ON-CHIP CELL GYM

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ABSTRACT

A novel microfluidic system for applying cyclic pressure to cells during incubation is developed and tested in this work. The cyclic pressure generates stress stimulus to the cells, and is named "Cell Exercise" in this work. The goal of this paper is to design an "On-Chip Cell Gym" where we can observe what happens during the cell exercise in real-time. We design the cell gym on a PDMS chip composed of two parallel chamber arrays, so that we can directly observe the difference with and without Cell Exercise. Cells in one group of chamber is cultured under cell exercise mode and the other one is under none cell exercise mode. Dramatic growth of cell stress fibers is observed in the group of cell exercise with respect to the group without any exercise.

INTRODUCTION

"Cell Stress Test" is known as a test performed by imparting periodic stress to a cell until it loses its deformability eventually [1], [2], [3]. Instead of causing damage to a cell, "Cell Exercise" introduces a relatively gentle stress to cells for assisting cell growth during incubation, and the cells with such exercise are found having improved elasticity. Figure 1(a) illustrates the idea of cell exercise with an analogy of a human doing push-ups. Figure 1(b) and (c) explain how cells are cultured under atmospheric pressure and under cell exercise, respectively. The pictures on the right of Figure 1 are examples of cultured cells, and it can be seen that the cells under Cell Exercise are bigger than those under constant atmospheric pressure. We would like to know what is happening in the cell level during the Cell Exercise. This is the motivation of this work.

EXPERIMENTAL

An important issue is how to simultaneously observe cell groups cultured with and without Cell Exercise. To solve this issue, we design the cell culture device as shown in Figure 2. The chamber arrays are placed in symmetry to the central line, and they are connected to two independent microfluidic channels. Through this device, we can impart pressure to cells with different pressure sources. This configuration allows us to simultaneously observe two cell groups. During the test, the cells are firstly fed from the inlets, and the cells are gradually settled on the bottom of the chambers due to gravity. After the cells attach to the chamber, the designated frequency of cyclic pressure starts to apply to one side of chamber array while the other side is open to atmosphere as the control group. Figure 3 shows a schematic view of the experimental system which is composed of a compressor, a pressure sensor, a microfluidic chip, and a camera for recording the cell responses. Human smooth muscle cells are used for experiment. As for cell exercise, the pressure of 180 kPa and 110 kPa is applied.

RESULTS

Figure 4 shows preliminary results where the pressure cycling between 180 kPa and 110 kPa every 250 seconds. From Figure 4, we can see a reasonably well controllability in pressure where an error is roughly less than 1% with

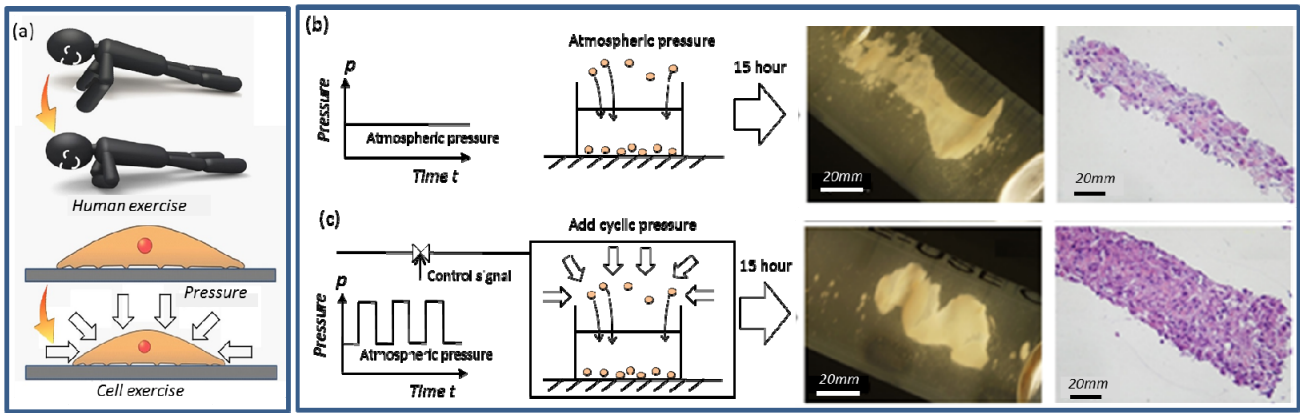

Figure 1: Overview of Cell Exercise. (a) An analogy and a conceptual illustration of the Cell Exercise. Pressure stimulus applied to a cell is like human doing pushups. (b) Experimental results of cultured cell sheet under atmospheric pressure. (c) Experimental results of cultured cell sheet under cyclic pressure, the Cell Exercise.

respect to the target value. Figure 5 shows an example of cell growth under the cell exercise after 0 hour, 6 hours and 12 hours. It demonstrates the feasibility of cell incubation in the device. Figure 6 shows fluorescence images of the cultured cells from each chamber array. Figure 6(a) and (b) are under atmospheric pressure and cell exercise, respectively. The stress fibers are colored in green, and we can see greater amount of stress fibers after cell exercise. We believe that this is the reason why we can obtain cells with greater size under cell exercise.

