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Self-assembled scaffolds for cultured cells and tissues with biomedical and biotechnological applications

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Abstract

The scaffolds must possess appropriate: i) porosity and inter-connective network for mass transport and cellular 3D organization; ii) biocompatibility; iii) a suitable surface for cell attachment, proliferation, differentiation; iv) adequate mechanical properties similar to those of natural organs. Porous structures with pore size between 50 and 200 µm (adequate for cultured tissues) are required and proper chemical modification of the polymer may be needed to promote cell adhesion. We are now proposing a new series of functionalized scaffolds based on polyvinyl alcohol (PVA) cross-linked by sodium trimetaphosphate (STMP) using an original two step method.

Experimental: A volume of 100 mL of PVA (10 % solution) was first cross-linked with sodium trimeta-phosphate (STMP) under two-speed steering, until a foam was formed. Then, 1 mL of NaOH (30 %) was added and the foam was molded into 6 well plates followed by freeze-drying. Derivatized scaffolds were prepared in the same way and conditions also adding galactose, collagen, chitosan or modified starch. Scaffold strips were placed into a 12 well plates and seeded with isolated Rat (Sprague-Dawley) hepatocytes at a density of 2 x 10^6 cells/strip. The proposed method produces high porous matrices (≥ 70 %) with a porosity distribution between 50 and 1000 µm (scanning electron microscope [SEM] micrographs - Fig 1). The re-organization of the cells inside the pores looked surprisingly to tissue like structures. The porous scaffolds were able to retain hepatocytes, facilitating their ability to adhere to the support. The PVA scaffolds show hepatocyte adhesion higher than 80% and viability of more than 50% (superior to the values reported for the two-dimension [2D] cultured cells). The addition of chitosan to obtain a derivatized scaffold generated a higher efficiency of cellular adhesion in the 3D PVA micro environment, favoring interactions between the membrane proteins of cultured tissue and the matrix.

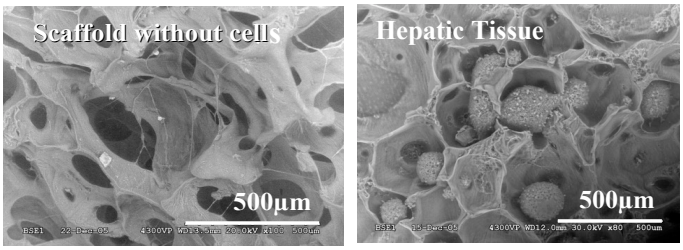

Fig. 1 – Top view of PVA-STMP-CM-Starch without cells and at 48h after inoculation of 10^6 cells (SEM accelerating voltage 15-30 kV)

Recent Publications

1. El Zein R, Ispas-Szabo P, Jafari M, Siaj M, Mateescu MA. *Molecules* 28/24 (2023) 8105.
2. Labelle MA, Ispas-Szabo P, Vilotte F, Mateescu MA. *J Pharm Sci.* 113 (2023) 725-734.
3. De Sousa Sabino, L.B., Copes, F., Saulais, S., De Brito, E.S. Da Silva Júnior, I.J.; Le, T.C, Mateescu, M.A., Mantovani, D. *Molecules* 27 (2022) 7271.
4. Leonida, M., Ispas-Szabo, P., Mateescu, M.A. (2018). *Bioactive Materials* 3 (2018) 334-340.
5. Zehtabi*F., P. Ispas-Szabo, D. Djerir, L. Sivakumaran, B. Annabi, G. Soulez, M. A. Mateescu, S. Lerouge,. *Acta Biomaterialia* 64(2017) 94-105.

Mircea Alexandru Mateescu graduated in Chemistry-Biochemistry from University of Bucharest and earned a PhD from Bucharest Polytechnic University. He is Full Professor of Biochemistry at the Université du Québec à Montreal (UQAM) Canada. He is frequently invited as visiting professor at Rome University *"Sapienza"* and at Université Paris Nord.

He has his expertise along two axes: *i)* self-assembled materials as pharmaceutical excipients for controlled drug delivery and as biomaterials for implants, xenografts or biotechnological applications, and *ii)* therapeutic copper-enzymes for treatments of inflammatory and oxidative damaging conditions.

As main achievements: more than 200 articles, 38 patents, one book, 11 book chapters and launching of Contramid®/Cross-Linked Starch - Drug Delivery: a patented technology.

Awards: ACFAS - Prize for Technological Innovation in Canada (1999); Prize Venezia: Italian Chamber of Commerce for major contributions to science and collaboration with italian universities (2012); Prize "Career in research" Faculty of Sciences – UQAM (2014) and several others. H-index 35 on Scopus.