Strengthening Cardiomyocytes: Proliferation Independent Effects of Mechano-Transducer YAP1

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Population aging increases the occurrence of chronic heart disease characterized by decrease of cardiomyocyte number and their contractility. The absence of natural heart self-repair mechanisms creates a need for new treatments to stimulate cardiomyocyte proliferation and/or their strengthening. Potential therapeutic target is mechanosensitive Hippo effector YAP1. While YAP1 promotes cardiomyocyte proliferation, its proliferation-independent effects remain to be identified. I hypothesized YAP1 to induce cardiomyocyte strength by increasing expression of cardiomyocyte biomarkers (sarcomere organization and calcium handling genes) and increasing hypertrophic response. This study used genetically modified and pharmacologically treated in vitro differentiated cardiomyocytes. YAP1 impact on cardiomyocyte biomarkers expression and effects of transcriptional activity induction were quantified by western blot. YAP1 role in myofibrillar maturation and hypertrophic response was examined using immunofluorescence followed by imaging and data analysis. YAP1 induces expression of cardiomyocyte biomarkers, such as cTnT, SERCA2A and LTCC, and hence also increases myofibrillar maturity. Moreover, YAP1 promotes BNP expression and induces cardiomyocyte hypertrophic response. Additionally, I tested pharmacological and mechanical stimuli to promote YAP1 activity. Intriguingly, I observed novel YAP1 transcriptional activity, present specifically in cardiomyocytes. Taken together, this study shed new light on the previously unknown crucial role of YAP1 in expression of cardiomyocyte biomarkers, cardiomyocyte structure, and myofibrillar maturity. YAP1 hence appears to be essential for proper heart function with potential to improve heart regeneration even in a proliferation-independent manner.

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