

University of Houston - Biomedical Engineering Seminar

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Via Zoom: <https://uofh.zoom.us/j/92470065206>

Post-Translational Regulation of Cardiac Muscle Contraction by Myofilamental Acetylation



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Abstract

We report, for the first time, that reversible myofilament protein acetylation carried out by histone acetyltransferases (HATs) and deacetylases (HDACs) can also regulate cardiac muscle contractile activity. Immunohistochemical and electron microscopic analyses revealed that both HDAC4 (a Class II HDAC) and PCAF (a HAT) associate with the Z-disc and I- and A-bands of cardiac sarcomeres. Increased acetylation of myofilament proteins by HDAC inhibition under *in vitro* conditions enhanced myofilament calcium sensitivity. The Z-disc-associated protein, MLP, a sensor of cardiac mechanical stretch was acetylated. Also HDAC inhibition increased myofilament calcium sensitivity of wild-type, but not of MLP knock-out mice, demonstrating a role of MLP in acetylation-dependent increased myofilament contractile activity. Current studies are to develop novel therapeutic approaches for enhancing cardiac muscle contractile activity using this new regulatory pathway under *in vivo* conditions.

Biosketch

Dr. Sanjeev Shroff is the McGinnis Chair of Bioengineering and Professor of Medicine at the University of Pittsburgh. Previously he was in the Dept of Medicine at the University of Chicago. Trained as an electrical engineer (B.Tech., IIT Kanpur, M.Eng., McMaster), Dr. Shroff obtained his Ph.D. in Bioengineering from the Univ. of Pennsylvania. Dr. Shroff's research *has* two main focus areas: **(1)** Contractile and regulatory proteins and post-translational regulation of cardiac contraction. **(2)** Role of vascular stiffness in cardiovascular function and potential therapeutic applications of vascular stiffness-modifying drugs and/or hormones (e.g., relaxin). Honors include AHA Established Investigator Award; Fellow of the American Physiological Society, *AIMBE*, *BMES*, and *IAMBE*. He received the University of Pittsburgh Chancellor's Distinguished Teaching Award. Dr. Shroff is PI of both a T32 training grant since 2005 and the Coulter Translational Research Partnership II Program since 2013.