

## PLLA and BMP-2 containing PLLA nanofiber scaffolds for growth and differentiation of hMSCs and bone regeneration

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**INTRODUCTION:** The reconstruction of large bony defects often requires the use of graft material. Here, scaffolds based on nanofibers, produced by electro spinning, offer great advantages. These fibers mimic the extracellular matrix and allow the differentiation of human mesenchymal stem cells (hMSC) towards osteoblasts [1]. Due to the fabrication process nanofibers offer the chance to incorporate growth factors in order to use them as a drug carrier system.

**METHODS:** The preparation of PLLA nanofibers by electrospinning has been reported in detail earlier [2]. Human mesenchymal stem cells were obtained according to [2]. Cells were seeded at a density of  $3 \times 10^4$  cells/cm<sup>2</sup> on cover slips and cover slips coated with PLLA and also with BMP-2 containing PLLA in growth and differentiation medium. Gene expression analysis was according to [3]. Animal experiments were performed as described in [4]. The nanofiber scaffolds were placed “press fit” into critical size rat skull defects, without further fixation. Histomorphometrical, radiological and immunohistochemical analysis was performed time dependent.

**RESULTS:** The use of PLLA or BMP-2 containing PLLA nanofibers had no influence on growth of hMSC *in vitro*. However, the presence of PLLA nanofibers initially diminished the gene expression of the osteoblast linkage, whereas the incorporation of BMP-2 resulted in an enhanced differentiation of hMSC (Fig. 1).

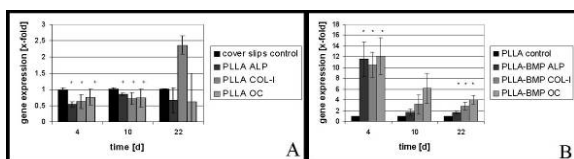


Fig. 1: Effect of PLLA (A) and PLLA-BMP-2 (B) nanofibers on gene expression *in vitro*.

Implanted into critical size defects, PLLA nanofibers facilitates the ingrowth of cells into the defect, whereas the BMP-2 containing

fibers enhanced the bone formation *in vivo* (Fig. 2)

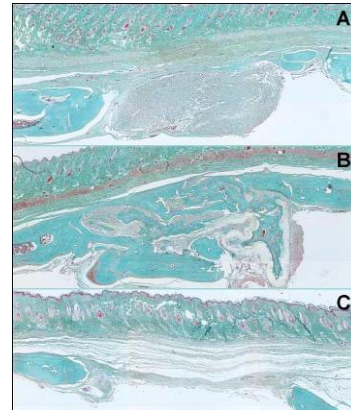


Fig. 2: Effect of PLLA (A) and PLLA BMP-2 (B) nanofibers on bone formation as compared to controls (C) *in vivo*.

**DISCUSSION & CONCLUSION:** FDA approved PLLA can easily be electrospun into a 3-D non-woven network that supports the growth of hMSC as described earlier [2]. Although PLLA is known to possess poor protein release properties [5], the large surface and the porous structure of PLLA nanofibers might facilitate contact to the BMP-receptor of the growing cell. Therefore the PLLA-BMP nanofiber scaffold allows a local control of bone healing.

**REFERENCES:** <sup>1</sup>Greiner, A, *Angewandte Chemie International Edition* 2007 46, 5670-5703. <sup>2</sup>Schofer, MD, *J Mater Sci Mater Med* 2009 20, 767-774. <sup>3</sup>Fuchs, TF, *TheScientificWorldJournal* 2007 7, 2012-2020. <sup>4</sup>Jones, L, *Journal of Cranio-Maxillofacial Surgery* 2007, 35, 350–357. <sup>5</sup>Maretschek, S, *Journal of Controlled Release* 2008 127, 180-187.

**ACKNOWLEDGEMENTS:** R. Dersch, M. Rudisile, C. Wack, C. Gräbedüchel, P. Rößler, J. Schäfer, U. Boudriot and J. Heverhagen were further involved in this study.