Book Review

Troponin: Regulator of Muscle Contraction

Editors: J.-P. Jin (Department of Physiology, Wayne State University School of Medicine, Detroit, MI)

As part of his development of the Ca^{2+} concept of muscle contraction and relaxation in the 1960s, Setsuro Ebashi discovered the first intracellular Ca^{2+} binding protein which he named troponin. In 1971 Marion Greaser and John Gergely determined that troponin consisted of three subunits. They named the subunits based on their observed function: TnC bound Ca^{2+}, TnI inhibited actomyosin ATPase activity in the presence or absence of Ca^{2+} and TnT bound to tropomyosin. In 1973 they made one of the classic understatements in the muscle literature when they stated that "there appears to be a rather complicated series of protein-protein interactions" in troponin. As this book clearly exemplifies, forty years later these rather complicated protein-protein interactions are still under intense investigation but now not only to elucidate basic mechanism but also to understand disease, especially in the heart.

Editor J.-P. Jin, Wayne State University, has gathered together experts in various facets of troponin research in both health and disease and charged them to write review chapters on a wide range of topics. The result is a comprehensive introduction to the ever expanding field of troponin research with well over 1,000 references. The emphasis is primarily on troponin in the heart.

The book starts with a very readable chapter of the history of the troponin field by R. J. Solaro, University of Illinois at Chicago, who has been an active participant in troponin research for nearly fifty years. His chapter emphasizes major discoveries in troponin research which he calls "tipping points". P. Reiser, Ohio State University, describes the tremendous diversity of troponin subunit isoforms found across the animal kingdom. J.-P. Jin provides an overview of the evolution of troponin subunit genes with the provocative hypothesis that TnI and TnT genes evolved from a common ancestor gene. S. K. Gollapudi and M. Chandra, Washington State University, give an in depth review of the biochemistry of Tn and its subunits. D. C. Rieck and W.-J. Dong, Washington State University, describe the methods and results of investigation of the conformational states of Tn *in vitro* and *in situ*. They emphasize the importance and challenges of studying Tn structural changes within the architecture of the myofilament. They conclude that there is an on-going need for a multi-faceted approach to investigating troponin conformational states. A. K. Sen describes the development of a kinetic model of the dissociation of troponin from the thin filaments under various conditions as a way to probe the various states of troponin in the myofilament. H.-Z. Feng and Jin provide an overview of the rapidly evolving field of developmental and adaptive regulation of troponin.

In a *tour de force*, M. Westfall, University of Michigan, comprehensively reviews the staggering complexity of established and emerging post-translational modifications of troponin with nearly 300 references. She emphasizes that the "on-off" signaling models of troponin function are increasingly being replaced by signaling cascades operating as mini-processes to modulate cardiac structure and performance in response to multiple environmental inputs. P. P. de Tombe, Loyola University Chicago, addresses the on-going challenge of investigating the mechanism of the century old Frank-Starling Law of the heart. He describes various hypotheses and experimental results with the enigma still unsolved. B. J. Biesiadecki and J. P. Davis, Ohio State University, discuss how abnormal troponin can be utilized as a tool to delineate the important troponin interactions involved in the Ca^{2+} regulation of cardiac contraction and also provide insights into potential therapies to treat cardiomyopathies. Finally P.-Y.

Jean-Charles, C. Nan, L. Zhang, J. Tian and X.-P. Huang, Florida Atlantic University, provide an overview of the effects of troponin mutations on diastolic dysfunction in the heart and possible therapeutic options. They start with a description of the effect of cardiac TnI mutations on diastolic dysfunction in humans and then move on to animal models of human disease and then to mechanistic studies of cTnI mutations on myofibrillar Ca^{2+} sensitivity. They emphasize that therapies for diastolic dysfunction should aim at modifying the Ca^{2+} sensitivity in the diseased hearts.

One comes away from reading this book realizing that an enormous amount has been learned in the forty years since the discovery of troponin but also that there is much more to be learned in this vibrant research field. This book makes a major contribution to understanding what is known and what are the major challenges ahead. J.-P. Jin has summarized it well in the preface when he states: "We are very proud of the completion of this work that is the very first of its kind and will facilitate progresses in the field." I agree.

Review provided by Jack A. Rall, Department of Physiology & Cell Biology, Ohio State University