PROACTIVE BIOMATERIALS: BIOMIMETIC INTERFACIAL PROPERTIES AND ADVANCED DELIVERY SYSTEMS

EMMANUEL PAUTHE*

BIOMATERIALS FOR HEALTH GROUP,
DEPARTMENT OF BIOLOGY,
UNIVERSITY OF CERGY-PONTOISE, FRANCE
*E-MAIL: EMMANUEL.PAUTHE@U-CERGY.FR

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Introduction

To heal and repair the human body, man has for centuries turned to biomaterials. Originally designed to be inert, contemporary applications such as tissue engineering and regenerative medicine demand biomaterials that can actively engage cellular matter, to direct and modulate the biological response, at the implant site and beyond. So, directing cell behavior is a key contemporary challenge in biomaterials science.
Since biomaterials interact with their surroundings via their surface, an attractive strategy toward truly bioactive materials is through the design of biofunctionalized coatings/interfaces. Of particular promise are three dimensional, cellularized, porous scaffold devices – with optimized interfaces to support and implant viable cells – promising breakthrough biomedical advances in the near future.

Results and Discussion

Engineering advanced materials, able to proactively and efficiently "dialogue" with surrounding tissues, is at the heart of the works developed at the University of Cergy-Pontoise, France in the Biomaterials for Health lab. Our activities are principally focused on the dynamics of extracellular matrix and biopolymer component assembly – at the molecular and supramolecular scales – in solution, at interfaces, and in biomaterials applications.
During the last decades, we made significant progress on projects that involves polyelectrolyte-based films, formed via layer-by-layer assembly.
In particular, strategies involving nanotemplating, to spatially and temporally release bioactive molecules (e.g. BMP2) [1], FIG. 1.

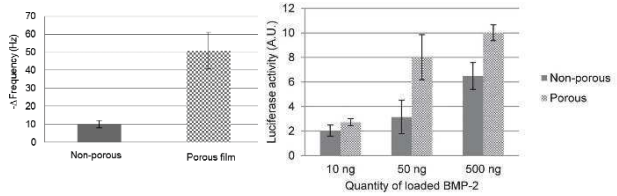

FIG. 1. Left, Quartz crystal microgravimetry measurements of BMP-2 loading onto/within cross-linked (PLL-PGA)14 (non-porous) and cross-linked ([PLL-PGA]5-PLL-NP)2-(PLL-PGA)2 exposed to THF (porous) films. Both films are incubated with 150 ng of BMP-2 (during 15 min) then extensively rinsed with buffer (10 min total). Right, Bioactivity induced by BMP-2 loaded onto/within non-porous and porous thin films. BMP-2 bioactivity is determined by measuring the luciferase expression of C2C12-BRE/Luc cells. The cells are cultured for 24 h on cross-linked (PLL-PGA)14 (non-porous) and cross-linked [(PLL-PGA)5- PLL-NP]2-(PLL-PGA)2 exposed to THF (porous) films loaded with 10, 50 or 500 ng/L of BMP-2. The results are normalized with the controls made in the absence of BMP-2.

We also developed research to generate intrafilm fibronectin placement, for films with exceptionally high matrix protein content [2], FIG. 2.

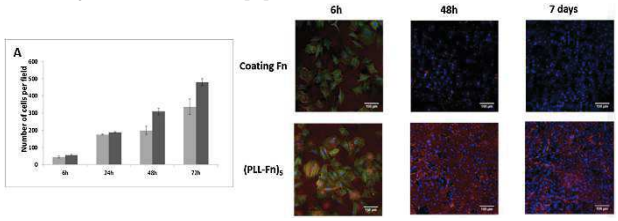

FIG. 2. (A) Cell adhesion and proliferation on the Fn monolayer (light grey) and the (PLL-Fn)5film (dark grey) after 6 h, 24 h, 48 h and 72 h. The experiment was performed three times independently, and the vertical lines represent the standard deviation. (B) Fn reorganization by MC3T3-E1 pre-osteoblastic cells. Cells were cultured for 6 h, 48 h and 7 days on either a Fn monolayer or a (PLL-Fn)5film, and stained for nuclei and actin. Fn was fluorescently labeled with Alexa Fluor 568.

These strategies represent appealing bioactive systems able to enhance cell adhesion, spreading, proliferation and differentiation, and offer great potential toward a variety of cell contacting applications, including antimicrobial.
On the other hand, we have proposed the engineering of a hydrogel scaffold glucose delivery system for enhancing mesenchymal stem cells survival. Such a system addresses a significant tissue engineering challenge: the massive death of transplanted cells that typically occurs following engraftment using currently available scaffolds. By supplying glucose in situ as a metabolic fuel for Mesenchymal Stem Cells (MSCs) in severe hypoxia, this new scaffold is shown to significantly enhance MSC survival.

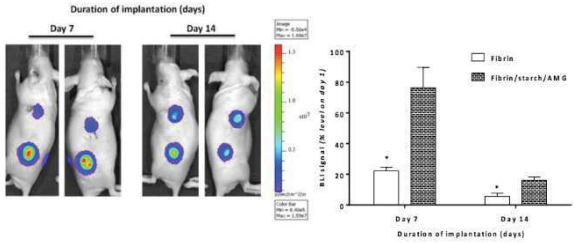

FIG. 3. Bioluminescence imaging and quantification of luciferase-labelled hMSCs loaded in fibrin and in fibrin/starch/AMG hydrogels, after subcutaneous implantation in nude mice.

References

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[2] A. Gand, M. Tabuteau *et al.,* Colloids Surf B Biointerfaces. 156 (2017) 313-319.
[3] J. Paquet, J. Boisselier *et al.,* Tissue Engineering Part A. 22 (2016) 22-