Application of plasma technologies to biological interface design

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One of the major challenges for the development of bio interfaces relies on the ability to design solid surfaces with controlled interactions with the biological entities. Surface functionalisation techniques can provide those bio-interfaces appropriate physico-chemical properties enabling the control of the conformation and activity of the immobilized biomolecules. The subsequent technological step is the combination of different bio-functions in micro- and nano-patterns on the surfaces. For instance, structuring the surface in adhesive and non adhesive zone in order to preferentially guide the cell growth is one of the most promising tools for the development of 'cell on a chip' devices and for tissue engineering. The requirement of further integration and the study of the special behaviour of the biomolecules interacting with nanostructures have been the two main motivations for the development of submicron patterning techniques. Plasma assisted deposition techniques are interesting methods to produce functionalized surfaces with controlled micro- and nano-patterns: they provide high-level functionality with good stability on different substrates and are compatible with different micro- and nano-patterning techniques.

In this work we show some examples of micro- and nano-functional surfaces provided by plasma processes in combination with Electron beam lithography, proteins micro-contact printing and micro-spotting, and their application as platforms for cell cultures and biosensing.

Nanopatterned surfaces were produced by a spatial arrangement of different functional domains by a combination of plasma polymer and E-beam lithography techniques. In particular bio-adhesive nano-spots in a PEO-like anti-fouling matrix have been produced (figure 1). We show that these chemical nano-patterns are able to immobilize proteins selectively in the adhesive nano-domains, leaving the anti-fouling matrix clear of biomolecules. We show with different methods (SPR and AFM) that nano-patterned surface constrains the immobilization of the antibodies in a biological reactive configuration, thus significantly improving the surface interaction as compared to more conventional non-patterned surfaces.

Two methods for protein patterning have been used as platform for cell patterning. Microcontact contact printing has been used as technique to transfer fibronectin through conformal contact, while piezoelectric deposition has been used as non-contact technique for producing arrays of fibronectin. Plasma deposited Poly(ethylene) oxide-like, PEO-like films have been used as non-fouling background to achieve the bioadhesive / biorepellent surface contrast. Both methods allow the direct fabrication of protein arrays on a non-fouling substrate and the formation of a stem cell pattern (figure 2). Microcontact printing produced fully packed homogeneous fibronectin patterns, much denser than microspotting patterns. In microspotting, the density of the protein layer was lower, but the immunorecognition of fibronectin targeted antibodies, as well as the cell density on the fibronectin spots could achieve similar levels to microcontact printing, thus were equally functional in both tested methods.

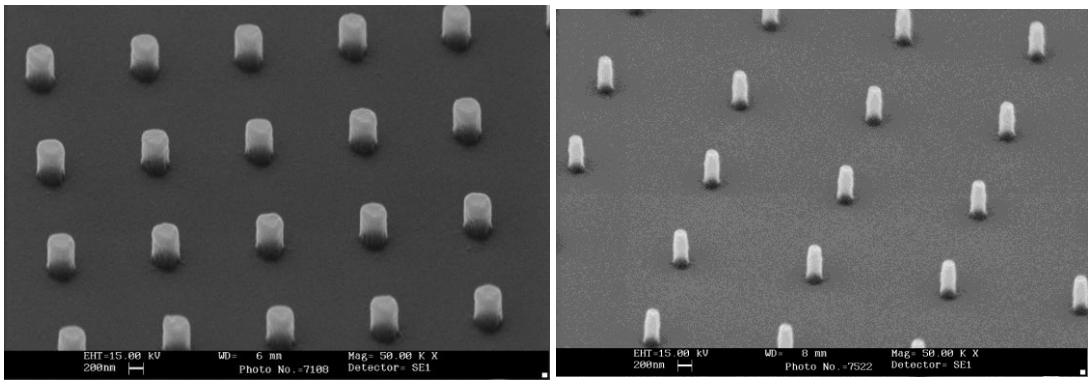

Figure 1. Plasma polymerised Acrylic acid nanostructure in a PEO-Like background.

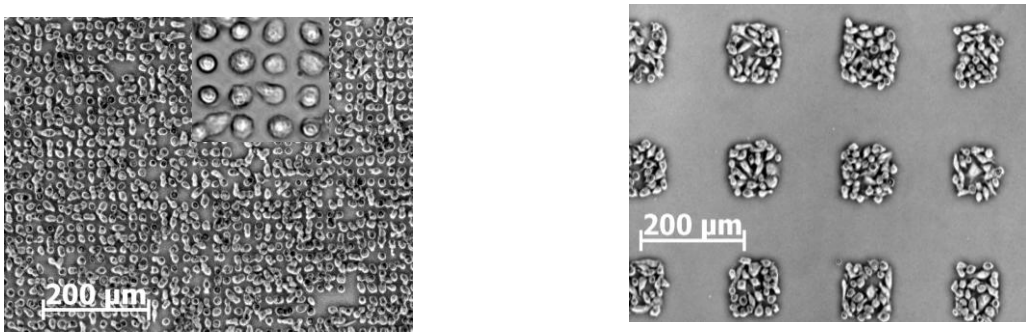

Figure 2: Human Umbilical Cord Blood Neural Stem Cell micro patterning.