World Academy of Science, Engineering and Technology International Journal of Biomedical and Biological Engineering Vol:11, No:07, 2017

## Shear Stress and Oxygen Concentration Manipulation in a Micropillars Microfluidic Bioreactor

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Abstract: Microfluidics is a promising approach for biomedicine cell culture experiments with microfluidic bioreactors (MBR), which can provide high precision in volume and time control over mass transport and microenvironments in small-scale studies. Nevertheless, shear stress and oxygen concentration are important factors that affect the microenvironment and then the cell culture. It is presented a novel MBR design in which differences in geometry, shear stress, and oxygen concentration were studied and optimized for cell culture. The aim is to mimic the in vivo condition with biocompatible materials and continuous perfusion of nutrients, a healthy shear stress, and oxygen concentration. The design consists of a capture system of PDMS micropillars which keep cells in place, so it is not necessary any hydrogel or complicated scaffolds for cells immobilization. Besides, the design allows continuous supply with nutrients or even any other chemical for cell experimentation. Finite element method simulations were used to study and optimize the effect of parameters such as flow rate, shear stress, oxygen concentration, micropillars shape, and dimensions. The micropillars device was fabricated with microsystem technology such as soft-lithography, deep reactive ion etching, self-assembled monolayer, replica molding, and oxygen plasma bonding. Eight different geometries were fabricated and tested, with different flow rates according to the simulations. During the experiments, it was observed the effect of micropillars size, shape, and configuration for stability and shear stress control when increasing flow rate. The device was tested with several successful HepG2 3D cell cultures. With this MBR, the aforementioned parameters can be controlled in order to keep a healthy microenvironment according to specific necessities of different cell types, with no need of hydrogels and can be used for a wide range of experiments with cells.

Keywords: cell culture, micro-bioreactor, microfluidics, micropillars, oxygen concentration, shear stress

Conference Title: ICMN 2017: International Conference on Microfluidics and Nanofluidics

**Conference Location :** Prague, Czechia **Conference Dates :** July 09-10, 2017