第76回応用物理学会秋季学術講演会 講演予稿集 (2015 名古屋国際会議場)

In Vitro Cardiomyocyte-Based Drug Profiling and Screening Application of the Designed Centrifugal Microfluidic Chip

°Wilfred Espulgar[1], Masato Saito[1], Jong-Kook Lee[2], Eiichi Tamiya[1]
[1] *Department of Applied Physics, Graduate School of Engineering, Osaka University, 2-1 Yamada-Oka, Suita, Osaka 565-0871 Japan,*
[2]*Department of Cardiovascular Regenerative Medicine, Graduate School of Medicine, Osaka University, 2-2 Yamada-Oka, Suita, Osaka 565-0871, Japan*
E-mail: wilfred@ap.eng.osaka-u.ac.jp

In vitro profiling of new chemical entities is essential in early phases of drug discovery and development. It is largely acknowledged that this works in combination with *in vivo* studies to predict the cumulative effects of a drug during chronic treatment and dose-related pharmacokinetic-pharmacodynamic (PK-PD) relationship in several clinical trials to evaluate the general pharmacological, toxicological, and predictive absorption, distribution, metabolism, and elimination (ADME) effect before its in-human administration and then registration. However, some profiling tests are not routinely done because of the needed additional technical skill and costly maintenance which leads to cases of unexpected side effects or adverse drug reactions (ADRs). In addition, a review of drug attrition in non-clinical and clinical development reports about serious ADRs and withdrawal from market place revealed that cardiovascular toxicity occurred more frequently than hepatoxicity. Thus, a cheap and easy platform for drug screening and profiling is very much desired. This study presents the design and operation of a centrifugal microfluidic chip for single-cell level cardiomyocyte-based drug screening and profiling as an alternative platform for this purpose. Primary culture neonatal rat cardiomyocytes were trapped using centrifugation of the chip where isolated single cells and groups of cells can be studied and compared in the same chip. Beat profiles of the cells were generated using image correlation analysis to study the contractile characteristics (beating rate, beating strength, and inter-beat duration). By utilizing this non-invasive tool, long term continuous monitoring, right after trapping, was made possible and cell growth and dynamics were successfully observed in the chip. Media replacement does not require large supporting equipment but instead utilize capillary flow only. The effect of carbachol (100 μM) and isoproterenol (4 μg/mL) to single cells and groups of cells were demonstrated and the feature for immunostaining (β-actin) applicability of the chip was revealed. Furthermore, these findings can be helpful for the headway of non-invasive profiling of cardiomyocytes and for future chip design and operation of high-throughput lab on-a-chip devices.

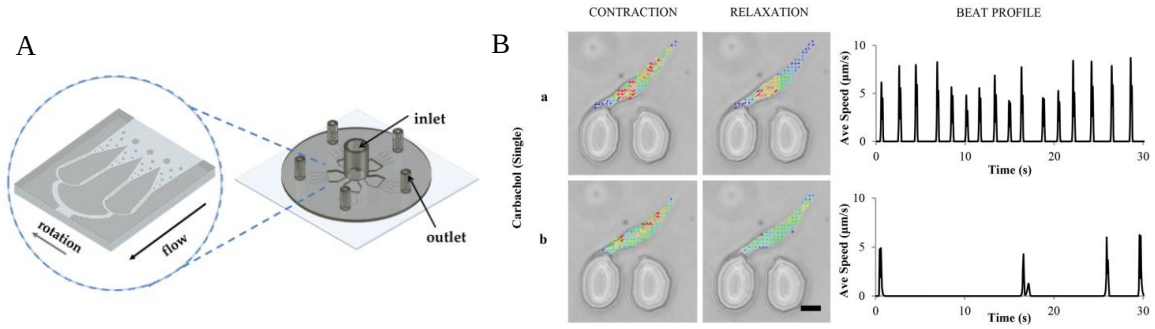

Fig. 1. Chip design (A) and Beat motions and beat profiles (B) before (a) and after (b) administration of 100 μM carbachol to 4 day old single cardiomyocyte.