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Introduction to Mini-Reviews

Molecular Basis for Calcium Release from Sarcoplasmic Reticulum

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The process that is generally called excitation–contraction coupling in muscle involves several important steps as follows. Excitation initiated at the muscle cell surface by the nerve impulse is propagated into the cell through the transverse tubular (T-tubule) system (Caille *et al.*, 1985). It spreads further to another membrane system, the sarcoplasmic reticulum (SR), which in turn releases the Ca^{2+} accumulated in the SR into the cytoplasm of muscle cell (Endo, 1977; Martonosi, 1984). Binding of the released Ca^{2+} to troponin located in the thin filaments releases the inhibition of the interaction between actin and myosin (Leavis and Gergely, 1984).

One of the most important unsolved questions in muscle physiology concerns how the signal elicited in the T-tubule, or other type of signal, induces Ca^{2+} release from the SR. Two major hypotheses have emerged from extensive studies on intact or skinned muscle fiber preparations. Firstly, the functional coupling between the T-tubule depolarization and Ca^{2+} release from SR may be mediated by a nonlinear charge movement and the mechanical processes occurring in the vicinity of the bridge between the T-tubule and SR membrane (the so-called foot). Secondly, chemical messengers (e.g., Ca^{2+}, and phospholipid metabilites such as inositol 1, 4, 5-trisphosphate) might be involved in the process. Chemical messenger-dependent Ca^{2+} release may play an important role especially in cardiac and smooth muscle fibers, where the T-tubule system is poorly developed or totally absent.

Most of the earlier studies on Ca^{2+} release from SR were done with skinned fiber preparations (Endo, 1977); however, this system has some

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limitations in an analysis of the process at the molecular level because of its complexity. On the other hand, isolated systems with various degrees of complexity, such as (1) a junctional complex consisting of the T-tubule and SR membranes and the feet, (2) individual components of the junctional complex, and (3) further purified molecular components, have enabled a remarkable advance in the understanding of the molecular mechanism of Ca^{2+} release in recent years.

The aim of this special issue is to provide one with an updated survey of the recent developments in the studies on Ca^{2+} release *in vitro*. The contributors are represented by a number of leading researchers in this particular field. Since the focus of the issue is on the *in vitro* system, studies on the fiber system are not included, although a solid historical background based upon extensive work in fiber physiology is carefully referred to in every article.

One of the important themes of this issue is the characterization of the membrane constituents that are relevant to the Ca^{2+} release mechanism. Several articles analyze this problem from different angles. First of all, general properties of the T-tubule membrane are thoroughly reviewed by Sabbadini and Dahms. The structures bridging the T-tubule and SR membranes, viz., the feet, and the junctional face membrane regions of the terminal cisternal SR have been found to be an essential for Ca^{2+} release. Several articles in this issue—Caswell and Brandt; Volpe; and Lai and Meissner—deal with various proteins located in these regions. A new technology in electrophysiology (single-channel conductance measurements) has provided a fascinating capability for direct examination of the Ca^{2+} channel functions that reside in the foot protein, as discussed in detail in the article by Lai and Meissner.

Another important theme of this issue concerns the functional aspects of Ca^{2+} release. Ikemoto, Ronjat, and Mészáros review the kinetic properties of Ca^{2+} release from isolated SR vesicles induced by various methods, and discuss the roles that various molecular components may play in the induction and release processes. A comprehensive review of the chemistry and function of one of the important Ca^{2+} release-inducing agents, inositol 1,4,5-trisphosphate, is provided by Hidalgo and Jaimovich. Another type of release induction mechanism, viz., chemical modification of thiol groups, is discussed by Abramson and Salama. Finally, the article by Palade, Dettban, Brunder, Stein, and Hals provides thorough coverage of a variety of pharmacological reagents that activate or inhibit Ca^{2+} release.

As seen in this mini-review series, the recent studies on the isolated muscle membrane system have begun to unveil some molecular components and their functions that seem to play critical roles in the signal transmission and Ca^{2+} release mechanisms. It is my hope that this issue not only provides a comprehensive summary of the recent rapid advance in the studies of the

molecular mechanism of Ca^{2+} release from SR, but also offers useful inputs into future studies of excitation–contraction coupling phenomena *in vivo* as well as *in vitro*.

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