CALIFORNIA STATE SCIENCE FAIR
2017 PROJECT SUMMARY

Name(s)

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Project Number

S0525

Project Title

Toward Precision Medicine: Harnessing Graphene Hydrogels, iPSCs, and Computational Models for Cardiac Tissue Engineering

Abstract

Objectives/Goals

In 2017 alone, over 8 million people around the world will die of cardiac diseases, most often induced by myocardial infarctions (MIs). Current treatment options, including heart transplants, are often too expensive, inaccessible, and fail to remediate the significant loss of heart function post-MI. The advent of induced pluripotent stem cells (iPSCs) has brought the goal of cardiac tissue engineering within reach: to create patient-specific muscle patches in vitro that can regenerate patients# hearts and be used for drug discovery. In this study, I sought to engineer novel hydrogel scaffolds to support iPSC-based cardiac tissue engineering. In addition, I sought to design computational tools to enhance heart disease diagnostics for labs and clinics.

Methods/Materials

To create my hydrogel, I began with biocompatible/biodegradable gelatin, enzymatically cross-linked the structure to achieve high physiological stability, incorporated graphene (nG) and graphene oxide (nGO) nanoparticles to enhance tensile strength and electrical conductivity, and added thermoresponsive NIPAM to enable the gels to form rapidly at body temperature. I gauged the biocompatibility, differentiation potential, and patterning of iPSCs on the gel substrates. Finally, I designed computational models in Matlab to classify the phenotypes of single-cell cardiomyocytes (CMs) and tissues based on their calcium transients and contractile properties.

Results

By tuning cross-linker, nG, and NIPAM concentration, the stiffness of the hydrogel was varied from 2 kPa to 26 kPa. Addition of nG also allowed the gels to become conductive, mimicking the heart#s microenvironment. Furthermore, Gelatin-NIPAM-nG hydrogels were fast-gelling, demonstrating potential as injectable vectors for non-invasive myocardial delivery of cells and drugs. iPSCs remained highly proliferative on the hydrogels and were successfully patterned into uniform colonies, ideal for drug testing applications. The computational tools that I designed were successful in rapidly analyzing and classifying calcium transients from normal/diseased CMs, and in evaluating the contractile phenotypes of beating tissue constructs over time using robust vector calculus models.

Conclusions/Discussion

Overall, I presented gelatin-NIPAM-graphene hydrogels as novel, low-cost scaffolds that, coupled with new, powerful computational tools, have the potential to enhance precision cardiovascular medicine.

Summary Statement

In this study, I successfully designed novel gelatin-NIPAM-graphene hydrogels to support iPSC-based cardiac tissue engineering; furthermore, I created computational tools to enhance heart disease diagnostics for laboratory and clinical use.

Help Received

I was honored to receive the guidance, training, and support of Dr. Oscar J. Abilez and Dr. Huaxiao Yang at the Joseph Wu Lab within the Stanford University School of Medicine as I completed my research study. I also want to acknowledge the 2016 SIMR Program at Stanford for giving me this opportunity.