THE BIOLOGICAL ROLE OF CaO/SiO_2 RATIO AND P_2O_5 CONTENT IN SOL-GEL BIOACTIVE GLASSES INCORPORATED INTO PLGA

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Introduction

We have prepared composite materials obtained on the basis of PLGA copolymer and sol-gel derived bioactive glasses (BG). Such composites have been shown by us to display high biocompatibility and some of them can stimulate osteogenesis in human bone marrow stromal cells (hBMSC) [1-4]. The aim of this study was to examine to what extent the chemical composition of sol-gel derived bioactive glasses (SBG) incorporated at 50 w% to PLGA matrix affects early osteogenesis events and BMP signaling in BMSC. The ion dissolution products obtained from materials were examined for biological activity as well.

Materials and Methods

Eight SBGs with different CaO/SiO_2 ratios with and without P_2O_5 were incorporated at 50% to PLGA matrix and structured into thin films suitable for cell culture (TABLE 1).

TABLE 1. Chemical compositions of gel-derived glasses and their CaO/SiO_2 ratio.

Material	Chemical composition (%mol)			CaO/SiO_2
	SiO_2	CaO	P_2O_5	ratio
A1	40	60	-	1.50
T1	50	50	-	1.00
D1	60	40	-	0.67
S1	80	20	-	0.25
A2	40	54	6	1.35
T2	47	47	6	1.00
D2	60	36	4	0.60
S2	80	16	4	0.20

Human BMSC were harvested from iliac crest of adult patients (42-67 years old, both genders) according to the approved Institutional Review Board protocol (nr 1072.6120.254.2017). After isolation and expansion, BMSC were either seeded directly on the films or cultured on tissue culture plastic with condition medium (CM) harvested from the materials (FIG. 1). BMSC were examined for mRNA levels of Runx-2 and Osx at 2-day culture, BMP-2 and BMP-6, phospho-Smad1, 5, 8 and phospho-Tak1 at 3-day culture, alkaline phosphatase activity at 7-day BMSC cultures as well as for culture mineralization 21 days post cell seeding.

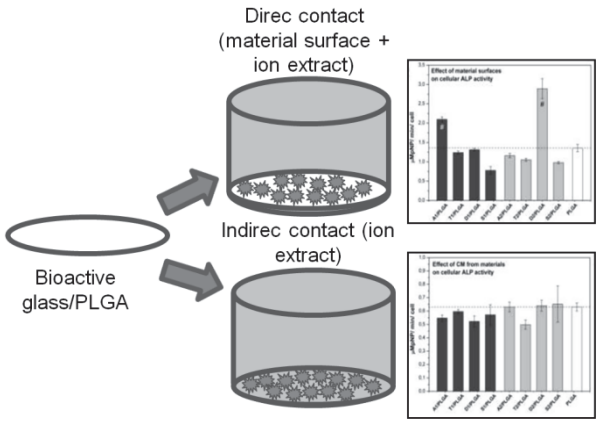

FIG. 1. General experimental scheme and representative results.

Results and Discussion

The materials without P_2O_5 stimulated higher RUNX-2 expression in BMSC and we observed higher mineralization level of the extracellular matrix in BMSC cultures grown in the presence of CM from these materials. In general, composites with higher content of CaO stimulated expression of OSX. CM from tested surfaces did not affect the activity of ALP, but culturing cells directly on some of the material surfaces resulted in ALP stimulation. P_2O_5 enriched materials stimulated the synthesis of BMP-2 and BMP-6 and the activation of Smad 1, 5, 8 proteins to a greater extent than these without P_2O_5. Moreover, most studied composite surfaces stimulated BMP-dependent TAK1 kinase.

Conclusions

Our studies confirmed osteoinductive properties of the studied composites although we have not found much correlation between the CaO/SiO_2 ratio in SBG, incorporated into PLGA, and BMSC response. The incorporation of P_2O_5 into SBG also played a significant role in a biological response. Furthermore, the examinations of ALP activity in cultures of human BMSC showed marked differences in cell behavior depending whether the cells were treated with culture medium conditioned with composite materials or they were directly seeded on the material surfaces. Although the ions released from some studied surfaces were sufficient to induce matrix mineralization in hBMSC, they were ineffective to activate cellular ALP activity in human BMSC. We believe the results obtained in this work may prompt further research regarding BMP pathways activation by composites that contain bioactive glasses as these pathways may be crucial to drive osteogenesis of BMSC on contact with bioactive materials. They also indicate the importance of studies dissecting the biological role of the ions released from bioactive materials and the role of the material surface itself.

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