

Program Outline

22 - 26 January 2017

(Sunday - Thursday)

Venue:

**Grand Copthorne Waterfront Hotel,
Singapore**



Riverfront Ballroom, Level 2

Achala KAMALADASA (A-14)

Difference in Anti-Viral Responses in Individuals with Past Asymptomatic and Symptomatic Dengue Individuals



Kamaladasa AI¹, Gomes L¹, Ogg GS^{1,2} and Malavige GN^{1,2}

¹Centre for Dengue Research, University of Sri Jayawardanapura, Sri Lanka, 2MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine, Oxford NIHR Biomedical Research Centre and University of Oxford, OX3 9DS, UK

Keywords: dengue, asymptomatic, symptomatic, cytokines

Introductions

Dengue viral infection in humans can manifest as asymptomatic or symptomatic infection, with a wide spectrum of clinical manifestations ranging from undifferentiated fever to life threatening illness. The majority of the dengue infections in humans are asymptomatic. Cells infected by dengue virus (DENV) are known to produce cytokines and other soluble mediators and increases in these factors are considered to contribute to disease pathogenesis. These different cytokines have been shown to have associations with different degrees of disease severity in acute DENV infections. One of the main cell types infected by DENV are monocytes, and virus infection induces the production of various anti-viral, pro-inflammatory and anti-inflammatory cytokines from monocytes.

Methods

Twelve healthy individuals with two past dengue infections with which resulted in either asymptomatic infection or dengue hemorrhagic fever (DHF) were recruited (6 people in each group). Monocytes were isolated with CD14 beads using MACS separating columns. Monocytes were then infected at a multiplicity of infection of one with DENV serotype 2 (DENV-2) and DENV serotype 3 (DENV-3) and incubated for 24 hours. Culture supernatant was assayed for levels of IFN- α , IFN- β , TNF- α , IL-10, IL-8, IL-6, IL-12p70, IL-17 and IP-10 with luminex assays.

Results

As expected, monocytes from those who had past asymptomatic group produced significantly more IFN- α when infected with DENV-2 and DENV-3, compared to uninfected monocytes (DENV-2; $p < 0.0001$, DENV-3; $P = 0.0001$). However, monocytes of those who had past DHF failed to produce significant levels of IFN- α when infected with either DENV-2 or DENV-3 (DENV-2; $p = 0.2988$, DENV-3; $P = 0.4435$). Further monocytes from those with past DHF spontaneously produced more than twice the amount of TNF- α ($p = 0.01$) and three times the amount of IL-8 ($p < 0.0001$) compared to monocytes of those who had past asymptomatic infection. In addition, monocytes of those with past DHF produced significantly more TNF (DENV-2, $p = 0.002$; DENV-3: $p = 0.02$) and IL-8 (DENV-2: $p = 0.008$; DENV-3: $p = 0.002$) when infected with DENV-2 and DENV-3. Significant amounts of IP-10 were produced by DENV-2 and DENV-3 infected monocytes of individuals with both past asymptomatic infection and those with past DHF. Production of IL-10, IL-12p70 and IL-6 from infected monocytes was not significantly different between asymptomatic and DHF groups. Neither uninfected nor infected monocytes produced IFN- β in both asymptomatic and symptomatic groups.

Conclusion

Failure to produce a significant amount of IFN- α in response to the DENV by monocytes of those with past DHF, is suggestive that they could be having impaired antiviral responses to the virus. In addition, since monocytes of those with past DHF also spontaneously produced significantly higher levels of TNF and IL-8, an altered immune response generated by their monocytes could contribute to severe clinical disease.