Reviewer’s report

Title: Differential proteomic analysis of virus-enriched fractions obtained from plasma pools of patients with dengue fever or severe dengue

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Reviewer: Alain KOHL

Reviewer’s report:

This study aims to elucidate the proteome associated with dengue viruses from patients with dengue disease (severe or fever). The authors use mass spec techniques on virus-enriched fractions to analyse dengue virions, and follow this up by ELISA. Mass spec analysis yields of dengue-virus containing fractions yielded interesting results, mainly that proteins of the complement system, coagulation system and the acute response signalling are found in fractions with virus. Could the ELISA studies be improved by immunoprecipitation of virus particles (from possibly larger serum volumes) before down stream analysis? The absence of success to confirm viroproteome results by ELISA is perhaps a technical issue that could be worked on. Nonetheless there is useful information in this manuscript as clearly there is an interesting question on why some proteins are enriched at significant difference between two types of patients in the respective virus-containing fractions, and this is of interest to the field. The authors put the data in context by carrying out detailed pathway analysis using IPA. The use of these molecules as prognostic markers would require a more detailed follow up of patients (especially as there appear to be some differences between Colombian and Vietnamese patients) but that is beyond the scope of the paper.

Specific points:

Introduction: other studies have looked at profiles of immune response/other markers in the serum of patients and while the introduction touches on this, it would be good for the reader to already have this introduced in more detail here.

Line 235: "non severe dengues" is not an adequate expression in English. I did spot similar points elsewhere in the manuscript and perhaps it should be re-read by a native speaker.

Methods: a more detailed description of statistics used and power calculations should be provided.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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