Synergistic Cell Type Specific Effect of Substrate Topography and Shear Flow on Cellular Alignment

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INTRODUCTION: Sever injury to the spinal cord will lead to permanent damage as the spinal cord is not able to regenerate itself. It has been proposed that the repair of spinal cord injury will require a combination of strategies such as integrating the biological influence of glial cells together with physical guiding cues on three-dimensional (3D) scaffold. Before preparing glial cells within in complex 3D scaffolds at relatively large scale for spinal cord injury, various scale-up issues need to be addressed. Thus, the aim of this project was to look at the influences of substrate topography and medium perfusion on various cellular behaviours using mini-bioreactor systems.

METHODS:
Cell culture: Type I astrocytes were purified and cultured in DMEM supplemented with 10% foetal bovine serum (FBS) and L-glutamine (2mM) as described previously¹.

Mini-bioreactor system: A mini bioreactor system consisted mainly of two commercially available tissue culture plates situated in two plastic boxes respectively, an 8-channel Ismatec peristaltic pump, 8 medium reservoirs (2.5ml) and 3-way valves. Corresponding to the 8 channels of the peristaltic pump, up to 8 perfusion chambers were fabricated and seeded with either astrocytes or fibroblasts. The entire system was then placed in a tissue culture incubator (37°C, 95% air/5% CO₂) and the cells subjected to medium perfusion with varying flow rates for defined periods of time.

RESULTS
Serial perfusion cultures of astrocytes and/or fibroblasts using the mini bioreactor system indicated that the supply of medium was crucial for the survival of the cells in closed mini chambers (volume = 0.125 ml). Systematic investigations demonstrated that aligned astrocytes and fibroblasts can be achieved on micro-grooved ε-polycaprolactone (PCL) substrates, and that this alignment is maintained throughout perfusion culture. More interestingly, it was also found that medium perfusion increased alignment of fibroblasts and influenced placement compared to static as more fibroblasts were observed to ‘hide’ in the grooves and could only rarely be found on ridges (Fig 1). In contrast astrocytes although aligned were not significantly influenced by flow (Fig 2).

DISCUSSION & CONCLUSIONS:
Our research demonstrated that:
(A) The susceptibility to respond to a combination of microtopographic, and physical cues is cell type dependant, with fibroblasts being responsive, whereas the astrocytes were not.
(B) The mini bioreactor systems can be used for systematic investigation of various scale-up issues in tissues engineering.

REFERENCES:

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