Reviewer's report

Title: Acute dengue virus 2 infection in Gabonese patients is associated with an early innate immune response, including strong interferon alpha production

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Reviewer: Daniel Libraty

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- Major Compulsory Revisions

1. This paper describes plasma cytokine levels in acute DENV-2 infections in a West African cohort of patients, and also adds a small number of surface activation marker measurements on T-lymphocytes. The potential uniqueness of the paper would be the examination of immune responses to dengue virus in a West African population, where severe disease (DHF) is generally not recognized. Unfortunately, this paper simply lists the levels of a large number of measured analytes, compared to healthy controls. They basically show that many cytokines/chemokines are elevated during an acute febrile viremic illness compared to healthy individuals, and that activation markers on T-cells are also increased. Their conclusions are overstated for this type of data, and the discussion is long and not well organized for the descriptive data.

2. The authors claim that their results demonstrate “the importance of IFN-alpha in modulating DENV infection”. Demonstrating measurable circulating levels of IFN-alpha in an acute viremic infection (dengue) compared to healthy controls does not by itself support a conclusion that IFN-alpha is important in modulating DENV infection. An attempt to correlate circulating IFNalpha levels with dengue viremia levels is a start, but no correlation was seen to support their stated conclusion. Their comparison to the existing literature on IFNalpha levels in dengue is incomplete- for example, another paper (Libraty et al. JID 2002) has measured IFN-alpha levels in dengue virus-infected children over time- also, the papers examining gene expression levels from blood samples of dengue virus infected children would be relevant to any discussion of circulating Type I IFN levels and potential comparisons to their data.

3. The authors state that "one originality of our study is that we included kinetic analyses..." Not clear what they mean- it is not clear in the paper, how many patients had serial daily blood collections (if any) or how many had single blood collections- several other papers in the literature have measured various cytokine levels over time during acute dengue virus infections. There is poor discussion of how their data compares to the existing literature and what their data would add to what has already been reported. Again, the authors are essentially reporting that the circulating levels of many cytokines/chemokines were higher in patients with an acute febrile viral illness (dengue) compared to healthy controls.

4. The authors conclude that their results "argue against the use of anti-inflammatory drugs to treat the symptoms of acute DENV infection". The
reasoning behind this statement is not clear.

5. Statistical comparisons- when performing many comparisons (approx. 50), a statistical test should be used that corrects for multiple comparisons.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have not competing interests