

**SY-I-4**

## **ACTIVATION OF HISTONE DEACETYLASE 2 BY INDUCIBLE HEAT SHOCK PROTEINS IN CARDIAC HYPERTROPHY**

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Diverse cardiac diseases are known to induce cardiac hypertrophy, which often ends up in disastrous leads to cardiac dilatation and heart failure. We have previously reported that cardiac hypertrophy could be blocked by class I histone deacetylase (HDAC) inhibitors, which prompted us to investigate the regulatory mechanism of class I HDACs in cardiac hypertrophy. Cardiac hypertrophy-inducing stimuli such as aortic banding, isoproterenol (ISP), or angiotensin II-infusion elevated the enzymatic activity of nuclear HDAC2, one of a class I HDACs. Among possible regulatory mechanisms, we ruled out alterations in protein amount, intracellular localization or phosphorylation level of HDAC2. Hypertrophic stimuli induced expression of heat shock protein (HSP) 72. HSP72 increased HDAC2 activity and directly interacted with HDAC2. Heat shock to of cardiomyocytes activated HDAC2 and the atrial natriuretic factor promoter. In HSP72 null mice, ISP infusion failed to increase both HDAC2 activity and heart weight. These results suggest that induction of chaperones in response to various stimuli and ensuing activation of HDAC2 mediate aspects of cardiac hypertrophy, and provide clue on how heart diseases such as myocardial infarction known to induce HSP cause cardiac hypertrophy.

**Key Words:** Cardiac hypertrophy, Class I histone deacetylases, Histone deactylase 2, Heat shock protein 72