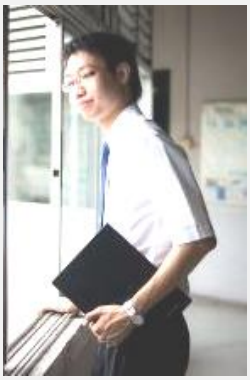
ImmunoTools *special* Award 2015



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Molecular Evasion by Dengue Viral Infection

Dengue virus (DENV) is important disease in tropical regions. Advancement in technology and science has not been successfully decreased dengue distribution. The world health organization (WHO) reported that from 1955 to 2007, the number of DENV infected patients has increased over one thousand folds. The countries reporting dengue cases have been increasing for more than four folds since 1970. Approximatly 50 million dengue infections occur annually. DENV is also expanding into new areas such as in North America and Australia, with the development of the traveling industry. Present, anti viral drug and vaccine are under investigated. Immunopathology is the main evident to relate the dengue infection and outcome of diseases. Severe disease (DHF and DSS) can cause high motility rate and associate with viral load.

Dengue virus hijack host molecule. There are several evident shown how the dengue suppress immune system. For example, dengue NS5 molecule regulates IFN type I signalling by binding with STAT2 degradation. Dengue viral protein NS2B/3 complex can act as protease enzyme activity to destroy STING protein which is the signalling molecule to enhance IFN type I expression. In this project, we try to investigate the new molecular mechanism of dengue virus subverts host immune response by system biology approach. We have several host targets from our system biological data. Regarding this data, I am interesting in innate immune system. Several adaptor molecules are targeted by dengue protein. In this study, we hypothesize that the specific host molecules play the role as host defences. The specific host molecules will be silenced by siRNA. Then, silenced cells will be infected by DENV. After infection, we will observe viral genome by realtime PCR. The importance cytokine, such as IFN-alpha, IFN-beta, TNF-alpha, IL-12 and IL-10, will be quantified the protein expression by ELISA. In this step, we will focus on type I

IFN and TNF-alpha which play impotents role to regulate viral infection. The TLR3, DDX41, RIG-I can activate IRF molecule to enhance type I IFN expression. The silenced cells with dengue virus will be treated with human recombinant protein to observe the viral titer. In this situation, the activation of several molecules will be observed, such as p-IRF3 and p-IRF7, by Western blot.

Regarding preliminary result, we found that the viral titer increase after we silent specific protein. Western blot analysis showed the activation of phosphoP38 and suppression of phosphoErk. The IFN-b alpha production will be considered it in this situation because the specific silencing protein regulates IRF7 activation. The recombinant IFN-b will be treated into this condition. Moreover, we also need to access the death cell by AnnexinV and PI staining.

Several molecules are still on the list of my work. In addition, the in vivo and ex vivo experiment are need to investigate the specific roles of these molecules. Now, we have the collaborator with Dr. Anavaj Sakuntabhai (Pasteur Institute) who has a lot of clinical samples.

In conclusion, the molecular event likes the puzzle. The ImmunoTools will help me to construct the complete figure. The ImmunoTools reagent will help me to understand the immune responses and immunopathology of viral infection.

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Publication

Poyomtip, T., Suwandittakul, N., Sitthichot, N., Khositnithikul, R., Tan-ariya, P., & Mungthin, M. (2012). Polymorphisms of the pfmdr1 but not the pfnhe-1 gene is associated with in vitro quinine sensitivity in Thai isolates of Plasmodium falciparum. Malar J, 11(7).

Dengue Virus and Host Interaction network (Manuscript in Preparation)

ImmunoTools *special* AWARD for **Teera Poyomtimp** includes 24 reagents

FITC - conjugated anti-human AnnexinV,

PE - conjugated anti-human IFN-gamma, IL-8, Annexin V,

APC - conjugated anti-human IL6,

human ELISA-set for 96 wells, human TNF-alpha, human IL12p40 total, human IL-10 (each 3 reagents),

recombinant human cytokines: rh IFNa1b, rh IFNa2a, rh IFNb1a, rh IFNb1b, rh IL-1alpha/IL1F1, rh IL-1beta/IL1F2, rh Myostatin, rh TNFalpha,

Soluble Human receptor: rh IL6rec, rh sTNFrec DETAILS more AWARDS