Abstract: Heart function relies on the contractility of myocardial muscle cells (cardiomyocytes). Induced pluripotent stem cells can be differentiated into cardiomyocyte progenitors (iPSC-CMs) and present high potential to replace damaged heart tissue and study heart disease (Robertson). Cardiomyogenic maturity increases in these cells with culture time. However, the shape and the organization of sarcomeres in single iPSC-CMs at known maturation stages do not resemble what is observed in mature cardiomyocytes from myocardial tissues. The expression of a set of cardiomyogenic markers is used to identify maturity in iPSC-CMs. No biomechanical markers of maturity are well established. We hypothesized that specific mechanical cues can increase maturation of iPSC-CMs and that cell maturation correlates to a biomechanical output. We seeded differentiated iPSC-CMs after at least 1 month of culture on 2000 \( \mu \)m\(^2\) rectangular protein patterns on polyacrylamide hydrogel substrates with a modulus of 10 kPa to resemble the morphology of ventricular cardiomyocytes. Cells were infected with rAV CMV-LifeAct-Tag RFP to observe myofibrils and sarcomeres in cells by labeling actin. Microbeads dispersed within the hydrogel move due to cell contractility. Their movement is transduced to force via traction force microscopy. Actin is simultaneously observed in these contractile cells to correlate structural maturity to biomechanical output. The contractility of beating iPSC-CMs mainly occurs along the cell main axis. Poorly developed sarcomeres are observed in cells with aspect ratios below 3. Compared with this aspect ratio, aspect ratios of 5 and 7 result in higher cell generated total force in the range of 6-10 \( \mu \)N. Directionality of force along the cell main axis is higher with an aspect ratio of 5. We are examining relationships between the organization and composition of myofibrils and beating rate in the forces generated by iPSC-CMs. We test the level of cardiomyogenic maturity of differentiated iPSC-CMs and aim to assess biomechanical and structural phenotypes consequent to differentiation and disease states.

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