Bone Tissue Engineering: In Vivo Evaluation of the Hybrid Biomaterial Calcium Phosphate/Poly(lactide-co-glycolide) and Osteoblastic Cells

MM.Beloti[1], PT.de Oliveira[1], JE.Davies[2], L.Guan[2], PSP.de Carvalho[3], AL.Rosa[1]

[1] Cell Culture Laboratory, School of Dentistry of Ribeirao Preto, University of Sao Paulo, SP, Brazil, [2] Institute for Biomaterials and Biomedical Engineering, University of Toronto, Ontario, Canada, [3] School of Dentistry of Bauru, University of Sao Paulo, SP, Brazil

INTRODUCTION: The combination of patient own cells and porous scaffolds to produce 3D hybrid osteogenic constructs is a common subject in bone tissue engineering research. Recently, a novel scaffold combining calcium phosphate and poly(lactide-co-glycolide) (CaP/PLGA) has been developed [1]. This study aimed to evaluate in vivo bone tissue response to the hybrid biomaterial obtained by seeding animal own cells into the CaP/PLGA scaffold.

METHODS: Rat bone marrow stem cells obtained by aspiration from femora of nine young adult male Wistar rats were cultured under osteogenic conditions until subconfluence. By using centrifugal force [2], subcultured cells were seeded into CaP/PLGA scaffold at a concentration of 4 x 10^4 cells/mg scaffold and the hybrid biomaterial was cultured for 0, 7 and 14 days. Bilateral critical-size (5 mm in diameter) defects were surgically created in calvaria of the same rats from which the cells were aspirated. Defects were filled with coagulum (n=4), scaffold alone (n=5), and hybrid biomaterial (scaffold plus autologous cells cultured for 0, 7, and 14 days (n=5, for each culture period). Histologic analysis was carried out under light microscopy at 4 weeks post-implantation.

RESULTS: In the sites filled with coagulum alone, newly formed bone was restricted to the defect borders, whereas a non-mineralized connective tissue was observed in the central portion of the defect (Fig. 1A). When scaffolds without cells were implanted, the presence of immature bone tissue took place all along the hybrid material surface (Fig. 1B). Immature bone tissue was also observed in the samples of the hybrid biomaterial implanted immediately after cell seeding procedure (time 0), although in a fewer amount (Fig. 1C). In the sites where the hybrid biomaterials cultured for 7 and 14 days were implanted, a non-mineralized connective tissue and the lack of immature bone tissue were noticed (Fig. 1D and E).

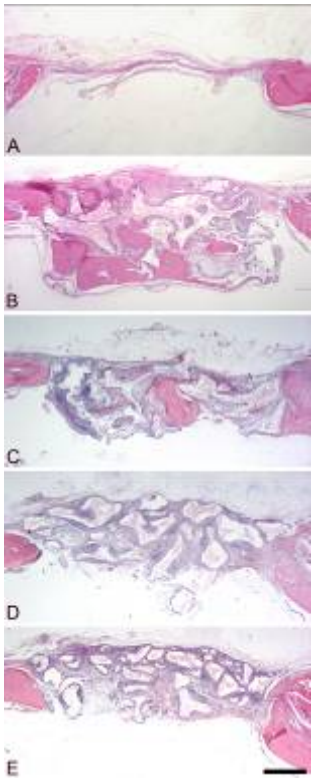

Fig. 1: Light microscopy of rat calvaria defects filled with (A) coagulum, (B) scaffold; (C) hybrid biomaterial (time 0), (D) hybrid biomaterial (7 days), and (E) hybrid biomaterial (14 days), at 4 weeks post-implantation. Bar = 1 mm.

DISCUSSION & CONCLUSIONS: These results point toward a negative influence of the time of culture of the hybrid biomaterial on in vivo bone response. Such finding could be related to the adsorption of serum proteins present in the culture medium. Further experiments must be carried out to test this hypothesis.

REFERENCES: [1] L. Guan, J.E. Davies (2004). *J Biomed Mater Res* **71A**:480-7. [2] M.M. Beloti, J.E. Davies, L. Guan et al. *Biomaterials in Regenerative Medicine*, Vienna 2006, p.54.

ACKNOWLEDGEMENTS: FAPESP for financial support.