Semana de Engenharia 2010
Guimarães, 11 a 15 de Outubro

CHONDROGENIC DIFFERENTIATION OF HUMAN BONE MARROW MESENCHYMAL STEM CELLS IN CHITOSAN FIBER MESHES USING A FLOW PERFUSION BIOREACTOR

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ABSTRACT

Native articular cartilage is subjected to synovial fluid flow during normal joint function. Thus, it is believed that the morphogenesis of articular cartilage may be positively regulated by the application of similar stimulation in vitro. In the present work, it is studied the effect of fluid flow over the chondrogenic differentiation of human bone marrow derived mesenchymal stem cells (hBMSCs). We aim at conclude if the shear stress caused by the medium perfusion trough the constructs is able of positively regulate the differentiation process.
Human BMSCs were seeded statically onto fiber meshes scaffolds, consisting of a blend of 50/50 chitosan and Poly(Butylene Terephtalate Adipate)–CPBTA. The constructs were cultured in a flow perfusion bioreactor for 28 days. An enhanced ECM deposition and collagen type II production was observed in the bioreactor samples, when compared to the static controls. The ECM accumulation in those samples is lower than in those cultured in the bioreactor, and there is a significant difference in the expression of collagen type I. It is shown that the flow induced shear stress has a beneficial effect on the chondrogenic differentiation of hBMSCs.

METHODS

Human BMSCs were isolated from bone marrow aspirates and were characterized by flow cytometry. After expansion, hBM-MSCs were seeded statically onto fiber meshes scaffolds, consisting of a blend of 50/50 chitosan and Poly(Butylene Terephtalate Adipate)–CPBTA. Constructs were cultured in the flow perfusion bioreactor for 28 days, using complete medium for chondrogenesis supplemented with TGF-β3.

RESULTS AND DISCUSSION

We observed an enhanced ECM deposition and collagen type II production in the bioreactor constructs, when comparedto the static controls. Moreover, it was observed a longer differentiation period in cells cultured in static conditions. The ECM accumulation in these constructs was lower than in the bioreactor, and a significant difference in the expression of collagen type I was observed (repeated from the abstract, change text and content). Our results are consistent with other studies in the literature (Fitzgerald *et al.*). They showed that dynamic shear, in the absence of hydrostatic pressure gradients, induced matrix protein transcription. These findings are consistent with other works that also found that dynamic shear increased the transcription of matrix proteins to a greater extent than dynamic compression, and at the same time augmented matrix biosynthesis, preferentially collagen synthesis (Jin *et al.* 2001).

CONCLUSIONS

In the present work, we found evidences that confirm our hypothesis that shear stress has a beneficial effect on the chondrogenic differentiation of hBM-MSCs.
We can also conclude that the CPBTA scaffolds are effective in supporting the chondrogenic differentiation of hBMSCs, being suitable for cartilage tissue engineering.

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ACKNOWLEDGEMENTS

Marta Alves da Silva would like to acknowledge the Portuguese Foundation for Science and Technology (FCT) for her grant (SFRH/BD/28708/2006). Authors would like to acknowledge the patients of Hospital de São Marcos, Braga, Portugal for donation of biological samples, and to its medical and nursing staff. Finally, we would like to acknowledge the European NoE EXPERTISSUES (NMP3-CT-2004-500283). This work was partially supported by the European FP7 Project Find and Bind (NMP4-SL-2009-229292).

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Marta Alves da Silva was born in Custóias, Matosinhos. She received her degree in Applied Biology by the University of Minho in 2001. Afterwards, she finished a Master in Molecular Genetics in 2005, also at the University of Minho. She is currently a PhD student in the 3B´s Research Group, and her thesis subject is “Articular cartilage repair strategies based on biomaterials”. During her PhD she has been awarded for the best oral communication at the “School of engineering day”, in 2007. She is the author of 3 published papers in international journal with referees.

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