

SELECTIVE MOLECULAR ASSEMBLY PATTERNING - A NEW APPROACH TO MICRO- AND NANO-CHEMICAL PATTERNING OF SURFACES FOR BIOLOGICAL APPLICATIONS

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INTRODUCTION: The repertoire of receptors and signalling markers expressed on the surface of cells *in vivo* is nothing else than a complex top-chemical pattern, the function of which is to elicit response from other cells. Our ability to investigate and manipulate the interaction between cells and extra-cellular environment (extra-cellular matrix or an implant) depends crucially on the availability of suitably patterned surfaces. Patterned surfaces have already been shown to affect growth, differentiation, and death of cells^{1,2}. Here, we present a novel techniques—Selective Molecular Assembly Patterning (SMAP)—for creating various chemical patterns by means of selective self-assembly on oxide surfaces.

METHODS: Standard photolithography was used to create patterns of titanium oxide within a matrix of silicon oxide. Using the fact that ordered SAMs of alkane phosphates form on the TiO₂, but not on the SiO₂, surfaces, by self-assembly from aqueous solutions, the TiO₂ structures were rendered hydrophobic and hence protein-adsorbing. Poly-L-lysine-g-poly(ethylene glycol) (PLL-g-PEG)^{3,4} was used to render the exposed SiO₂ protein-resistant, thus creating a contrast with respect to protein adsorption. X-ray photoelectron spectroscopy and imaging time-of-flight secondary ion mass spectrometry were used to characterize the surfaces in vacuum, while fluorescence microscopy was used for studies in aqueous media.

RESULTS: Quantitative XPS as well as qualitative ToF-SIMS results proved that dodecylphosphate adsorbed on the TiO₂ surface forming a self-assembled monolayer⁵, leaving SiO₂ bare. Subsequent modification with PLL-g-PEG resulted in protein-adhesive patches (TiO₂/DDP) in a matrix resistant to protein adsorption (SiO₂/PLL-g-PEG), as shown in Figure 1A. Human foreskin fibroblasts (HFF), incubated with such substrates in serum, exhibited clear preference towards attaching to the protein-adhesive (hydrophobic) areas (Figure 1B), where they form focal contacts. The non-adhesive areas remained cell-resistant for up to two weeks.

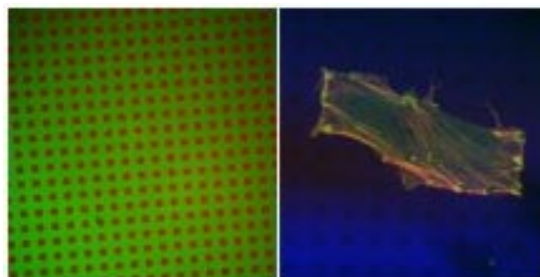


Fig. 1: A. Left: Rhodamine labelled streptavidin adsorbed to 5x5 μm TiO₂/DDP patches (red) surrounded by fluorescein labeled PLL-g-PEG (green) matrix. B. Right: HFF, incubated for 20h in serum on a patterned surface, fixed, and stained for actin (red) and vinculin (green).

DISCUSSION & CONCLUSIONS: Protein adsorption studies conclusively established that the resulting surfaces present protein adhesive (the TiO₂/alkane phosphate SAM region) and non-adhesive (the PLL-g-PEG-coated SiO₂) areas. Human foreskin fibroblasts were shown to selectively attach to the protein-adhesive areas. Current research is focusing on creating patterns in the sub-micrometer range and evaluating the response of a variety of cell types to pattern geometry and chemistry. The high quality, reproducibility, simplicity, and versatility of SMAP make it a promising technique for both scientific and industrial applications in the context of biomaterial and biosensor surface technology.

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