

SlgN Immunology Seminar



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Alphaviruses: from mosquitoes to brains and joints

Host
Dr Lisa Ng
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Date
Tuesday,
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Time
11am – 12pm

Venue
SlgN
Seminar Room,
Immunos Building
Level 4
Biopolis

Alphaviruses are distributed worldwide and cause diseases of medical importance including Chikungunya, equine encephalitis and Ross River fever. Explosive epidemics occur, as observed with Venezuelan equine encephalitis virus with hundreds of thousands of equine cases and tens of thousands of human cases and Chikungunya on the Island of La Reunion in 2006 where over a third of the human population were infected over a period of a few months. Estimates suggest that Chikungunya has infected several million people from its emergence in Central Africa in 2004/5 through its spread into India and South East Asia. In susceptible vertebrates, alphaviruses generate a high titre viraemia. This facilitates spread to mosquitoes where virus crosses the midgut barrier to infect salivary glands. Mosquitoes control levels of virus, principally through RNAi responses. The virus appears not to antagonise these responses; as shown by addition of an RNAi suppressor to the virus genome. At the cellular level the response of arthropod and mammalian cells to infection is completely different. In arthropod cells a persistence infection is established whereas, in mammalian cells, recognition of infection initiates apoptosis. In mammalian cells there is also a shut-off of host cell transcription and translation which converts infected cells into highly efficient virus factories. This and transient antagonism of interferon responses, the alphavirus non-structural protein-2 interferes with STAT signalling, establish the high titre viraemia. In turn this results for some alphaviruses, principally those from the New World, in virus dissemination across the blood-brain barrier into the CNS and viral meningoencephalitis. Old World alphaviruses generally cause a more systemic disease characterised by rash, myalgia and arthralgia but may cause severe disease such as encephalitis or chronic arthritis. For Chikungunya, a working hypothesis for the arthralgia / arthritis is that virus infected monocytes give rise to chronically infected joint macrophages.