NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by A/P Low Boon Chuan

Zebrafish VCAP1X2 regulates cardiac contractility and proliferation of cardiomyocytes and epicardial cells

By **Sheng-Ping Hwang**

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Sarcomeric signaling complexes are important to sustain proper sarcomere structure and function, however, the mechanisms underlying these processes are not fully elucidated. In a gene trap experiment, we found that vascular cell adhesion protein 1 isoform X2 (VCAP1X2) mutant embryos displayed a dilated cardiomyopathy phenotype, including reduced cardiac contractility, enlarged ventricular chamber and thinned ventricular compact layer. Cardiomyocyte and epicardial cell proliferation was decreased in the mutant heart ventricle, as was the expression of pAKT and pERK. Contractile dysfunction in the mutant was caused by sarcomeric disorganization, including sparse myofilament, blurred Z-disc, and decreased gene expression for sarcomere modulators (smyd1b, mypn and fhl2a), sarcomeric proteins (myh6, myh7, vmhcl and tnnt2a) and calcium regulators (ryr2b and slc8a1a). Treatment of PI3K activator restored Z-disc alignment while injection of smyd1b mRNA restored Z-disc alignment, contractile function and cardiomyocyte proliferation in ventricles of VCAP1X2 mutant embryos. Furthermore, injection of VCAP1X2 variant mRNA rescued all phenotypes, so long as two cytosolic tyrosines were left intact. Our results reveal two tyrosine residues located in the VCAP1X2 cytoplasmic domain are essential to regulate cardiac contractility and the proliferation of ventricular cardiomyocytes and epicardial cells through modulating pAKT and pERK expression levels.

About the Speaker

Dr. Sheng-Ping Hwang was born in Taipei, Taiwan in 1956. She graduated from the Department of Botany, National Chung-Hsing University, Taiwan in 1978. She received M. Sci in Marine Environmental Science in 1984 and her Ph.D. degree in Biochemistry and Cell Biology in 1989 from State University of New York at Stony Brook, USA. She did postdoctoral research in the lab of Professor W. J. Lennarz located in the same department working on sea urchin embryogenesis during 1990-1993. She joined the Institute of Zoology, Academia Sinica, Taiwan as an associate research fellow in 1993, and received tenure in the Institute of Cellular and Organismic Biology, Academia Sinica in 2010. Her research interest is the investigation of gene regulatory mechanisms involved in organ morphogenesis including GI tract and heart in zebrafish embryos. She is an Academic Editor at PLoS One. She is the coordinator of Taiwan Zebrafish Core Facility at Academia Sinica, which has provided various services to zebrafish community since 2010.

Artwork by Ann Nee, DBS, NUS