

IMCB Invited Speaker



Speaker : Dr. Jianming Jiang
*Research Associate, Department of Genetics,
Harvard Medical School, USA*

Date : 18 November 2013, Monday

Time : 10:00AM - 11:00AM

Venue : IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis

Host : Prof. Wang Yue

Seminar :

**Delineation of molecular mechanisms of heart diseases using
an adeno-associated virus mediated delivery system**

Mutations in sarcomere proteins such as the myosin heavy chains (MHC) and myosin binding protein C (Mybpc) are the leading genetic causes of human hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM). Mouse models, MHC^{403/+} and Mybpc^{U1}, recapitulate the genetics and pathology cardiomyopathy found in human patients. However, our knowledge of how mutations in sarcomere proteins lead to cardiomyopathy is limited due to tedious crossing, genetic modifiers in different mouse background and lack of tissue or cell type specific knockout mice. We developed an adeno-associated virus mediated RNA Interference (AAV-RNAi) system to better understand molecular mechanisms of cardiomyopathy *in vivo*. During my talk, I will present two projects. First, we used AAV-RNAi to rescue HCM by selectively silencing the expression of the mutant cardiac MHC gene in mice. RNAi-treated disease mice (MHC^{403/+}) developed no pathologic manifestations of HCM for at least 6 months. Because inhibition of HCM was achieved by partial reduction in the levels of the mutant transcripts, the variable clinical phenotype in HCM patients may reflect allele-specific expression and silencing of mutant transcripts may have therapeutic benefit. Second, we found that Mybpc deficient myocytes have delayed perinatal karyokinesis/cytokinesis and prolonged cell cycle progression, resulting in increased myocyte number and mononuclear myocyte proportion. Mybpc has unexpected inhibitory functions during postnatal myocyte cytokinesis and cell cycle progression. Unrecognized myocyte hyperplasia may contribute to increased heart mass that characterizes myopathy with human mutations reducing MYBPC levels.

About the Speaker :

Dr. Jianming Jiang is a research associate in the Department of Genetics at Harvard Medical School. After finishing undergraduate study in Zhejiang University, Dr. Jiang received his M.S. from Chinese Academy of Medical Sciences & Peking Union Medical College, and his Ph.D. from National University of Singapore & Genome Institute of Singapore.

Dr. Jiang's research focuses on the development of new therapies for heart diseases. He is specifically interested in understanding how the deregulated factors in heart contribute to the progress of disease development and how to reinstate the regenerative capacity of mammalian hearts.