Sr/Mg – doped bioceramic scaffolds for biomedical application

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INTRODUCTION: Bone is a mineralized connective tissue with remarkable self-healing capability. However, in the presence of large bone defects (≥ 2.5 cm), bone self-recovery is not efficient, necessitating surgical intervention and the introduction of a bone substitute. Hydroxyapatite (HAP) is a widely investigated material for bone tissue engineering (BTE) due to its similarity to the biological apatite found in bones and teeth. Mesoporous bioactive glasses (MBAGs), quickly bind to surrounding tissues and release ions promoting the formation of new bone [1]. The silica from glass enhances angiogenesis, which is a pivotal consideration given the high vascularization level of this tissue [2]. Ion-doping approach of both HAP and MBAG particles has gained great attention due to the ability of therapeutical ions to stimulate a certain cell response. The project aims to develop and characterize bioceramic scaffolds based on a combination of Sr/Mg-doped HAP and MBAG, thereby promoting osteogenesis and creating a favourable environment for the proliferation of endothelial cells.

MATERIALS AND METHODS: *Scaffolds fabrication*. Scaffolds were fabricated via sponge-replica technique sintered at 1400 ºC: pure HAP served as control; Sr, Mg-doped HAP = dHAP, combination of dHAP with 10% SrMg-MBAG = dBAG. *Mechanical properties.* A static compressive test has been used to verify the scaffolds strength. *Biological properties***.** The cytocompatibility of scaffolds towards human bone marrow-derived mesenchymal stem cells (hBMSCs) and human endothelial cells (Ea.hy926) has been verified with the Resazurin reduction assay after 1 and 7 days of cultivation. The viability of both cell lines was confirmed with the fluorescent assay Live/Dead. Scaffold suitability in sustaining Ea.hy926 adhesion and proliferation has been verified through FESEM and fluorescent microscope using phalloidin and DAPI after 14 days of cultivation. The pro-osteogenic behaviour of the scaffolds was assessed by culturing hBMSCs within the scaffolds for 21 days. The confirmation of osteogenic differentiation was achieved through a comparative analysis of the expression level of collagen I via real-time PCR. Furthermore, the correct differentiation toward an osteogenic lineage is verified with the collagen I/collagen II ratio. All samples were tested in biological triplicates (n=3).

RESULTS AND DISCUSSION: The results of the static compressive test indicate that the MBAG particles serve as sintering agent, leading to superior performance of dBAG. In contrast, the results of the Resazurin reduction assay didn't show any significant difference among the samples for both time points and cell lines in exam. Scaffolds' cytocompatibility is confirmed by the Live/Dead assay, highlighting not only cells' viability but also cells' distribution within the scaffolds. The morphological analysis revealed a better cell-cell and cell-material interaction in dHAP and dBAG scaffolds compared to HAP, demonstrating that these scaffolds provide an optimal environment for Ea.hy926 proliferation. The real-time PCR results suggest that all the scaffolds can sustain osteogenesis, however, dHAP and dBAG scaffolds show better performances. The collagen I/collagen II ratio in favour of collagen I demonstrate their differentiation toward an osteogenic lineage.

CONCLUSION: Bioceramic scaffolds based on Sr,Mg- doped HAP and MBAG present promising materials for bone tissue engineering.

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