課題番号　:F-18-KT-0146
利用形態　:機器利用
利用課題名（日本語）　:CUPAL　人材育成　MEMS 後期
Program Title(English)　:Liver/intestine on a chip
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キーワード／Keyword　:リソグラフィ・露光・描画装置、Microfluidic device, Body on a chip, disease modeling

1. 概要（Summary）

Prior to delivery of a drug to patients and markets, drug candidates need to be evaluated for their efficacy and toxicity at the stage of pre-clinical trials. However, the most of drugs do not reach to clinical trials, even showed serious the toxicity on patients at the trials. This is largely due to an absence of proper methods for disease modeling (e.g., shortcoming of *in vitro* cell-based assays and *in vivo* animal tests) to predict drug effect [1]. In this research project, a high-performance microfluidic device was fabricated by advanced micro fabrication techniques.

2. 実験（Experimental）

【利用した主な装置】

高速マスクレス露光装置、レーザー直接描画装置

【実験方法】

(1) Device fabrication

The microfluidic device was developed by our laboratory. The general fabrication method involved multi step lithography. By using the DMD lithography machine, the 3D semi-cylindrical shape microfluidic channel molds were fabricated. These channels were main parts of micro valve and micro pump. Then, by using the laser directly writing device, the photomask of control layer and microfluidic cell culture layer was fabricated. The photomask was used to fabricate the main mold for microfluidic device. After pouring the mold with PDMS materials and curing in 80 ℃, the microfluidic device was fabricated.

(2) Tissue modeling

Liver and intestine cell resources were HepG2 and CaCO2 cells, general cell lines for in vitro studying. They are co-cultured on chips under the DMEM cell culture medium, with 10% FBS, 1% P/S, 1%NEAA with density 2×10^6/ml.

3. 結果と考察（Results and Discussion）

(1) Device and system setup

Fig.1 shows the fabricated device. The microfluidic chip was previously reported in our previous project [2]. The main device structure consisted of a perfusion layer and a control layer. The perfusion layer was designed for cell culture. The control layer was used to actuate the micro pump and valve.

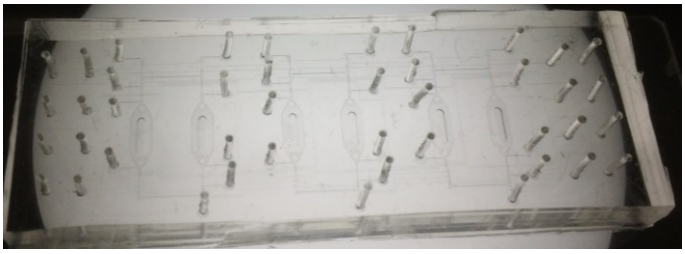

Fig. 1 the fabricated microfluidic device for cell culture.

(2) liver/intestine on a chip

After 1-week co-culture on a chip, Fig. 2, the liver cells and intestine cells shown normal cell viability and morphology. The liver/intestine on a chip was presented. In the next step, this liver/intestine on a chip could be used as the drug first-pass platform for pharmacokinetics.

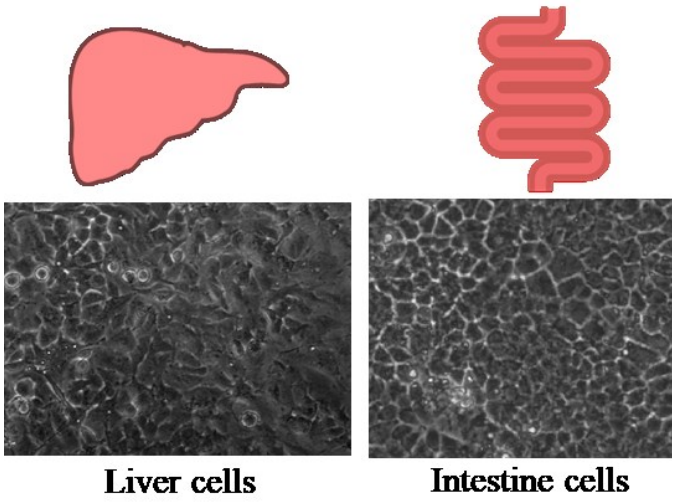

Fig. 2　Liver/intestine on a chip.

4. その他・特記事項（Others）

・参考文献

[1]Scannell, J. W., Blanckley, A., Boldon, H., & Warrington, B. (2012). Diagnosing the decline in pharmaceutical R&D efficiency. Nature reviews Drug discovery, 11(3), 191-200.

[2] Kamei K, Kato Y, Hirai Y, et al. Integrated heart/cancer on a chip to reproduce the side effects of anti-cancer drugs in vitro[J]. RSC Advances, 2017, 7(58): 36777-36786.

5. 論文・学会発表（Publication/Presentation）

None.

6. 関連特許（Patent）

None.