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

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Editorial

Skeletal muscle cells are excitable. They convert external electrochemical stimuli into signals that produce a variety of biological responses. For instance, voltage-gated Ca^{2+} channels, located in the sarcolemma and T-tubule system, trigger communication with internal Ca^{2+} stores, the sarcoplasmic reticulum, coupling voltage signals to Ca^{2+} release [1]. Once released, Ca^{2+} 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 Ca^{2+} 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-transcription (E-T) coupling [4]. In skeletal muscle E-T coupling, Ca^{2+} 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 Ca^{2+} [10]. Various components of Ca^{2+}-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 Ca^{2+}-regulated transcription pathways in skeletal muscle are mediated by the phosphatase calcineurin (CaN) and the kinase, CaMKII, both dependent on Ca^{2+}-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 Ca^{2+}-regulated genes have revealed that transcriptional regulation is fine-tuned both by the spatial and temporal features of the Ca^{2+} signal, permitting a wide variety of signals through a handful of mediators [5,18].

In spite of the large number of genes affected by Ca^{2+} signaling, only a small fraction of Ca^{2+}-dependent gene regulation signaling pathways have been partially decoded so far. This leaves rich opportunities for discovering new signaling pathways and gene targets of Ca^{2+} regulation. Future studies focused on less characterized Ca^{2+}-dependent transcriptional programs, and the role of global vs. local Ca^{2+} signaling domains may provide a better understanding 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

1. Schneider MF (1994) Control of calcium release in functioning skeletal muscle fibers. Annu Rev Physiol 56: 463-484.
2. Melzer W, Herrmann-Frank A, Luttgau HC (1995) The role of Ca^{2+} ions in excitation-contraction coupling of skeletal muscle fibres. Biochim Biophys Acta 1241: 59-116.
3. Berchtold MW, Brinkmeier H, Muntener M (2000) Calcium ion in skeletal muscle: its crucial role for muscle function, plasticity, and disease. Physiol Rev 80: 1215-1265.
4. Gundersen K (2011) Excitation-transcription coupling in skeletal muscle: the molecular pathways of exercise. Biol Rev Camb Philos Soc 86: 564-600.
5. Chin ER (2010) Intracellular Ca^{2+} signaling in skeletal muscle: decoding a complex message. Exerc Sport Sci Rev 38: 76-85.
6. Dunn SE, Simard AR, Bassel-Duby R, Williams RS, Michel RN (2001) Nerve activity-dependent modulation of calcineurin signaling in adult fast and slow skeletal muscle fibers. J Biol Chem 276: 45243-45254.
7. Liu Y, Cseresnyes Z, Randall WR, Schneider MF (2001) Activity-dependent nuclear translocation and intranuclear distribution of NFATc in adult skeletal muscle fibers. J Cell Biol. 155: 27-40.
8. Schiaffino S, Sandri M, Murgia M (2007) Activity-dependent signaling pathways controlling muscle diversity and plasticity. Physiology (Bethesda) 22: 269-278.
9. Rana ZA, Gundersen K, Buonanno A (2009) The ups and downs of gene regulation by electrical activity in skeletal muscles. J Muscle Res Cell Motil 30: 255-260.
10. Dolmetsch R (2003) Excitation-transcription coupling: signaling by ion channels to the nucleus. Sci STKE 2003: PE4.
11. Liu Y, Shen T, Randall WR, Schneider MF (2005) Signaling pathways in activity-dependent fiber type plasticity in adult skeletal muscle. J Muscle Res Cell Motil. 26: 13-21.
12. Bassel-Duby R, Olson EN (2006) Signaling pathways in skeletal muscle remodeling. Annu Rev Biochem 75: 19-37.
13. Shen T, Liu Y, Randall W R, Schneider MF (2006) Parallel mechanisms for resting nucleo-cytoplasmic shuttling and activity dependent translocation provide dual control of transcriptional regulators HDAC and NFAT in skeletal muscle fiber type plasticity. J Muscle Res Cell Motil. 27: 405-411.
14. Chin ER, Olson EN, Richardson JA, Yang Q, Humphries C, et al. (1998) A calcineurin-dependent transcriptional pathway controls skeletal muscle fiber type. Genes Dev 12: 2499-2509.

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15. Shen T, Liu Y, Contreras M, Hernandez-Ochoa EO, Randall WR, et al. (2010) DNA binding sites target nuclear NFATc1 to heterochromatin regions in adult skeletal muscle fibers. Histochem Cell Biol 134: 387-402.

16. Chin ER (2005) Role of Ca^{2+}/calmodulin-dependent kinases in skeletal muscle plasticity. J Appl Physiol 99: 414-423.

17. Rose AJ, Kiens B, Richter EA (2006) Ca^{2+}-calmodulin-dependent protein kinase expression and signalling in skeletal muscle during exercise. J Physiol. 574: 889-903.

18. Carrasco MA, Hidalgo C (2006) Calcium microdomains and gene expression in neurons and skeletal muscle cells. Cell Calcium 40: 575-583.