THE HARTWELL FOUNDATION

2019 Individual Biomedical Research Award

Rebecca Schulman, Ph.D.

Associate Professor
Department of Chemical and Biomolecular Engineering

Johns Hopkins University

Engineered Cardiac-Tissue Patches: Correcting Arrhythmia in Beating Heart Cells with DNA Nanotubes

Over 40,000 babies are born in the United States each year with a congenital heart defect inside the heart or in the large blood vessels outside the heart. In order to reduce the risk of life-threatening heart failure, 25% of the malformations will require surgical intervention to correct or improve either blood flow abnormalities or weakened heart muscle (myocardium) in order to reduce the risk of life-threatening heart failure. One promising approach for regenerative repairs has been demonstrated in animal models. The approach is to supplement the damaged tissue using human heart muscle cells (cardiomyocytes) to provide mechanical support and the necessary biochemical cues for growth. Unfortunately, the ability to construct a functioning piece of laboratory-grown heart tissue (cardiac patch) derived from patient stem cells grown in an extracellular matrix, that will both survive implantation and support contractions powerful enough to augment the ability to pump blood, has yet to be achieved. This is because it has not been possible to get cardiomyocytes when transferred as a cardiac patch to beat in synchrony with each other and the rest of the underlying myocardium. Normally, the heartbeat is triggered by electrical impulses that originate from the rhythmic pacing discharge from certain heart muscle cells that function as a pacemaker. In effect, the heart beats efficiently to pump blood because of the organized flow of electric charge, which requires transfer of the charge from one contracting cell circuit to another. In the heart, intercellular channels between adjacent cell membranes enable this transfer, whereas transmission between distant heart cells occurs by nerve fibers. By contrast, the cardiomyocytes in a patch are separated from each other in a stabilizing matrix of biomaterials and other support cells that lack nerve fibers and thus, cannot sufficiently propagate electrical signals to support synchronized contractions and maintenance of a stable rhythm. Scaffold-free patches can achieve sufficient conductivity but at the expense of required mechanical support. To ensure that all cardiomyocytes within a cardiac patch will beat in synchrony with each other, Rebecca proposes to use nucleic acids as a non-biologic building block to organize conductive polymers using self-forming nanoscale tubes as templates that will function essentially as wires to carry current between each cell. The non-genomic strands of DNA that form these structures will take shape in a controlled chemical process that emanates from each cardiomyocyte surface and favors self-assembled connections between cells. The process will take place during preparation of the cardiac patch, under conditions favorable for cell growth. If she is successful, it will be possible to construct cardiac patches that offer an effective intervention to halt the progression of heart failure and improve the health of those children affected by a congenital heart defect.