Single-cell-culture experiment made easier for researchers

Single-cell-culture experiment is widely used for biological researches concerning cell heterogeneity. This experiment although straightforward to performed by the limiting dilution method with manual pipetting and cell culture well plates, is time consuming and not cost-effective. To perform such single-cell experiment, a researcher needs to first prepares a diluted cell suspension and then place a small volume of the cell suspension into a well of a cell culture well plate, hoping to get just one cell in a well. However, the probability of getting one-cell-in-a-well is low; typically about 10 – 20% even performed by a trained personnel. As a result, it is common that researchers have to plate cells in tenth of cell culture well plates in order to just get enough cells for an experiment.

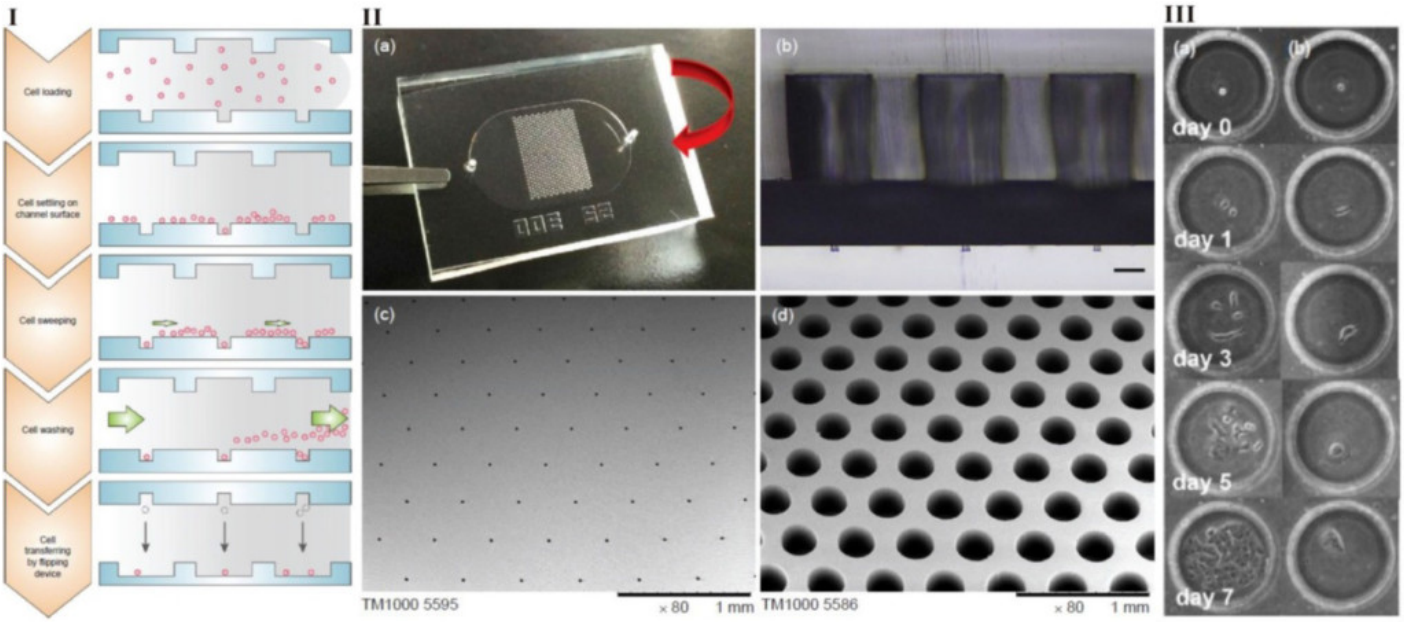

Fig. 1. (I) Design concept and operation procedure of the DW device. (II) Appearance of the DW device. (II-a) A PDMS DW device held by a tweezers. (II-b) Micrograph of the cut cross-section of a DW device. (II-c) SEM image showing small capture wells. (II-d) SEM image showing big culture wells. (III) Time-lapse images of two culture wells each contained a single A549 human lung carcinoma cell after cell loading. The cell in well (III-a) proliferated, whereas the cell in well (III-b) remained single after 7 days of cell culture, showing differential abilities in cell proliferation between the two cells.

A research team led by Prof. Chia-Hsien Hsu at the National Health Research Institutes in Taiwan has developed a simple method to make single-cell-culture experiment easier using a microfluidic chip-based technique. The microfluidic device has a dual-well (DW) design which allows for high-

efficient loading of single cells in large microwells whose size can be made significantly larger than a single cell for single-cell culture application. The increased efficiency of single-cell loading in large microwells is achieved by utilizing a novel concept of using small microwells to trap singles cells followed by using gravidity to transfer the captured cells to large microwells for the cells to spread and grow during cell culture (Fig. 1 (I)). The efficiency of single cell loading in the larger wells of the DW device is nearly 80%, which is much higher than that of the conventional limiting dilution method. Due to its small size, the DW device only requires minimal cell culture medium consumption, further reducing the cost of the experiment. The utilities of the DW device have been demonstrated with cell proliferation, differentiation and single-cell colony formation assay experiments using mouse brain neural stem/progenitor KT98 cells, as well as two cancer cell lines: A549 and MDA-MB-435 cells. The DW device is made of polydimethylsiloxane (PDMS) material, which is transparent thus it is also convenient for microscopic observation of the cultured cells Fig. 1. (III). The ability of this new approach to allow for high-efficiency loading of single cells in large microwells should be useful for a broad range of applications where on-device culture and analysis of single cells are required.

Publication

A microfluidic dual-well device for high-throughput single-cell capture and culture.
Lin CH, Hsiao YH, Chang HC, Yeh CF, He CK, Salm EM, Chen C, Chiu IM, Hsu CH.
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