The Death of Transcriptional Chauvinism in the Control and Regulation of Cardiac Contractility

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ABSTRACT: In the last 25 years we have witnessed the triumph of the genome. There are now well over 200 complete genome sequences and the application of modern solid state technologies to genomic sequencing promises affordable, personalized sequences for the individual in the very near future. With this explosion in DNA sequence data, the focus in the immediate past has been on the primary DNA sequence, the cis-trans interactions that underlie controlled transcription, cataloging the transcriptome and applying rudimentary systems analysis to those datasets in an attempt to assign molecular signatures to normal and abnormal physiological states. However, it is becoming clear that the post-transcriptional processes, which operate at the levels of RNA stability and selection for translational initiation, as well as the post-translational processes of protein stability, trafficking and secondary modifications such as phosphorylation, all play key roles in the homeostasis of the contractile apparatus and its overall function. Defining the interplay of these processes, in concert with the signaling pathways that allow transcription, translation and post-translational processes to be quickly modified in response to events outside of the cardiomyocyte, are leading to an understanding of the spatial and temporal requirements for each of these processes in controlling cardiac output. We wished to confirm the importance of post-translational modification in controlling cardiac contractility *in vivo*. We therefore examined the role that post-translational modification of an important component of the cardiac contractile apparatus, myosin binding protein C, plays in the normal and diseased heart by creating transgenic mice in which the effects of chronic cardiac myosin binding protein C (cMyBP-C) phosphorylation/dephosphorylation could be determined.

KEYWORDS: cardiac myosin binding protein C, phosphorylation, hypertrophy, signaling

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