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"YAP Promotes Cardiac Hypertrophy Through Metabolic and Epigenetic Regulation"

By

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B.S. Huaqiao University, 2015
M.S. Stevens Institute of Technology, 2018

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Monday, October 20th, 2025
Medical Science Building, G-609
11:00 A.M.

Join Zoom presentation

https://rutgers.zoom.us/j/2745332614?pwd=j965CKUlHTlUm1KGoGaAEHTIRdIJ3V.1&omn=95890770831

Meeting ID: 274 533 2614
Password: 10202025

ABSTRACT

Heart failure (HF), a global health challenge affecting over 64 million people worldwide, can be delayed by activating compensatory cardiac hypertrophy—an adaptive response to increased workload that helps preserve cardiac function. However, the mechanisms behind this process are not fully understood. Yes-associated protein (YAP), a key effector of the Hippo pathway, has been shown to play a protective role by mediating compensatory hypertrophy during the acute phase of pressure overload. To better understand the role of YAP during this process, we explored its involvement in cellular metabolism and epigenetic modifications. We first observed that YAP specifically upregulated H3K4me3 in cardiomyocytes under stress. H3K4 methylation is promoted in the presence of methyl donors, S-adenosyl methionine (SAM), and the histone methyltransferase (HMT) complexes. Firstly, we found YAP upregulated the expression of serine synthesis pathway (SSP) enzymes. Metabolomic analysis revealed that YAP increased SSP-related metabolites in the heart under stress, including SAM. Using cardiac-specific SSP-deficient mice, we demonstrated that SSP is essential for maintaining cardiac function, promoting cardiac hypertrophy, inducing SAM production, and preserving H3K4me3 expression levels. Secondly, we found that YAP upregulates and recruits an HMT specifically responsible for H3K4me3 to regulate cardiac function under stress. Cardiac loss of this HMT impaired cardiac function and exacerbated cardiac fibrosis and apoptosis. By integrating RNA-seq and ChIP-seq analyses, we further identified six downstream target genes co-regulated by YAP and H3K4me3. Taken together, our findings suggest that YAP promotes compensatory cardiac hypertrophy under stress by regulating SSP- and HMT-dependent metabolic and epigenetic pathways, thereby inducing H3K4me3-mediated control of key downstream genes. These results highlight the potential therapeutic targets for preventing the progression of heart failure under stress conditions.