Long Term Monitoring of Single and Multiple Cardiomyocytes Trapped in a Centrifugal Microfluidic Chip

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The purpose of this study is to develop a microfluidic chip that can trap, culture, and monitor cardiomyocytes with the ultimate goal of understanding the behavior of the different types of cardiomyocytes (atrial, ventricular and nodal). Microfluidics technology has been exploited in cell study because of its ability to manipulate particles and control over culture conditions. This can be utilized in a range of cell related applications such as cell manipulation, cell separation, cell culture, and cell lysis. The use of this technology can greatly reduce the cost in cell research; however, operation of microfluidic device in laboratories is hindered for the need of additional machines and technical know-how in fluid dynamics and control. In this study, centrifugal microfluidics (at 50 x g) is utilized to trap single and multiple cells of primary cultures of neonatal rat cardiomyocyte. Centrifugation is a common practice in general chemical and biological laboratories which makes the operation of the chip less likely to pose a problem even for those who are not familiar with microfluidics technology. The trapped single cells are separated (100 μm) with the assumption that no cell interaction will occur while the trapped multiple cells are trapped in such manner that interaction in all direction is maximized. Cell growth, coupling, and beating are successfully observed and monitored in the fabricated microfluidic device without large supporting equipment which is done right after trapping. In the previous study, cardiomyocytes can be kept in the centrifugal microfluidic chip for 3 days. Fig. 1 shows the bright field image of a studied cardiomyocyte incubated for 4 days and its corresponding beating profile. It can be seen that the cell has a stable beating behavior at a rate of 23 bpm. With this microfluidic chip, the cells are monitored and kept alive for 7 days when observed and analyzed daily but can be kept for as long as 2 weeks if left alone inside an incubator.

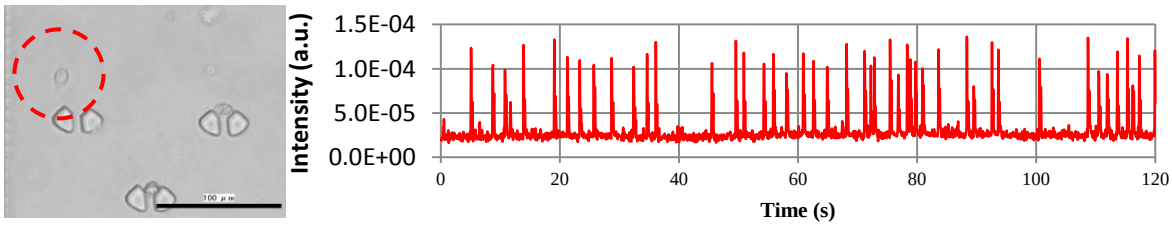

Fig. 1. *Single Cardiomyocyte after 4 days of incubation with beat rate of 23 bpm*

Fig. 2 presents a summary of the beating profile fluctuations of 23 single cardiomyocytes observed in 7 days. It can be gleaned from the diagram that the maximum beating is within the range of 72h – 120h (3–5 days). After 5 days, the cells decrease in beat rate and eventually die. Thus, observation and analysis of the cells should be done on the 3rd-5th days of incubation. By comparing the beating profile of the cells, it is expected to determine the ventricular types from atrial types. Nodal cardiomyocytes do not exhibit beating which makes this method not applicable. From literature, atrial cardiomyocytes have higher beat rate and shorter beat interval than ventricular cardiomyocytes. With this approach, a non-invasive method for identification can be eventually realized.

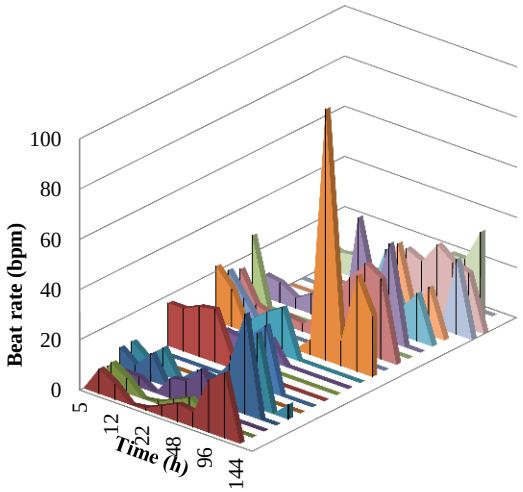

Fig. 2. *Beating profile fluctuations of 23 single cardiomyocytes monitored for 7 days*