MICROMECHANISTICALLY MODULATED CARDIOMYOCYTE ALIGNMENT IN VITRO

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Abstract- World Health Organization reports that 18 million people died from cardiovascular-related diseases in 2015, representing 31% of all global deaths. Recent studies of human cardiomyocyte in vitro have been generating scientific insights beyond traditional approaches. However, human cardiomyocyte in general is difficult to study due to limited sample availability and its in vitro fragile nature. In this work, we studied HL-1 cells, a tumor-cell derived cardiomyocyte, to ultimately quantify the relationship between cell contractility and the influence of external stimuli. The motivation is to use cardiomyocyte contractility as a quantifiable indicator for cardiotoxicity. The intermediate step is to understand the implications of biomechanical cues on cardiomyocyte orientation. HL-1 cells have the ability to grow in vitro indefinitely while maintaining the ability to rhythmically contract autonomously upon reaching confluence. These HL-1 cells can mimic the characteristics of human cardiomyocyte, making them an excellent candidate for proof-of-concept demonstration. They differ from human cardiomyocytes in that they lack a natural orientation and striation in vitro. With the success of integrating substrates with nano-scale precision texture and tissue engineering, the physiological environment of cells and tissues can be re-capitulated in vitro. The purpose of this research was to align HL-1 cells on a polymer substrate to quantify their uniform contractility. We created an effective tool to observe cardiac contractility where the HL-1 cells are mechanically supported with a polymer substrate micromachined with grooves and ridges with nano-scale precision. Herein, we report on the quantitative efficiency of HL-1 cardiomyocyte alignment on various micro-patterned surfaces. The experimental results suggest that our microplatform can promote cardiomyocyte alignment in vitro, which is the crucial intermediate step towards rapid drug screening for cardiotoxicity.

Keywords- cardiomyocyte, micro-pattern, cardiac orientation, alignment