Reviewer’s report

Title: Serum IL-10 as a marker of severe dengue infection

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Reviewer: Katja Fink

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“Serum IL-10 as a marker of severe dengue infection”

The authors measure blood cytokines in 259 patients during fever and in 65 of those a subset of cytokines is also measured at defervescence. The aim of the study is to assess whether IL-10 levels can be used as a predictive marker for severe dengue, comparing levels in the first and the second sample.

The introduction is well written and some of the numerous studies measuring the same cytokines in dengue patients are cited. The methods used are accurate.

The conclusion is that IL-10 is not useful as a predictive biomarker, and the authors mention the large variability within the patient groups, representing the complexity of dengue pathology and its underlying mechanisms.

The conclusion that dengue is an extraordinarily complex disease has been reached in many other studies, and there is a consensus that one biomarker alone will not be sufficient to predict severity with a reasonable sensitivity. It is therefore somehow surprising that the authors try to assess the predictive value of IL-10 alone.

Major compulsory revisions:

1. the authors mention that the value of this study lies in the fact that a “large cohort” of patients was analyzed. Even though the number 259 is certainly large, the critical analysis including the second time point was only done in a subset of patients, and it is not clear from the tables and figures how many patients were included for those calculations. N=… should be added to all tables and figures.

2. primary and secondary patients were mixed for the analysis. It could be more informative to split these two groups and calculate correlations separately. However it might be difficult to assess the status if the first sample is drawn only at day 7 (IgG is already present even for primary). How did the authors do that?

3. the figure numbers in the text do not tally with the figures. Figure 1 and 2 do not seem to be mentioned at all in the text and figure 4 as mentioned in the text is missing.

4. why does IL10 have to rise or fall after the febrile phase to be suitable as a predictive biomarker? (discussion). The important value is the febrile phase IL-10, and that value does not necessarily seem to correlate with eventual severe
disease, hence is not a suitable predictive biomarker.

5. the comparison with MCMV is very hypothetical, the pathology of the two viruses is rather different.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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 no competing interests