UNIVERSITY OF CALIFORNIA AT DAVIS

PHYSIOLOGY & MEMBRANE BIOLOGY

SCHOOL OF MEDICINE

IN-HOUSE SEMINAR SERIES

SAMANTHA HARRIS, Ph.D.

Assistant Professor

Neurobiology, Physiology & Behavior

"Myosin Binding Protein-C: A Novel Regulator of Cardiac Contraction Through Thick and Thin"

Myosin binding protein-C (MyBP-C) is a thick-filament protein that limits cross-bridge cycling rates and reduces myocyte power output in vertebrate striated muscles. Mutations in cardiac (c) MyBP-C are the most common cause of familial hypertrophic cardiomyopathy, the leading cause of sudden death in adolescents and young adults. To investigate mechanisms by which MyBP-C affects contraction we assessed effects of recombinant N-terminal domains of cardiac (c) MyBP-C on contractile properties in permeabilized rat cardiac trabeculae. Here we show that N-terminal fragments of cMyBP-C containing the first two Ig domains of cMyBP-C (i.e., C0 and C1) plus the unique linker sequence termed the MyBP-C "motif" increased Ca2+ sensitivity of tension and increased rates of tension redevelopment (i.e., k*tr*) at sub-maximal levels of Ca2+. At concentrations ≥ 20 μM, recombinant proteins also activated force in the absence of Ca2+ and inhibited maximum Ca2+-activated force. Recombinant proteins that lacked the combination of C1 and the motif did not affect contractile properties. These results suggest that the C1 domain plus the motif constitute a functional unit of MyBP-C that promotes activation of the thin filament.

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4:00 PM
TUPPER HALL ROOMS 2419A & 2419B

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