Joint Faculty Candidate Seminar between Chemical and Biomedical Engineering

in
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The role of the extracellular matrix in cardiac cell proliferation and differentiation in the healthy and diseased developing heart

By
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Seminar abstract

Congenital heart defects (CHDs) are a leading cause of death in infants and young children. Hypoplastic left heart syndrome (HLHS) is a particularly severe CHD that is fatal without surgical intervention. However, standard repair of HLHS does not recapitulate native heart anatomy and function, and many patients suffer from secondary complications throughout life. Compared to the healthy developing heart, the HLHS heart is characterized by altered cell differentiation, decreased cardiomyocyte proliferation, and immature extracellular matrix (ECM). Mimicking healthy extracellular cues may be an effective approach for cardiovascular regeneration in HLHS patients, but it remains unclear whether HLHS cells are inherently defective or whether they can be stimulated to proliferate and differentiate. In this talk I will describe three projects which collectively aim to understand the role of developing cardiac ECM in healthy and diseased cardiac cell behavior. In the first project, I studied the complex composition of the developing and mature cardiac ECM in a healthy rat model and found that fetal cardiac ECM significantly promoted the proliferation of neonatal rat cardiomyocytes. Next, I investigated alterations in cell proliferation and ECM composition in an experimental model of heart hypoplasia in the developing rat fetus. The major findings from this project suggest that cardiomyocytes from the HLHS heart can compensate for impaired proliferation and differentiation when removed from the unhealthy cardiac environment. Finally, I have begun to isolate and characterize c-kit+ cardiac progenitor cells (CPCs) from pediatric patients with CHDs, including those with HLHS. We developed cardiac ECM-fibrin hybrid scaffolds with tunable composition and stiffness, and show that CPC differentiation is affected by changing these properties. This work is laying the foundation for the development of novel tissue engineering and regenerative medicine strategies for treating HLHS patients in the future.

Biosketch

Corin Williams completed her PhD at Boston University under the mentorship of Prof. Joyce Wong and is currently a postdoctoral fellow in Prof. Lauren Black's lab at Tufts University. Her research interests are engineering approaches to understanding and repairing congenital heart defects in the developing fetal and neonatal cardiovascular system. Her doctoral research focused on the development of micropatterned cell sheets that mimic the complex organization of smooth muscle cell layers in the artery. Her postdoctoral research has largely focused on young developmental age cardiac ECM as a biomaterial for cardiac regeneration. Corin has been supported by the American Heart Association (Founder's Affiliate Predoctoral Fellowship), the NSF East Asia and Pacific Summer Institutes Award to conduct research in Japan during the summer of 2007, and is currently funded by the NHLBI Ruth L Kirschstein NRSA individual postdoctoral fellowship. In the fall of 2012, she had a unique opportunity to teach an Intro to Bioengineering course at Olin College, one of the top undergraduate engineering schools in the nation. In addition, Corin has enjoyed participating in various STEM outreach programs to high school students while at BU and Tufts, and has been actively involved in mentoring young women who are interested in STEM fields.

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