Public Abstract

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Heart disease is the leading cause of death in the United States and many other industrialized countries. My dissertation focuses on the molecular mechanisms that regulate heart function at the cellular and subcellular level in the hope of providing an important base on which to build treatments for cardiovascular disease. Specifically, I measured the ability of single heart muscle cells to shorten against a load and, thus, generate power, in conditions that mimic those encountered in the body. It was found that single myocytes that lack a specific thick filament protein were able to shorten at a faster rate against a given relative load, which resulted in an increase in power generating capacity. These myocytes were also able to generate force more quickly. It was also found that normal myocytes shortened more slowly at a short length than at a long length, and this affect was more pronounced in myocytes expressing the slower of two thick filament molecular motors. However, shortened myocytes generate less force, and equalizing the force between long and short caused myocytes to shorten more quickly. This result has implications for heart function when the amount of blood entering the heart is altered (i.e., more blood means longer cells and vice versa). Overall, this research provides important mechanistic insight into the molecular regulation of heart function.