Excitation-Contraction Coupling and Excitation-Transcription Coupling in Skeletal Muscle

Erick O. Hernández-Ochoa* and Patrick Robison
Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

Editorial

Skeletal muscle cells are excitable. They convert external electrochemical stimuli into signals that produce a variety of biological responses. For instance, voltage-gated Ca2+ channels, located in the sarcolemma and T-tubule system, trigger communication with internal Ca2+ stores, the sarcoplasmic reticulum, coupling voltage signals to Ca2+ release [1]. Once released, Ca2+ binds to myosin-actin contractile machinery and permits the production of force or shortening [2,3]. This process of excitation-contraction (E-C) coupling, is regulated by short-term signaling mechanisms to control the supply of Ca2+ required for cycling myosin-actin contractile machinery activation [1,2].

The molecular signals coupling excitation and contraction also regulate the transcriptional activity of the cell over a much longer time scale by a process known as excitation-contraction- (E-T) coupling [4]. In skeletal muscle E-T coupling, Ca2+ released from internal stores during E-C coupling triggers communication to the nucleus to regulate gene expression and thereby shape the transcriptome [4,5]. In response to external cues, such as electrical activity at the neuromuscular junction, skeletal muscle exhibits plastic changes, reprogramming gene expression to sustain a specific muscle performance by activating signaling pathways according to excitation pattern [6-9].

Genomic approaches have identified hundreds of genes and dozens of transcription factors that are regulated by the fluctuations in concentration of intracellular Ca2+ [10]. Various components of Ca2+-dependent signaling pathways and multiple transcription factors, coactivators and corepressors have been shown to be involved in skeletal muscle remodeling [8,11,12].

The two most well characterized Ca2+-regulated transcription pathways in skeletal muscle are mediated by the phosphatase calcineurin (CaN) and the kinase, CaMKII, both dependent on Ca2+-calmodulin (CaM) [4,5,11,13]. The CaM-CaN pathway activates the transcription factors nuclear factor of activated T-cells and myocyte enhancer factor 2 (MEF2) to control slow-type muscle fiber gene expression [9,14,15]. The CaM-CaMKII pathway signals histone deacetylase and the transcription factors serum response factor and MEF2 [11,13,16] to regulate the metabolic responses to exercise [5,17]. New insights into the regulation of specific Ca2+-regulated genes have revealed that transcriptional regulation is fine-tuned both by the spatial and temporal features of the Ca2+ signal, permitting a wide variety of signals through a handful of mediators [5,18].

In spite of the large number of genes affected by Ca2+ signaling, only a small fraction of Ca2+-dependent gene regulation signaling pathways have been partially decoded so far. This leaves rich opportunities for discovering new signaling pathways and gene targets of Ca2+ regulation. Future studies focused on less characterized Ca2+-dependent transcriptional programs, and the role of global vs. local Ca2+ signaling domains may provide a better understanding of the role of E-T coupling as it relates to genomic effects on skeletal muscle phenotype. Understanding the biochemical and molecular mechanisms involved in modulating skeletal muscle phenotypes is critical to the development of targeted pharmacological tools to ameliorate muscular diseases. Biochemistry and Pharmacology is an open access journal with a wide scope in biomedical sciences, manuscripts in the field of muscle biochemistry, E-C and E-T coupling will provide new insights into the fascinating muscle machine.

References

*Corresponding author: Erick O. Hernández-Ochoa, Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA, E-mail: ehern001@umaryland.edu

Received April 11, 2012; Accepted April 12, 2012; Published April 13, 2012


Copyright: © 2012 Hernández-Ochoa EO, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

