Combinatorial Screening of Cell Response to Surface Chemistry Gradient on a Soft Biomaterial

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Statement of Purpose: Factors that influence cellular response are both numerous and complex. A combinatorial high throughput platform allows screening of different biological, chemical and mechanical properties in a systematic and efficient manner in comparison with individual testing of parameters. In this manner positive hits for a specific biomedical application may be identified from a large field of variables.[1,2] A combinatorial approach has been reported for screening of dendritic cells, smooth muscle cells and osteoblasts on glass surfaces with chemical or ligand density gradients.[3-5] Presented in this study is Human Umbilical Vein Endothelial Cell (HUVEC) response to polydimethylsiloxane (PDMS), a soft biomaterial with tunable elasticity engineered to have a surface chemistry gradient.

Methods: Cross-linked networks of PDMS were prepared using Sylgard®184 Elastomer Kit (Dow Corning). Surface chemistry gradients were generated by Ultraviolet Ozone Oxidation (UVO) of a hydrophobic monolayer (chlorodimethyloctylsilane-Sigma Aldrich) on glass[4,5] and PDMS substrates. The gradients were characterized using water contact angle measurements. Following sterilization, HUVECs were seeded on fibronectin coated gradient substrates. Automated microscopy (Nikon NIS Elements, Melville NY) was used to capture and analyze images of fluorescently stained (AF488 C_5-maleimide, Invitrogen) cells.

Figure 1(a) Water droplet profiles along PDMS substrate

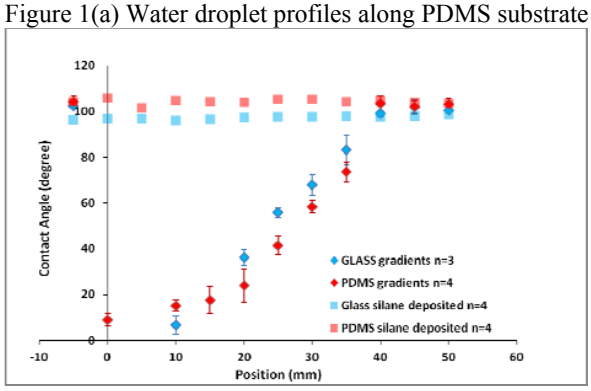

Figure1(b)Contact angle measurements demonstrate range in surface wettabilities on glass and PDMS substrates

Results: In this study, uniform silane chemistry (~102°) on glass and PDMS substrates were converted to linear chemical gradients after UVO treatment (Figure 1). Water contact angle measurements ranged from <10° to ~100°, demonstrating the monotonic change in surface chemistry. HUVEC spreading on PDMS gradients increased as a function of position (primary x-axis) that corresponds to increasing hydrophobicity (secondary x-axis) along length of gradient (Figure 2). The spreading on hydrophobic end of PDMS is approximately twice as much on the hydrophilic end of gradient. Interestingly, this trend appears to be much weaker on rigid glass substrates with similar surface chemistry gradients. As expected, plain glass slides did not show any specific trend, indicating that the observed trends in cell morphology are in response to the underlying gradients and not an artifact of the cell seeding procedure.

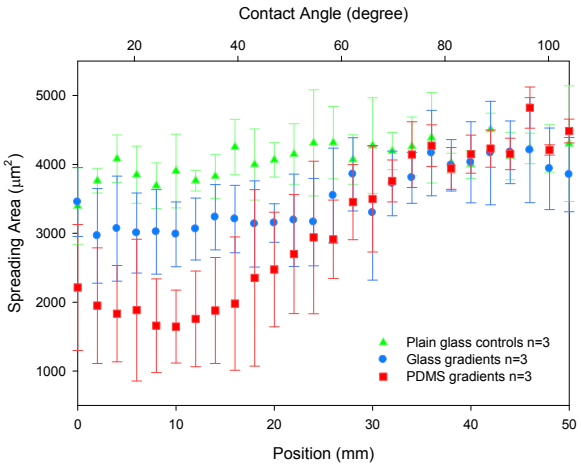

Figure 2(a). HUVEC spreading area on gradient materials

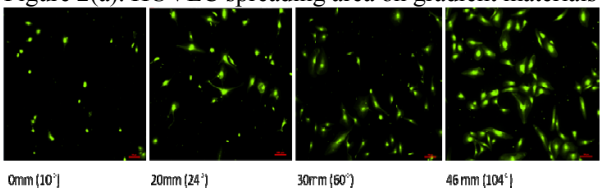

Figure 2(b). Images of HUVEC along PDMS gradient

Conclusions: Preliminary results are presented here showing the response of HUVECs to a surface chemistry gradient and indicate a strong dependence of cell adhesion and spreading on the hydrophobicity which is enhanced on soft PDMS substrates. Future experiments will probe underlying mechanisms such as protein adsorption and conformation that influence cell morphology. A combinatorial material that displays both a range in surface chemistry and mechanical stiffness will be fabricated to study comprehensive HUVEC cell response. The long term objective is to develop instructive biomaterials with optimized properties that precisely control cell adhesive interactions to direct cell fate.

References:

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