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Bioinspired superhydrophobic patterned surfaces as chips for high-throughput analysis of biomaterials viscoelastic properties

MB Oliveira[1,2], GM Luz[1,2] and JF Mano[1,2]
[1]*3B's Research Group – Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, AvePark, 4806-909 Taipas, Guimarães, Portugal;* [2]*ICVS/3B's - PT Government Associate Laboratory, Braga/ Guimarães, Portugal*

Tissue-constituent cells are usually anchorage-dependent cells. Their viability is compromised when they are in a fluid suspension. The adhesion of these cells in the body occurs in solid elastic tissues. Mechanical properties of biomaterials were reported to have a role in modulating cells response, affecting their function and structure, as well as the direction of differentiation [1]. Cells like neurons, muscle cells, mesenchymal stem cells are examples of cells previously reported to be dependent on substrates stiffness. It is well known that interactions occurring in the area of tissue engineering and regeneration are not easily predictable. As such, we previously developed arrays of wettable spots in polystyrene superhydrophobic surfaces in order to use these structures as high-throughput platforms for biomaterials development. We patterned biomaterials precursors in the wettable spots, keeping them confined in such regions by the wettability contrast caused by the superhydrophobic surroundings. The method was used to study several cells-biomaterials interactions in 3D milieu. We studied the effect of distinct combinations of biomaterials in encapsulated cells [2], as well as cells-porous scaffolds interactions [3]. Adapted chips based on the same concept were also used to develop an on-chip drug-release quantification device [4]. By using the same type of chips developed for cells-biomaterials interactions studies, we aimed to adapt the system for the rapid study of miniaturized biomaterials viscoelastic properties. Most living tissues show a viscoelastic behavior, i.e., besides showing a particular stiffness, they have the ability to dissipate energy during cyclic stimulation. We used superhydrophobic chips to pattern miniaturized hydrogels, and adapted a mechanical dynamic analyzer (DMA) so on-chip viscoelastic properties of those materials could be assessed under physiological-like conditions. For the proof-of-concept we performed a three-factor combinatorial study targeting bone tissue engineering applications. A system consisting of distinct combinations of polymeric matrix concentration, crosslinking was systematically studied. We believe this system will facilitate the on-chip rapid study of miniaturized biomaterials for the future discovery of the role of the viscoelastic properties of tissues and materials in cell response.

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High-throughput drug screening using cell spheroids in superhydrophobic patterned chips

MB Oliveira[1,2], AI Neto[1,2], MI Rial-Hermida[3], C Alvarez-Lorenzo[3] and JF Mano[1,2]
[1]*3B's Research Group – Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, AvePark, 4806-909 Taipas, Guimarães, Portugal;* [2]*ICVS/3B's - PT Government Associate Laboratory, Braga/ Guimarães, Portugal;* [3]Department. Farmacia y Tecnología Farmacéutica, Universidad de Santiago de Compostela, 15782-Santiago de Compostela, Spain

High-throughput studies in biotechnology areas such as drug screening and tissue engineering have been carried out mainly in 2D environment. However, low clinical and biological relevance of 2D models is well known. Both in tissues and tumor masses, cells lie in a 3D configuration organized in the self-secreted microenvironment: the extracellular matrix (ECM). In this milieu, cells interact in a totally natural manner, without the interaction of foreign factors, such as materials. The demand for studies using organotypic models is increasing, in order to improve the relevance of the findings achieved in these areas of study. A solution to create such organotypic models is the in vitro construction of cell spheroids. These are micro-masses of cells formed from a cell suspension, where the attachment of cells to any surface is not promoted. As such, cells tend to attach between themselves and form an organized mass, constituted by cells in combination with ECM. Some types of spheroids are grown in order to mimic tumor models: the living spheroid structure contains a necrotic core, similarly to the native tumors. Cell spheroids are also useful as models for the development of complex microtissues [1], and can also be used as building blocks of larger tissues. Several methods to produce cell spheroids are reported in the literature. The hanging drop method is one of those methods: the cells are pulled to the concave bottom of a hanging droplet by gravity effect, and tend to start the natural organization by cell-cell attachment and production of ECM. We propose the use of superhydrophobic surfaces patterned with wettable regions as platforms for the affordable and scale-up production of cell spheroids by the hanging drop method. Moreover, we used the platform - whose wettable regions are transparent and whose drop has its surface totally exposed to the external media allowing its facilitated manipulation – as high-throughput screening platform for drug testing and on-chip cell response analysis by microscopy. For the proof-of-concept we dispensed cell suspensions of distinct cell types (L929 and SaOs-2) with different cell concentrations in the array of wettable regions of the chips. We tested the effect of a cytostatic drug used in clinical practice (doxorubicin), also dispensed in a combinatorial logic in each spot of the chip. By on-chip microscopy analysis we proved the suitability of such platforms for drug screening using tumor-like models.

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