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ELASTOMERIC DROPLET GENERATION OF VASCULARIZED CARDIAC SPHEROIDS FOR THE USE OF HIGH-THROUGHPUT DRUG SCREENING

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With recent advancements in tissue engineering, several cardiac constructs have been utilized for drug screening. However, many systems are still not applicable for medium to high throughput workflow commonly found in drug discovery settings. Adapting techniques from biomaterial and polymer sciences, microfabrication, and fluid mechanics, we use new biocompatible and biodegradable elastomers to generate particles for vascularized cardiac tissue engineering applications. We create a novel three-dimensional in vitro model of the heart by co-culturing endothelial cells, cardiac fibroblasts, and iPSC-derived cardiomyocytes to form vascularized cardiac spheroids. Using biodegradable UV-curable elastomer poly(octamethylene maleate (anhydride)) (POMAC) and a droplet microfluidic device, we create a high throughput droplet system by generating prepolymer particles that are highly controllable and uniformly sized, ranging from 50-200 μm in diameter. The microfluidic design is optimized for appropriate channel dimensions and flow rates to efficiently produce large quantities of monodisperse elastomeric particles and crosslink these particles off-chip. Leveraging the elastic deformation and autofluorescent signals of the POMaC droplets, we can monitor cardiac tissue force generation and other functional characterization in a non-invasive manner. This engineered 3D cardiac spheroid will be validated by demonstrating various drug responses, in which the addition of isoproterenol increases the contractility, whereas treatment of diltiazem produces negative inotropic effects. We will also show that SU5416, a selective inhibitor of the vascular endothelial growth factor receptor, inhibits vascularization without affecting cardiac tissue function. We aim to use this model to investigate potential future therapeutic targets for cardiovascular disease in a high-throughput screening workflow.