in nature and presence in the mammalian calcified tissues.

Hydroxyapatite (HA) is the most well-known CaP material, since it is crystallographic ally and chemically similar to the mineral phase of human bone. Therefore, it has been intensive studied for use of biomaterial and scaffold for bone tissue regeneration. However, it is an important to note that the native bone apatite differs from the stoichiometric HA in a number of ways, including the non-stoichiometry, nanosized crystal dimensions, and a relative crystallinity when assuming 100% for stoichiometric HA. The non-stoichiometry of the biological apatites is mostly caused from the incorporation of the foreign ions into the crystal lattice. Studies confirmed that substituting ions (anions or cations) present in native hard tissues such as strontium (Sr), magnesium (Mg), zinc (Zn) and niobium (Nb) into CaPs can lead to the beneficial effects on the biomaterial properties, such as the degree of structural order (i.e., crystallinity), morphology, thermal stability, solubility, mechanical properties, degradability, surface charge, and dissolution rate under physiological conditions. Furthermore, the doping with ionic species can play an important role in the biological responses for bone cells [1-5].

Conclusion

Masato Tamai reported that Nb(V) incorporated as niobates to biphasic calcium phosphate (HA and β-tri calcium phosphate, β-TCP) significantly promoted to the calcification of normal human osteoblasts and have the potential to promote alkaline phosphatase (ALP) activities an important factor in the generation of the new bone. Consequently, Nb(V) species can be considered as a key dopants for the incorporation in HA, as most niobium salt precursors (e.g., NbCl5) undergoes hydrolysis in alkaline aqueous medium leading to the formation of oxyanions (generic formula NbxOyz−) instead of Nb5. Thus, the main goal of this study is the synthesis and characterization of niobium-modified bio ceramics for potential use as a biomaterial in bone tissue repair. Although there were few published studies in this field, no research was found in the consulted literature where a systematic and an extensive characterization of morphology, structure, and the cytotoxicity of Nb-doped HA produced by a co-precipitation method under the same experimental conditions has been performed.

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Conflict of Interest

The authors declare that there is no conflict of interest associated with this manuscript.

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