Controlling Cell Behaviour using Nanopatterned Surfaces

N. Gadegaard, M Dalby, C Wilkinson and M Riehle
Centre for Cell Engineering, University of Glasgow, Glasgow, G12 8QQ, Scotland

There is a growing interest in fabricating biomedical materials with increased functionality to meet the demands for the next generation of medical devices [1]. It has become apparent that by carefully controlling the surface of an implant or a scaffold, its performance can be enhanced. This increased functionality can be achieved by chemical coatings or by applying specific topographies. We have developed particularly effective model system to study the behaviour of cells on substrates with well-defined nanotopographies. Using electron beam lithography we are able to write large areas (>1 cm^2) of high density dots (up to 10^{10} per cm^2) [2]. By using a single exposure approach in our electron beam lithography tool we have precisely control over diameter, pitch and even geometric arrangement. This has allowed us to systematically investigate the importance of feature size as well as geometric arrangement of such nanodots. For the cell experiments we use hot embossing of a silicon master or nickel shim in a thermoplastic polymer. This provides an easy and fast method of preparing the required number of samples for the biological experiments.

Surfaces with highly ordered nanopits low provide low adhesive substrate for different cell lines, Figure 1. Although the surface area is typically reduced by 15%, the reduced cell adhesion is far greater [3]. If msenchymal stem cells are culture on similar surfaces but with differing geometric layout of the nanopits we have observed that such cells respond differently despite the available surface area is practically identical, Figure 2. Moreover, if we reduce the degree of order of the nanopits the stem cell will specifically differentiate into bone forming cells [4]. This is normally only achieved by treating the cells with hormones. Finally, we will give an example of how our knowledge of specific cell response from different topographic patterns can by combined and form a new type of all engineered tissue scaffold for small blood vessel repair.

[1] K. Seunarine *et al.*, Nanomedicine **1**, 281 (2006).
[2] N. Gadegaard *et al.*, Microelec. Eng. **67-8**, 162 (2003).
[3] A. S. G. Curtis *et al.*, IEEE Transactions on Nanobioscience **3**, 61 (2004).
[4] M. J. Dalby *et al.*, Nature Materials **6**, 997 (2007).

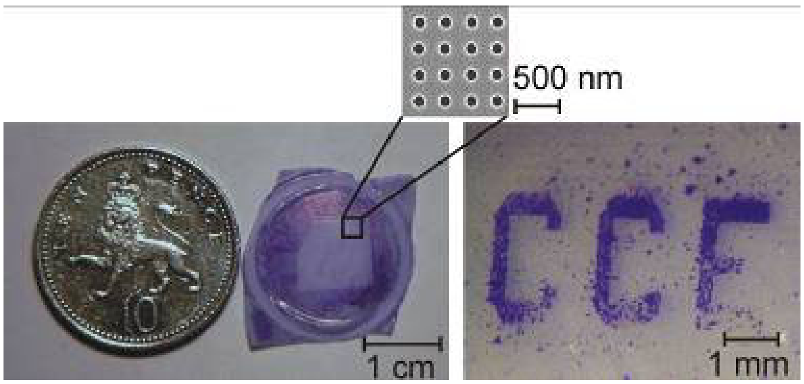

Figure 1. Left, photograph of cells on a nanostructured substrate. The cells are stained blue and as can be seen the patterned area (1x1 cm^2) is free of cells. Right, cells are confined to the flat region making up the letters CCE. Insert, SEM of the nano patterned region of 100 nm deep pits with a diameter of 120 nm on a 300 nm pitch.

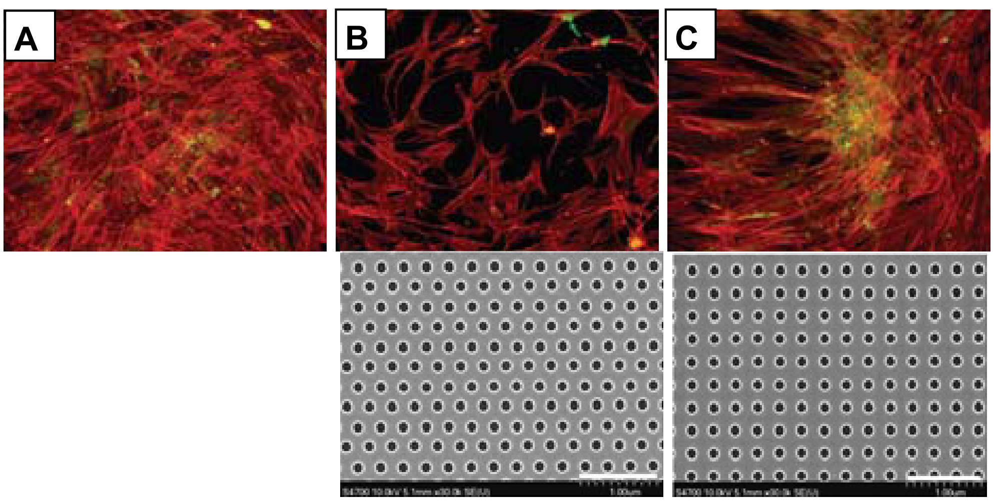

Figure 2. Mesenchymal stem cells culture on different substrates. (A) On a flat control surface the cells adhere well, whereas a (B) hexagonally and (c) square ordered symmetry have significant reduced adhesion.