EDITORIAL

Mechanisms of Excitation Contraction Coupling in Skeletal Muscle

Calcium (Ca^{2+}) ions play an important role as second messengers in virtually all cell types including being the primary mediator of muscle contraction. Since several pathophysiological conditions of skeletal muscle (malignant hyperthermia, central core disease, etc.) result from compromised Ca^{2+} handling and signalling, manifesting themselves as an alteration of the force generating capacity, it is extremely important to understand the fundamental mechanisms by which Ca^{2+} is released from internal stores. Over the last several years much effort has been focused on elucidating the specific mechanisms involved in excitation-contraction (EC) coupling - the mechanism that controls Ca^{2+} release from the sarcoplasmic reticulum (SR) and the consequent muscle contraction – in hopes of gaining an understanding of the role of the EC process in health and disease.

In muscle, the fine balance of cytoplasmic [Ca^{2+}] is achieved and maintained through an extremely well organized system of tubules and vesicles known collectively as the sarcoplasmic reticulum (SR), a highly specialized version of the endoplasmic reticulum that closely surrounds myofibrils and that efficiently sequesters and releases Ca^{2+} [3]. The SR forms highly specialized junctions called calcium release units. In these structures the SR terminal cisternae and the sarcolemma's invaginations, or transverse-tubules (TTs), are closely associated with one another [2]. CRUs are the *loci* where the excitation-contraction (EC) coupling mechanism takes place [6]. It took several years after the elucidation of the structures of the SR and TT [3, 5], before the molecular components that allow the communication between these two sets of membranes could be identified. One of the first structures described as an integral component of the triads were the large electron-dense structures that bridge the narrow gap separating the SR from the T-tubule/sarcolemma now known as *feet*, [(Franzini-Armstrong, 1970). Feet were later identified as the cytoplasmic domains of RyRs and RyRs in turn were identified as the Ca^{2+} release channels of the SR. Another extremely important component of CRUs is the dihydropyridine receptor (DHPR), an L-type Ca^{2+} channel, localized in specific areas of the exterior membranes that face junctional arrays of feet. The DHPRs are responsible for initiating EC coupling by triggering Ca2+ release from the RyRs (Rios and Brum, 1987; Tanabe et al., 1987). While DHPRs and RyRs are still recognized as the two key elements in the communication between the SR and exterior membranes, many other proteins involved in the mechanism have been identified in the last decade (β-DHPR, calsequestrin, triadin, junctin, FKBP12, mitsugumin, junctophilin, etc).

In this special BAM Issue, two original papers from Ward and collaborators discuss Ca^{2+} activation of muscle contraction and actomyosion ATSase activity investigating role of fiber types, and the effects of Mg^{2+} and temperature. Papers by Coronado et al., Sharma and Wagenknecht, Rossi and Sorrentino, and Schreiber et al. review the role, structural interactions, and tissue related expression of some of the key EC coupling proteins, while the review by Lueck et al. offers an excellent overview of muscle disorders linked to mutation of the Ryanodine receptor gene.

I believe that the collection of papers presented in this special BAM issue represent a valuable contribution to the field of EC coupling and I hope that it will stimulate further scientific research and encourage young investigators to become myologists.

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