TEMS

Temasek External Monthly Seminar

TEMASEK LIFESCIENCES LABORATORY

ALL ARE WELCOME

21 May 2018 (Monday), 3.00pm

The Auditorium (Level 1)

Hosted by: Dr Cai Yu

Two C type Lectins on Zika and Dengue Pathogenesis: from mosquito to human

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Dr. Chen completed his undergraduate education at National Taiwan University (NTU) in 1991, master's thesis research in plant viruses from 1993-1995 at NTU. His doctoral research in RNA splicing mechanisms in yeast was performed in the laboratory o at National Yang-Ming University/IMB, Academia Sinica, In 2003, He began his postdoctoral study of microRNAs (miRNAs) in *Drosophila melanogaster* in laboratory of Dr. Bruce Hay at the California Institute of Technology. In 2007, he led the Hay's group in the development of a novel method of miRNA-mediated RNA interference (RNAi) in *D. melanogaster*, and he generated a population of *D. melanogaster* using a synthetic *Medea* gene drive element. The *Medea* element can potentially be used in other insect vector species, including malaria vectors, to drive anti-pathogen genes into wild populations for controlling disease transmission. In 2008, the Medea project received funding from the Bill and Melinda Gates Foundation. The development of the *Medea* gene drive element received a Scientific American Top 50 award in 2007, and was also selected for a Top 10 article by Faculty 1000. He began his career at the National Health Research Institute (NHRI) in 2009. In his laboratory at the NHRI, his group is carrying out our studies in two model systems, *D. melanogaster* and the dengue vector *Aedes aegypti*. He received the Herbert Tabor Young Investigator Award from the Journal of Biological Chemistry in 2011 for the work on virus and mosquito. From 2016, he is Deputy Executive Secretary, National Mosquito-borne Disease Control and Research Center, NHRI and as Chief Executive Officer, National Tropical Disease Control and Research Center from 2017. Now he developed CRISPR/Cas 9 system in Aedes. And he also tries to establish some animal model for Dengue and Zika in his lab.

C-type lectins are a family of proteins with carbohydrate-binding activity. Several C-type lectins that have been shown to have vital roles in immune activation and viral pathogenesis, which are employed as receptors or attachment factors to facilitate flavivirus invasion. Dengue virus (DENV) and Zika virus are two of the most threatening and fastest spreading mosquito-borne disease of the world. DENV have four serotypes (DENV-1 to DENV-4). And the yellow fever mosquito, Aedes aegypti, is the principle vector transmitting dengue virus. In this study, we used CRISPR/Cas9 technology to knockout C-type lectin-3 (GCTL-3) gene which is susceptibility factors for dengue infection in A. aegypti. Aedes GCTL-3 Gene disruption by homology directed repair at the target locus. The data show that GCTL-3 mutant mosquitoes could reduce DENV1,2,3 viral load after a blood meal. GCTL-3 homology mutant mosquitoes could reduce amount of oviposition and hatch rate. GCTL-3 mutant also causes embryo melanization in the ovary of Aedes mosquito, suggesting this protein also play role on the development of reproduction organs for Aedes. So far there is few cues for the pathogenesis in the testis cause by Zika, Here, using an immune compromised mouse-model, we found one c type lectin CLEC5A is crucial for testis pathology during Zika infection. The findings to which these observations in mice and mosquito may translate to a potential treatment for ZIKV-infected humans.

Recent Publications:

1. Yi-Ping Kuo; Kuen-Nan Tsai; Yin-Chiu Luo; Pei-Jung Chung; Yu-Wen Su; Yu Teng; Ming-Sian Wu; Yu-Feng Lin; Chao-Yang Lai; Tsung-Hsien Chuang; Shih-Syong Dai; Fan-Chen Tseng; Cheng-Han Hsieh; De-Jiun Tsai; Wan-Ting Tsai; **Chun-Hong Chen**; Guann-Yi Yu, **2018** "Establishment of a mouse model for the complete mosquito-mediated transmission cycle of Zika virus", accepted PLOS Neglected Tropical Diseases Co-corresponding author
2. Yen, P.S., James, A.A., **CHEN, C.-H**., Failloux A.B., **2018**. miRNA-based transgenic *Aedes aegypti* mosquitoes reduce the transmission of arboviruses from two distinct families. *Nature communication Biology*, doi:10.1038/s42003-017-0011-5. Co-corresponding author
3. Wu, R.H., Tsai, M.H., Tsai, K.N., Tian, J.N., Wu, J.S., Wu, S.Y., Chern, J.H., **Chen, C.H**., Yueh, A., **2017**. Mutagenesis of dengue virus protein NS2A revealed a novel domain responsible for virus-induced cytopathic effect and interactions between NS2A and NS2B transmembrane segments. J. Virol., 91(12). Co-corresponding author