

## Publication

## A recombinant antibody increases cardiac contractility by mimicking phospholamban phosphorylation

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Many cardiovascular disease states end in progressive heart failure. Changes in intracellular calcium handling, including a reduced activity of the sarcoplasmic reticulum calcium pump (SERCA), contribute to this contractile dysfunction. As the regulatory protein phospholamban can inhibit the calcium pump, we evaluated it as a potential target to improve cardiac function. In this study, we describe a recombinant antibody-based protein (PLN-Ab) that binds to the cytoplasmic domain of phospholamban. Fluorescence resonance energy transfer (FRET) studies suggest that PLN-Ab mimics the effects of phospholamban phosphorylation. PLN-Ab accelerated the decay of the calcium transient when expressed in neonatal rat and adult mouse ventricular cardiac myocytes. In addition, direct injection of adenovirus encoding PLN-Ab into the diabetic mouse heart enhanced contractility when measured in vivo by echocardiography and in ex vivo Langendorff perfused hearts. The PLN-Ab provides a novel therapeutic approach to improving contractility through in vivo expression of an antibody inside cardiac myocytes.

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