Targeted nanopatterning for medical applications

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The function and fate of cells are influenced by many different factors, one of which is surface topography. There are numerous of examples in the literature of fabricated micro- and nanotopographies used to study biological systems. The majority of the studies have worked on relative few shapes and patterns, thus systematic studies of topography and cell response have typically been limited to single cell types and a small set of topographical variations. Recently there has been a move towards significantly larger systematic studies, now coined *materiomics*[1]. Such studies depend on making 100s or 1000s of different topographies on the same sample and then analyse the cell responses using high-content imaging[2]. The fabrication of such samples is only really possible using lithographic processes where design files are generated by computer algorithms and then realised by either photo- or electron beam lithography. That process provides binary patterns across the sample. We have taken a different approach and in this presentation we will show our advances towards high-content topographical surfaces for screening cell-substrate interactions.

The aim has been to develop a substrate presenting a continuous range of different topographic features. For example, we have used photolithography to define a linear grating where the pitch changes continuously along one axis, *Figure 1*, while the height of the gratings changes along the other axis. The height variation is fabricated by plasma polymerisation of a sacrificial etch mask. This provides a non-binary pattern where anywhere on the pattern there will be a unique combination of height and pitch[3]. We have used this substrate to investigate the response from different cell types and as is seen in Figure 1, fibroblasts and endothelial cells respond differently. In a different study, we use the same sacrificial mask on an array of nanopillars. Here the height of the pillars changes along one axis and by co-culturing two cell types we were able to demonstrate separation of the cells and at the same time find the optimal conditions for cell adhesion[4]. Common for all our samples is that they are fabricated as polymer substrates by injection moulding enabling large number of samples to be produced.

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[1] S.W. Cranford et al, Advanced Materials (2013)
[2] H.V. Unadkat et al, PNAS (2011)
[3] P.M. Reynolds et al , Small (2012)
[4] P.M. Reynolds et al, NanoLetters (2013)

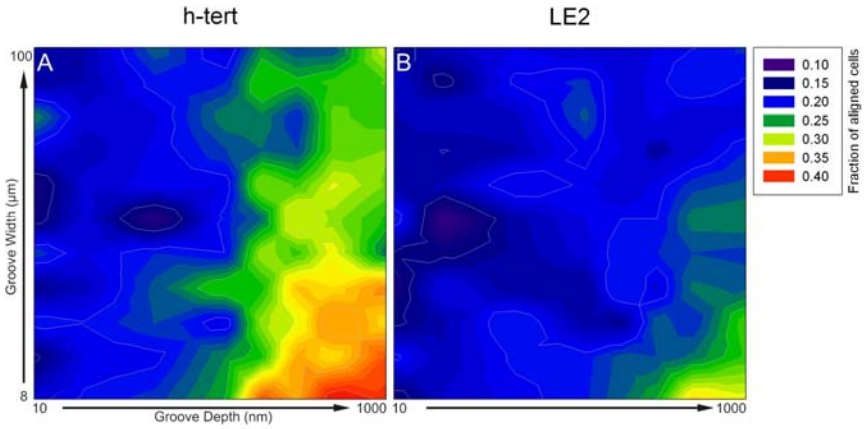

Figure 1: Left, fibroblast cells cultured on a dual gradient substrate. The colour scaling indicates the degree of cell alignment with respect to the underlying micropattern. Right, same experiment for endothelial cells.

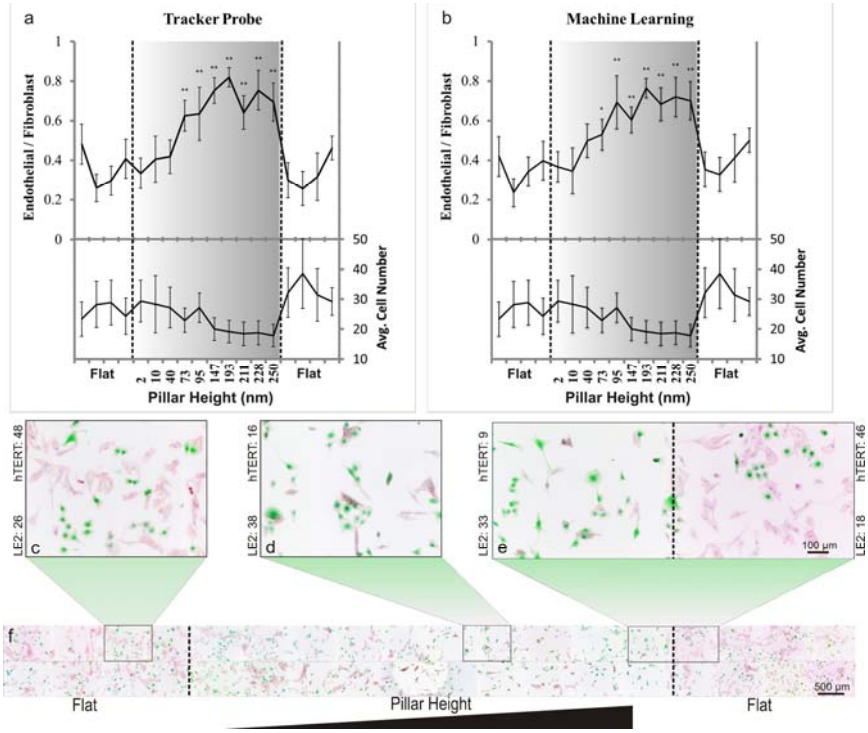

Figure 2: Response of fibroblast and endothelial (LE2) cells in co-culture to a gradient of nanopillar height is shown. From this analysis, we can suggest that a nanopillar height in excess of 75 nm is sufficient to induce a statistically significant change in the ratio of endothelial / fibroblast cells on the nanopattern.