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EDITORIAL

Progress on the regulation of myofibrillar function: Part 2

Henk L. Granzier[1] and Richard L. Moss[2]

This issue of *JGP* is the second of two special issues dedicated to muscle and nonmuscle contractile systems. The content in this issue was submitted by attendees of the 2018 Myofilament Conference (https://cvrc.wisc.edu/myofilament-conference/#meeting-home) and handled by *JGP*'s Editors according to the Journal's editorial process.

The goal of the Myofilament Conference is to further the mechanistic understanding of force generation and its regulation in contractile systems. Accordingly, the research papers in this issue investigate force development, mechanical stiffness, and length-dependent activation in both skeletal and cardiac muscle. In doing so, the papers increase our understanding of the roles and mechanisms of action of regulatory proteins such as titin, nebulin, myosin-binding protein C (MyBP-C), and actin-capping protein (CapZ), as well as the myofilaments themselves.

This second special issue includes a focus on the molecular motor myosin and includes a Milestone in Physiology by Moss and Solaro on the relationship originally described by Michael Bárány between the speed of muscle contraction and myosin ATPase activity. Furthermore, Reda et al. present new insights into how the developmental increase in expression of myosin heavy chain β (β-MHC) enhances sarcomere length–dependent activation of the myocardium. The issue also includes a detailed Commentary by Irving and Craig that evaluates the emerging strain-dependent model of thick filament activation in which the activation of cardiac contraction depends on positive feedback between stress on the filament and the graded process of switching "ON" individual myosin motors.

Other contributions include studies on MyBP-C, a protein located in the C-zone of each half-thick filament that is thought to be an important regulator of contraction. The work by Robinett et al. shows that the slow skeletal isoform (sMyBP-C) regulates sarcomere contraction through a combination of cross-bridge recruitment, modification of cross-bridge cycling kinetics, and alteration of drag forces that originate in the C-zone. These findings are further highlighted in a Commentary by Colson.

Thin filament regulation is also a focus of this issue, including work by Heeley et al. on how physiological levels of regulation are dependent upon the liganded state of the thin filament as well as the conformation of myosin. Solís and Russell study the thin filament accessory CapZ, located in the Z-disk, and its role in responding to mechanical stimuli, and Gregorich et al. determine the role of the Z-disk-located enigma homologue in contraction. Finally, to integrate many of the findings, including the roles played by titin and nebulin in the regulation of contraction, Mijailovich et al. present a computational platform "muscle simulation code" (MUSICO). This model of contraction takes into account cross-bridge cycling kinetics, the explicit 3-D geometry of the myofilament lattice including variation in actin filament lengths and titin-based passive elasticity, and thin filament regulatory processes. A Commentary on this work is provided by Chase.

The editors hope you enjoy this final installment of the Myofilament Conference special issue and encourage those who are interested to consider attending the 2020 meeting.

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[1]Department of Cellular and Molecular Medicine, University of Arizona, Tucson, AZ; [2]Department of Cell and Regenerative Biology, University of Wisconsin, Madison, WI.

Correspondence to Henk L. Granzier: granzier@email.arizona.edu.