302g Building a Tissue Engineered Microfluidic Bioreactor Array for High-Throughput Assays

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As the progress of functional genomics, the number of drug candidates has by far outgrown the present capability of cytotoxicity studies. In addition, early discoveries of toxic side effects of drugs in test can greatly reduce the risk of a lengthy and expensive drug development process. Increasing interest in toxicity study systems in vitro has made cell-based platforms an attractive approach to uncovering the toxicity effects at cellular and subcellular levels. However, conventionally, cells cultured statically on 2D surfaces may not well exhibit authentic responses upon external stimulation. We have designed and fabricated a mcirofluidic device using multiple layers of poly(dimethylsiloxane) (PDMS) through photolithography and replica molding. Each layer was designed to specifically serve part of a network of microfluidic channels for medium flow, drug serial dilution, mixers and cell culture chambers with the same dimension as the round wells of a 384 well plate. Tissue engineering scaffolds were placed in the chambers for three dimensional cell cultures on the chip. The alignment and bonding of different PDMS layers were investigated. The fluid ports were also engineered for prolonged medium flow and for convenience of the chip to be scanned within a 384 well plate reader. Optimal designs for uniform fluid distribution in the highly parallel system were also studied. Computational fluidic dynamics was also explored for the simulation of the flow rate and mass transport properties of serial dilution channels, cell culture chambers, mixers and overall fluid distribution with FluentTM. The microfluidic bioreactor array was designed to test the effects of 6 different concentrations of a drug with controls on two different types of cells in a perfusion 3D culture without interference. The numbers of cell types and drugs for the test can be easily expanded with similar designs. In this study, embryonic stem cells stably transfected with fluorescent proteins cultured in the microfluidic bioreactor array were studied for high throughput assays of drugs. The test results based on the cellular fluorescence intensity change caused by the drugs will be presented in the paper.