Induction of Mechanical and Structural Maturity in Single Cardiomyocytes Differentiated from iPSCs

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Heart function relies on the contractility of myocardial cells (cardiomyocytes). Induced pluripotent stem cells can be differentiated into cardiomyocytes (iPSC-CMs). The shape and the organization of sarcomeres and other subcellular structures in single iPSC-CMs do not resemble what is observed in mature cardiomyocytes from myocardial tissues.

Here we mechanically and structurally mature iPSC-CMs with a platform for culture of cells on polyacrylamide hydrogels, where cell shape is forced to mimic the elongated morphology of mature cardiomyocytes. We simultaneously measure generated forces and sarcomere organization of live contractile cells. We force cells to different levels of elongations by using microcontact printing to pattern cell adhesive proteins on gels. To visualize sarcomeres, we infect cells with LifeAct to fluorescently label actin fibers.

We quantified cell contractility and sarcomere maturity by processing videos of beating cells. We determined forces using traction force microscopy of moving microbeads, which was measured with particle image velocimetry of different video frames. Z-lines, myofibril alignment and sarcomere maturity were determined from fluorescently labeled actin in live cells. On our patterned hydrogels, iPSC-CMs mainly contracted along their major axis. The magnitude and directionality of contractility related to sarcomere organization and varied with pattern elongation. Single cell contractility and developed sarcomeres were rarely observed in cells with a shape aspect ratio below 3.

This culture platform tests the level of cardiomyogenic maturity of differentiated iPSC-CMs and may allow the assessment of biomechanical and structural changes consequent to disease states.

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