RUTGERS
School of Graduate Studies

Office of Student Affairs and Admissions
SGS at New Jersey Medical School
Rutgers, The State University of New Jersey
185 South Orange Avenue, MSB C-696
Newark, NJ 07103

http://njms.rutgers.edu/gsbs/
p. 973-972-4511
f. 973-972-7148

YOU ARE INVITED TO ATTEND THE

DEFENSE OF THE DOCTORAL

DISSERTATION

"Deficiency of Yes-Associated Protein (YAP) Promotes Structural and Functional Cardiac Maladaptation in Response to Acute Pressure Overload"

by
Jaemin Byun

Cell Biology, Neuroscience and Physiology Program

M.S. 2004, Handong University, Pohang, South Korea
B.E. 2001, Handong University, Pohang, South Korea

Thesis Advisor:

Junichi Sadoshima, M.D., Ph.D.
Department of Cell Biology and Molecular Medicine

Tuesday, November 20th, 2018
12:15 P.M.
Medical Science Building, G609-B

ABSTRACT

Cardiovascular disease (CVD) remains the leading cause of death globally. Among many CVDs, heart failure (HF) is a critical risk factor for cardiac death. The development of cardiac hypertrophy in response to hemodynamic overload is considered initially beneficial. However, the adaptation has its limits and in the presence of prolonged stress, HF may develop. Yes-Associated Protein (YAP), the central downstream effector of the Hippo signaling pathway, regulates cell proliferation and survival in mammalian cells. Our previous work demonstrated that cardiac-specific loss of YAP leads to increased cardiomyocyte (CM) apoptosis and impaired CM hypertrophy during chronic myocardial infarction in the mouse heart. Due to its documented cardioprotective effects, we sought to determine the importance of YAP in response to acute pressure-overload (PO). Our results indicate that endogenous YAP is activated in the heart during acute PO. YAP activation was also observed in CMs subjected to cyclic stretch, which dependent on RhoA. To examine the function of endogenous YAP in acute PO, Yap+/flox;Creα-MHC (YAP-CHKO) and Yap+/flox (WT) mice were subjected to transverse aortic constriction (TAC). We found that YAP-CHKO mice had attenuated cardiac hypertrophy and significant increases in CM apoptosis and fibrosis that correlated with worsened cardiac function 7 days after TAC. Loss of CM YAP also impaired activation of the cardioprotective kinase Akt, which may explain the YAP-CHKO phenotype. Together, these data indicate a pro-hypertrophic, pro-survival function of endogenous YAP and suggest a critical role for CM YAP in the adaptive response to acute PO.