Stimulation of Bone Tissue Formation in vitro by Lactate Released from PLA Scaffolds.

Joanna Wójtowicz,1 Tomasz Ciach,2 Małgorzata Lewandowska - Szumieł1, Corresponding Author: jwojtowicz@wum.edu.pl

1Department of Biophysics and Human Physiology, Medical University of Warsaw, Warsaw, Poland
2Faculty of Chemical and Process Engineering, Warsaw University of Technology, Warsaw, Poland

Introduction
Lactate is a known stimulating factor of collagen production by fibroblasts in vivo (1) and in vitro (2). On the other hand, lactate is a product of resorption of PLA-based scaffolds used in tissue engineering (TE). Therefore, it would be useful to verify if lactate may play a role of a bioactive agent which stimulates in vitro tissue formation in TE constructs for bone regeneration.

The aims of the study were: 1) to determine if lactate stimulates collagen production by osteoblasts in vitro and 2) to prepare bioactive scaffolds of controlled lactate release in order to obtain enhanced bone tissue formation during biomaterial degradation in vitro.

Materials and Methods
Human bone derived cells (HBDCs) were cultured in lactate containing media. Cell viability/number (XTT/PicoGreen), differentiation (ALP activity, osteocalcin content) and collagen production (ELISA, hydroxyproline content) were determined. Expression of the selected genes was measured in a real-time PCR. PLA 3-dimensional scaffolds with controlled lactic acid release (determined enzymatically) were prepared by means of electrospinning. In vitro culture of HBDCs was performed within those scaffolds up to 21 days. Cell viability/number, differentiation and collagen production were measured.

Results
It was found that lactate activated collagen expression and synthesis (Fig.1A.) and additionally stimulated differentiation of the HBDCs (Fig.1B.). Stimulating and nontoxic lactate concentrations (5-25mM) were selected as desired during the controlled lactate release from the PLA fibrous scaffolds. Both cell proliferation and differentiation were confirmed in HBDCs culture within the scaffolds. Tissue-like structures were observed (Fig.2).

Discussion and Conclusions
The results confirm for the first time a stimulating effect of lactate on human osteoblast function in vitro. In particular, lactate induces collagen I production and HBDC differentiation. Controlled lactate release from resorbable scaffolds may be a useful tool in a culture of osteoblasts designated for transplantation in TE constructs. The system can be used in obtaining tissue-like constructs prior to implantation.

References

Disclosures
Authors have no commercial conflict of interest to disclose.