

MINI DENGUE SYMPOSIUM

2ND JULY 2015, 2PM – 5.30PM

Department of Microbiology, National University of Singapore
Block MD4A, Level 2, Seminar Room, 5 Science Drive 2

Free Registration. Please kindly register with Ms June Koh, mickgn@nus.edu.sg



Prof. Shie-Liang Hsien, Academia Sinica, Taiwan

Distinct Features of Dengue Virus Produced from Human & Non-Human Cells

Abstract: Dengue is caused by four serotypes of dengue virus (DV) through mosquito bite, and is one of the most common arboviral diseases in the world. More than 40% of the world's population are living in risk areas for DV infection. DV infection in humans causes a wide spectrum of illnesses such as mild dengue fever (DF) and severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Despite the medical importance, there is still no effective vaccine or antiviral drug against DV infection. The latest un-satisfactory results of the phase III clinical trial of the tetravalent vaccines developed by Sanofi demonstrate that our knowledge to DV is still very limited. It is obvious that the current VERO cells-based plaque neutralization test (PRNT) is unable to predict the protective efficacy of DV vaccines. In addition, VERO cells do not express Fc receptor, thus it is impossible to understand whether the anti-DV antibody in dengue patient sera will induce antibody-dependent enhancement (ADE) or not using VERO cells as targets. Thus, a reliable assay to reflect protective efficacy and prevention of ADE is urgent for the development of successful vaccines against DV infection. Recently, we found that DV produced from human cells (macrophages, dendritic cells) are distinct from DV produced from VERO cells, BHK cells, and C6/36 cells. We compared the virus copy number (by real time RT-PCR) versus virus titer (in BHK and VERO cells) ratio using DV isolated from different resources, and found the (virus copy number/titer) ratio is distinct in DV produced from different cell types. In addition, DVs produced from human primary cells have higher infectivity and induce higher amount of inflammatory cytokines from macrophages. These features suggest that DV produced from non-human and primary human cells are distinct, and can explain why the VERO cells-based PRNT test has low correlation with protective efficacy in vaccine recipients. We are identifying the human host factor(s) contributing to the distinct features of DV produced from human and non-human cells actively to resolve this mystery.



Prof. Yee-Shin Lin, National Cheng Kung University, Taiwan

Dengue Virus Non-Structural Protein 1 Antibody Therapy and Vaccine Strategy.

Abstract: We previously showed that antibodies against dengue virus (DENV) nonstructural protein 1 (NS1) cross-react with human platelets and endothelial cells. The C-terminal regions of DENV NS1 possess cross-reactive epitopes. We recently found a monoclonal antibody (mAb) which did not recognize the C-terminal region of DENV NS1 and had certain therapeutic effects both in vitro and in vivo, suggesting that NS1-specific mAbs could be potential candidates for anti-dengue disease therapy. We further used polymer-based nanocomplexes or alum as an adjuvant to examine the protective effects of DJ NS1 (consisting of N-terminal DENV NS1 and C-terminal JEV NS1) in the DENV-induced hemorrhage mouse model. Polymer-based nanocomplexes provide better adjuvant activity than alum. Active immunization with DJ NS1-encapsulated nanocomplexes induced longer antibody persistence than alum and caused long-term protection. These results provide support for new strategies for the development of high efficacy vaccines using nanocomplexes as the adjuvant.



Dr. Guey-Chuen Perng, National Cheng Kung University, Taiwan

Megakaryocytic Lineage Cells in Dengue Virus Infection.

Abstract: Dengue is one of the most important vector-borne human viral diseases globally. The disease is resulting from the bite of mosquito carrying infectious dengue virus. Variety of clinical manifestations can be registered in affected subjects. Viremia is the most salient clinical laboratory finding in dengue patients. And yet its entity including origination and morphology in circulation of acute plasma remains an enigma. The presentation addressed the viral morphology in circulation and the phenotypes of the cells accounting for the origination of the virus. Utilization of molecular biology assays, multi-color FACS analysis, and electron microscopy, we showed that a distinct infectious dengue virions circulated in dengue plasma, and that megakaryocytic lineage cells were likely responsible for the unique viral morphology during acute stage. Results reveal a new avenue engaging in dengue pathogenesis and can guide to a new strategy in developing protective index for evaluation of dengue vaccine clinical trials.



Dr. Brian Chia, Experimental Therapeutic Centre A*STAR, Singapore

Peptide Inhibitors of the Dengue Virus NS3 Protease.

Abstract: The Dengue virus is a mosquito-borne infectious disease infecting 50–100 million people annually in over 100 countries, putting almost half of the world's population at risk. There is currently no approved drug or vaccine. A plausible drug target is the viral non-structural serine protease (NS3) and our medicinal chemistry effort using a peptide-based protease inhibitor strategy at the Experimental Therapeutics Centre will be presented.



Dr. Tzong-Shiann Ho, National Cheng Kung University, Taiwan

Rapid Diagnostic Tests for Acute Dengue Infection.

Abstract: Early recognition of dengue is challenging because initial symptoms are often non-specific, viremia may be below detectable levels and serological tests confirm dengue usually late in the course of illness. There is an unmet need for specific, inexpensive dengue diagnostic tests that can be used for clinical management, surveillance and outbreak investigations. In previous studies, we found that NS1 binds to coagulation factor II (thrombin) and forms NS1-thrombin complex in dengue patients' sera by enzyme-linked immunosorbent assay. Higher sensitivity for detecting dengue infection is achieved by using anti-NS1 monoclonal antibodies to detect NS1-thrombin complex in dengue patients' sera. Based on the previous findings, we developed a new rapid diagnostic kit for acute dengue infections and conducted clinical validation of the kit during the major dengue outbreak in 2014. The results will foster an evidence-based dengue diagnostic test and hopefully a more accurate and affordable tool for global dengue control.