A new look at phospholamban in pressure-overload hypertrophy

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THE QUESTION OF THE MECHANISMS of pathological cardiac hypertrophy and the relationship of changes in cellular function to a myriad of clinical symptoms has long been an important and intriguing puzzle to researchers. How is it that exercise induces signaling changes that are beneficial to heart function but pathological conditions such as hypertension or valvular disease are associated with a loss of hemodynamic function and neurohumoral response, although both produce muscular hypertrophy? What are the interactions between hypertrophic and contractile signaling pathways? One point of interest is the pertrophy? What are the interactions between hypertrophic and neurohumoral response, although both produce muscular hypertrophy and the relationship of changes in cellular function to a unified signal to the sarcoplasmic reticulum and as an element in modulating the β-adrenergic pathway itself. If intracellular Ca^{2+} fluxes change in response to other diseases or treatments, how can PLB modify adrenergic signaling under these conditions?

In that context, the data of Mills et al. (3) raise interesting questions in light of previous work in a rat model where the loss of sensitivity to isoproterenol in spontaneously hypertensive rats was associated with elevated abundance of PLB along with reduced phosphorylation at Ser^{16} and Thr^{17}. Additionally, phosphorylation was restored at both of these sites by treadmill exercise training, increasing the Ca^{2+} available for release and, subsequently, contractility. This result is similar to the pacing of single cat myocytes in the increase of Thr^{17} phosphorylation while at the same time GRK2 was decreased, improving β-adrenergic responsiveness (2). Although there are obvious species differences in the two studies, why did PLB phosphorylation go down in the hypertensive rat and up in the PO cat when both had reduced adrenergic response? The changes in morphology, signaling, and function of the heart in these disease states leave many questions remaining to be answered, and this step in the progress of linking whole heart function to specific regulatory changes brings us closer to that goal.

REFERENCES