

2012 SATU Joint Research Scheme Project Sample	
Project Title	Dissecting the Role of Viral Population Diversity in Pathogenesis of Enterovirus 71
Project Description	Human enterovirus 71 is a common causative agent of hand, foot and mouth disease (HFMD). In the recent years, EV-71 has emerged as a more neurovirulent virus killing many young children in many parts of Asia especially Taiwan and Malaysia (Huang <i>et al.</i>, 2011, Chan <i>et al.</i>, 2011). EV-71 outbreak occurs in a cyclical pattern of every two-three years. Continuous surveillance of EV-71 in different parts of Asia especially Taiwan, Malaysia and Thailand will enable a better control of future outbreaks. In the first part of our study, we propose to initiate EV-71 surveillance in Taiwan, Malaysia and Thailand. The surveillance data will be updated weekly or monthly and the three countries will be alerted if there's any increase in EV-71 cases. The second part of the study will include the understanding of the mechanism of EV-71 virus neurovirulence. In this study, we hypothesize that virus population diversity influence pathogenesis. EV-71 is RNA virus, and has genome that is error-prone due to low fidelity of their RNA polymerases. This thus creates a population of viruses with related sequences termed as quasispecies. The high mutation rate of RNA viral replication is beneficial at the population level because it increases the probability of virus adaptation to a new environment during infection (Lauring and Andino, 2010). In poliovirus, increasing the fidelity of viral RNA polymerase reduces the viral diversity and leads to loss of neurovirulence in mice (Vignuzzi <i>et al.</i>, 2006). It is postulated that the neurotropic EV-71 is highly quasispecies in nature and that contributes to higher virulence in human. Different EV-71 virus strains from Taiwan, Malaysia and Thailand will be pyrosequenced using next-generation DNA sequencer to determine the quasispecies

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	characteristics. The viral population diversity of these strains isolated from fatal and mild cases will be compared. The understanding of viral quasispecies will reveal the actual antigenic changes in the virus. The study will help us to understand how the viral populations can adapt and evolve in human, and has great implication in the design of vaccine and antiviral drug.
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