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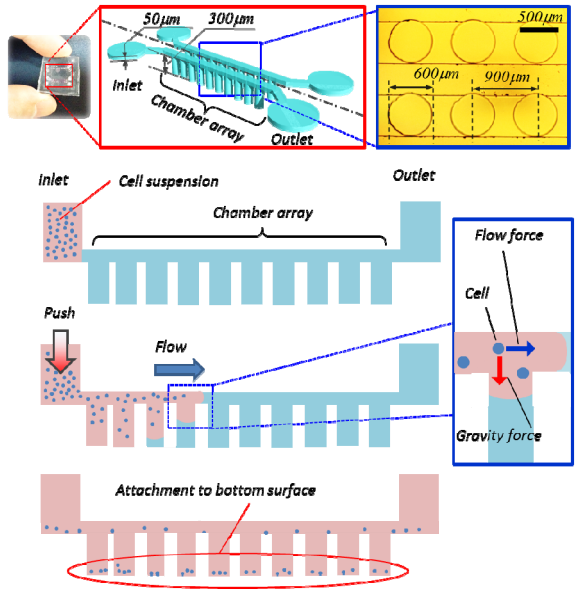

Figure2: Microscopic view and schematic of the microfluidic device for the On-Chip Cell Gym. Microfluidic device consists of a chamber array and a channel. Cells are fed from the inlet and settle at the bottom of the chamber array by gravity.

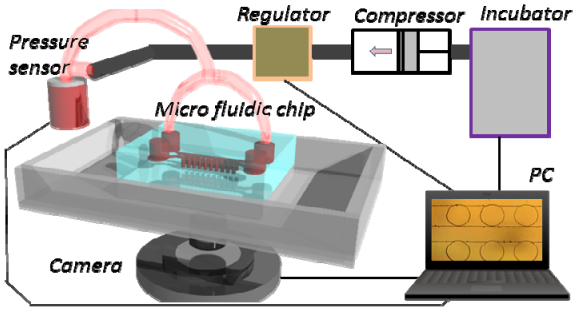

Figure 3: A schematic view of the experimental system. This system allows us to apply loads to cells with different cyclic pressures for Cell Exercise.

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CONTACT

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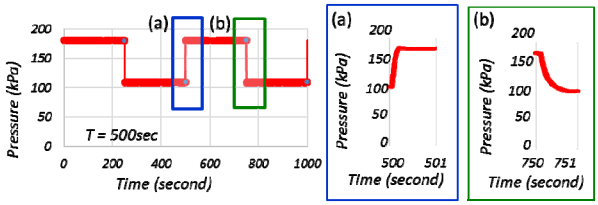

Figure4: The performance of pressure control in Cell Exercise. (a) A close view of increasing pressure. (b) a close view of decreasing pressure.

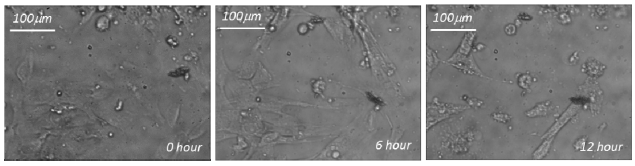

Figure5: Example images of cells in the On-Chip Cell Gym. The On-Chip Cell Gym provides the possibility of realtime observation during Cell Exercise.

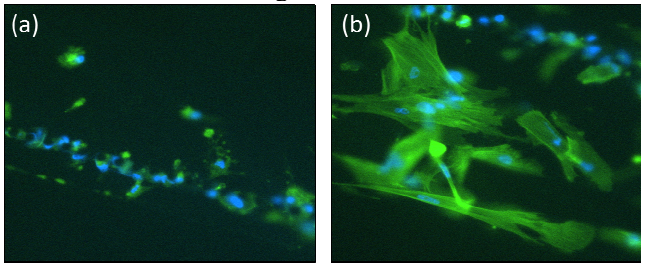

Figure 6: The fluorescence images of the cultured cells without and with Cell Exercise. (a) Without Cell Exercise. (b) With Cell Exercise.