

SgN Immunology Seminar

Prof Douglas Golenbock

Chief, Division of Infectious Diseases & Immunology
University of Massachusetts Medical School
USA



Innate Immunity and Malaria: Synergistic roles of Hemozoin and Plasmodial DNA

Host
Prof Laurent Renia
Singapore
Immunology
Network, A*Star

Date
Thursday
27 March 2014

Time
2pm – 3pm

Venue
SgN Seminar
Room
Immunos Building
Level 4
Biopolis

Malaria is an acute cytokine mediated febrile illness. We sought to better understand the cause of the cytokine storm in malaria. We focused on the malarial pigment, hemozoin. We found that natural hemozoin activated TLR9 because it trafficked plasmodial DNA into a phagolysosomal compartment. We found that hemozoin could interact with DNA- primarily from dying parasites- even before erythrocytes released merozoites and shed hemozoin during schizogony. Evidence emerged suggesting that in addition to the TLR9-mediated response, there was a cytosolic DNA sensor that activated an type I interferon pathway. We investigated these events and found that hemozoin itself is responsible for liberating DNA into the cytosol because it causes the loss of phagolysosomal integrity, permitting the contents of the phagosome access to the cytosol. These events are followed by the activation of multiple inflammasomes and the production of IL-1b. Indeed, activated inflammasomes could be observed by both biochemical means and by confocal laser microscopy analysis of cells from human patients. Hence, the plasmodial parasite has multiple mechanisms by which it can activate the innate immune response, and many of these mechanisms involve hemozoin working in collaboration with DNA.