The Cardiac Tissue System: A Novel Technique Capable of Inducing Hypertrophy in Excised Heart Muscle

Anna Jokiel Raskin,1 Masahiko Hoshimiijima,2 Andrew McCulloch1, and Jeffrey Omens1,2

1Department of Bioengineering, University of California, San Diego, La Jolla, California 92039-0412
2Department of Medicine, University of California, San Diego, La Jolla, California 92039-0608

ABSTRACT

Altered mechanical stresses and strains in cardiac myocytes can induce modifications in gene expression that can affect cardiac remodeling and myocardial contractile function. Most studies of myocardial mechanotransduction use isolated neonatal rat myocytes. To study the genetics of these pathways it is helpful to be able to probe alterations in gene expression in intact muscle from genetically engineered mice.

The main goal of this study was to develop a chamber that facilitates straining of cardiac tissue, while measuring its force within a physiological environment. The system was developed to house intact right ventricular (RV) papillary muscles, such that cell to extracellular matrix adhesion as well as cell to cell adhesion, which influence cardiac remodeling, were undisturbed. The tissue chamber is isolated from the external environment and provides control of I, supply, temperature, and supersaturation delivery. Isolated papillary muscles are suspended within the chamber in modified M199 cell culture media, thus enabling a non-invasive technique to study the effects of short-term mechanical strain on gene expression. Through this mechanism, contractile parameters were studied and hypertrophy can be induced in specimens for a period up to 12 hours. By quantifying mRNA levels of hypertrophic markers (BNP, SOCS3,ANP) we are able to monitor the development of hypertrophy within normal specimens and within specimens obtained from knock-out mice that may have a dysregulated hypertrophic or biophysical signaling. Preliminary results reveal that 

**BACKGROUND**

Mechanical loads are known to elicit adaptive hypertrophy in myocytes through multiple signaling pathways in the cell. 

**METHODS**

**Objectives:** To develop a system that is capable of inducing hypertrophy (analogous to chronically) by increasing the level of stress acting on intact cardiac muscle specimens, with the mechanisms leading to dysregulated hypertrophic signaling in genetically engineered mouse models can be studied.

**IV Papillary Muscle Culture System**

**SYSTEM OPTIMIZATION**

**SYSTEM CAPABILITIES**

**RESULTS**

**FUTURE WORK**

**REFERENCES/ACKNOWLEDGEMENTS**