

Research backed by the John Taylor Babbitt Foundation continues to make significant strides in elucidating the mechanisms that cause HCM and identifying approaches for treatment. Thanks to the generosity of its supporters and benefactors, the Foundation provides a \$75,000 grant for basic and clinic research to Dr. M. Roselle Abraham at Johns Hopkins in Baltimore. Dr. Abraham is the Director of Research and Co-Director of Hopkins' Hypertrophic Cardiomyopathy (HCM) Center of Excellence.

HCM is the most common inherited cardiac disease and is estimated to affect up to 1 in 500 individuals. Most cases of HCM are benign; however, some patients will develop serious disease with risk of sudden cardiac death, atrial fibrillation, stroke, and heart failure. Due to its high prevalence, HCM remains the most common heart-related cause of sudden death in young athletes. Currently, the causal mutations for HCM are unknown in about 40% of patients and there are no known therapies that can prevent or mitigate the development of cardiac disease in patients.

Research in Dr. Abraham's lab is aimed at developing blood and imaging techniques for effective preclinical diagnosis and risk stratification of HCM patients and their family members and at identifying customized therapies to prevent or mitigate disease. Since HCM was described as a disease ~60 years ago, several therapies have been tested successfully in animal models, but none has proved effective for patients.

Last year with funding from the Foundation, Dr. Abraham's lab identified *mutation-specific* differences in cardiac function in two different HCM mouse models, thus establishing that different mutations cause different cardiac pathophysiology and will likely require different treatments. Work this year has focused on investigating differences between the physiology between mouse and human hearts and on developing methods to examine the effects of exercise on cellular cardiac function in mouse models. Exercise-induced effects are of particular interest says Dr. Abraham because the most common symptom presented by her patients is chest pain and related difficulties in exercising.

Research this year successfully characterized differences in genetic expression in two mouse models. A post-doctoral fellow in the lab received a Travel Award from Johns Hopkins to present these important results at the European Society of Cardiology meeting in Rome. Significant progress made in clinical studies, resulting in one published manuscript and three additional manuscripts which have been accepted for publication in prestigious peer-reviewed journals, pending revisions.

In addition, the Abraham lab made important findings related to cellular models for heart muscle cells (cardiac myocytes or CMs). The lab showed that existing cell culture protocols result in generation of immature CMs which function like heart cells at a juvenile stage of development. Current work is aimed at maturing cells, including exciting developments in culturing CMs on nanogrooves to mimic the 2-D architecture in developing heart muscle tissue.

Looking forward to next year, Dr. Abraham is particularly enthusiastic about a collaboration with John Hopkins' Applied Physics Laboratory to use 3-D printer technology to mimic the 3-D architecture of human cardiac tissue. The end goal is to generate *HCM hearts-in-a-dish* to use to investigate disease mechanisms and to develop and test mutation-specific therapies. Clinical research in the coming year will continue to develop the understanding on exercise effects in patients, with a focus on prediction of atrial fibrillation and stroke in HCM patients using non-invasive imaging techniques.