NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

Friday, 12 Feb 2016 | 4pm | DBS Conference Room 1

Hosted by Professor RM Kini

Dengue Virus: A Sting In The Tail



Brief Biosketch

Ooi Eng Eong completed his medical studies at the University of Nottingham and thereafter pursued PhD training in molecular epidemiology under the mentorship of now Emeritus Professor Chan Soh Ha at the Department of Microbiology, National University of Singapore. His background in clinical medicine and molecular biology enables him to position his research at the interface between clinical epidemiology, including early phase clinical trials, virology and immunology. Specifically, his research interests are to elucidate how antibodies either protect against or enhance dengue virus infection and what factors determine the outcome of dengue virus infection or transmissibility and hence explain its epidemiological phenotype. By understanding these mechanisms, he hopes to contribute to the development of effective dengue vaccines and therapeutics.

By **Ooi Eng Eong**

Program in Emerging Infectious Diseases, Duke-NUS Medical School, Singapore

The high incidence of dengue virus (DENV) infections around the globe has led to increasing viral genetic diversity, some of which appears to be associated with greater epidemic potential. The underlying mechanisms of viral fitness in an epidemiological setting, however, remain poorly defined. We recently combined epidemiological, phylogenetic and virological analyses with molecular and mechanistic studies to examine the Puerto Rico dengue outbreak in 1994. We show using clinical isolates that the epidemiologically fitter dengue virus produces lower levels of genomic RNA for greater levels of subgenomic RNA than the viruses endemic to Puerto Rico before 1994. These subgenomic RNA plays a critical role in dengue virus replication as it binds the protein TRIM25 to inhibit its deubiquitylation. Deubiquitylation of TRIM 25 is a key enzymatic process needed to activate this protein to engender sustained and amplified RIG-I signaling. Without which, type-I interferon expression becomes attenuated. Our findings suggest that this inhibition of type-I interferon expression then allows this strain of dengue virus to spread more effectively epidemiologically, resulting in the emergence of the epidemic of 1994 in Puerto Rico. I will discuss this set of data as well as new findings on how nucleotide changes in the 3' tail of the DENV genome influence epidemiological fitness of this virus.

Artwork by Ann Nee, DBS, NUS