Singaporean Society for Immunology

SgSI Seminar Series: Infectious Diseases

Date & Time: 29 January 2015 (Thursday), 4.30 - 5.45pm

*Venue: Venue: CeLS Auditorium @ NUS

Host: Dr. Katja Fink, SIgN

Registration is based on first-come first-served.
Click here to register now!

Dr. Justin Chu

Asst. Professor
NUS

Human Genome-wide RNAi Screen Identifies Host Susceptibility and Resistance Factors that Mediate Human Enterovirus 71 infection

Enterovirus 71 (EV71) infections usually manifest as hand, foot and mouth disease (HFMD) although it can also result in severe neurological disease and death. EV71 remains a recurring health threat to children due to the lack of antivirals and vaccines. Given the compact genome of EV71, many cellular proteins are likely to be required for its successful replication. To date, only a handful of these factors have been identified. Here we report the identification of 273 host factors affecting EV71 infection from a genome-wide RNAi screen in human rhabdomyosarcoma cells. Bioinformatics analyses revealed the involvement of a plethora of cellular processes including transcription regulation, translation initiation and membrane biogenesis etc. Among the hits, Misshapen/NIKs-related kinase (MINK), a host susceptibility factor was selected for detailed analysis due to its strong inhibitory profile upon gene silencing in EV71-infected cells. Through proteomic analysis and infection inhibition assay, we found that the activation of MINK was triggered by early replication events of EV71 and MINK plays an essential role in the IRES-mediated translation of EV71 viral RNA. This study provides a comprehensive map of cellular components involved in EV71 replication that can form the basis for antiviral targeting and our understanding of virus pathology.

Dr. CC Khor

Principal Investigator
GIS

Human Genetic susceptibility to typhoid sepsis

Typhoid is predominantly a disease of the developing world, predominantly caused by inadequate sanitation systems and / or contamination of food and water. The vast majority of individuals exposed to the typhoid bacteria clear the infection with only mild symptoms. However, a small but significant proportion progress to life-threatening sepsis. We conducted a genome-wide association study on >400 patients with typhoid sepsis and contrasted their genetic profiles to >2000 controls. Potentially promising initial findings were forwarded for validation analysis in further independent patient collections totaling and additional >700 cases and >1000 controls. We note very strong association mapping near the class II HLA region, whereby individuals carrying certain genotypes showed >3-fold resistance to typhoid sepsis compared to non-carriers of the genotypes. I will discuss how modern day genetics and genomics can be used to robustly identify such susceptibility genes, as well as the long road from association to function.

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