

QUANTIFICATION OF PROTEIN PHOSPHORYLATION IN CARDIAC TROPONIN I AND MYOSIN BINDING PROTEIN-C

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Approximately 5 million Americans currently suffer from heart failure, a symptomatic syndrome in which the heart muscle weakens and is unable to pump enough blood and oxygen to support other organs in the body. Molecular alterations of calcium and contractile proteins have been implicated in heart failure, and several animal studies have shown that there is a reduction in cardiac muscle contraction resulting from abnormal phosphorylation of several sites in troponin I (TnI) and myosin binding protein-C (MyBP-C). However, the precise location and degree of phosphorylation of these sites in the human heart are still poorly understood due to analytic challenges in identifying and quantifying phosphorylation in small human heart biopsies; thus, approaches with high sensitivity, such as mass spectrometry, are needed. Palmer et al. (2011) used a mass spectrometry-based proteomic method to quantify indirectly phosphorylation of MyBP-C in mice, but the method is highly labor-intensive and does not allow phosphorylation to be measured directly. We hypothesize that a novel and facile sample preparation method for mass spectrometry-based analysis can be developed to identify and quantify directly phosphorylation of both TnI and MyBP-C sites in precious human heart samples. Ultimately, this method will lead to a greater understanding of molecular alterations in failing human hearts.