Cell Culture on MEMS Materials in Micro-Environment Limited by a Physical Condition

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Abstract— We propose an integrated micro cell culture system to control physical conditions in a micro-environment. We quantitatively evaluated the cytotoxicity of commonly-used MEMS materials, i.e. Glass, SU-8, Polystyrene, and PDMS, by using the proposed system. In consequence, these materials were not seen the cytotoxicity regarding the proliferation. Since the cellular adhesiveness and the proliferation were correlate roughly with the surface energy. So, the surface energy is one of the important parameters for evaluating the cytotoxicity of MEMS materials.

Keywords- cell culture; cytotoxicity; microchannel; micropump

I. INTRODUCTION

In BioMEMS field, cell culture in a microchannel have been focused for controlling the local environment around cells. There are several factors that influence for the cell culture in the microchannel. The influences are mainly divided into two factors, physical and chemical factors. The conventional studies about the cytotoxicity evaluated complex effects with these chemical and physical factors such as the channel material, the cell concentration, the channel dimension, the pressure and the flow rate [1, 2]. So, it has not been individually clarified that each chemical/physical factor affect the cytotoxicity. In this study, we propose an integrated micro cell culture system and strictly control the physical influence to evaluate the cytotoxicity of the channel material.

By integrating the total perfusion system on a chip, the proposed device has good portability and controllability for each separated factor in the micro-environment. A cross-sectional view of a culturing microchannel is shown in Fig. 3. To evaluate the adhesiveness and the proliferation potency, HeLa-H2B-GFP cells are cultured in the microchannel. Number of cells was counted by image analysis in fluorescence observation images as shown in Fig. 4.

II. INTEGRATED MICRO CELL CULTURE SYSTEM

The factors affect the cells in a microchannel are illustrated in Fig. 1. Since the cell culturing microdevice are made of novel materials and a culturing chamber is closed to a small space, the physical and/or chemical factors for cell culturing become obvious. To control the several factor individually by minimizing the dead volume, the proposed system with about 100mm square integrates a battery-powered small peristaltic pump [3], a culturing microchannel, and a reservoir as shown in Fig. 2.

![Fig. 2: A photograph of an integrated micro cell culture system.](image)

![Fig. 1: Cells in a micro-environment.](image)

![Fig. 3: A SEM image of cross sectional view of the channel.](image)

![Fig. 4: Photographs of HeLa-H2B-GFP cells in the microchannel.](image)
III. EVALUATION OF PHYSICAL INFLUENCE

To evaluate the controllability of the physical condition, the proliferation profile in the change of the shear stress was measured on a glass-bottom microchannel. From the experimental result as shown in Fig. 5, the cell culturing in the micro-environment needs the perfusion system, but good cell proliferation was achieved under low shear stress from 0.9 to 3.6 Pa. Moreover, the profiles of the static incubation on a dish and incubation in the microchannel under low shear stress are similar tendency. So, the low shear stress induced by the flow do not affect the cells in the microchannel.

IV. CHEMICAL CYTOTOXICITY TEST

A chemical cytotoxicity test in the change of the bottom materials, i.e. Glass, SU-8, polystyrene and PDMS, was carried out under the low shear stress. The initial cellular adhesiveness and the proliferation profile are shown in Figs. 6 and 7, respectively. Cellular adhesiveness is differences between four materials, but no toxicity was found on the proliferation forms from which the similar doubling time was calculated between tested materials.

The adhesion rate and the doubling time as a function of the surface energy is shown in Fig. 8. Generally, the proliferation increases with the adhesion. However, the adhesion and proliferation were not correlated. Since the HeLa-H2-B-GFP cells may have the maximum doubling time of 26hours as the proliferative capacity, the measured proliferation is saturated.

In conclusion, the proposed integrated micro cell culture system can be used for a micro-cytotoxicity test and the surface energy is one of the important quantiative evaluation parameters for biocompatibility in the micro-environment.

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REFERENCES