Reviewer's report

Title: Dengue type 4 in Rio de Janeiro, Brazil: cases characterization following its introduction in an endemic region

Version: 0 Date: 14 Feb 2017

Reviewer: Anthony Jin Shun Chua

Reviewer's report:

This is a relatively straightforward paper on the characterization of endemic DENV-4 cases in Rio de Janeiro, Brazil. However, other than identifying that the circulating DENV-4 virus belonged to Genotype II, there was no new information nor insight contributed by this paper to the literature. The authors may wish to highlight potential takeaway points from this study for the readers in the Discussion section.

It is highly recommended that the authors engage the help of a native English speaker to proofread the manuscript. There are many sentences with awkward structures in the prose, which may result in confusion in readers.

Major Revisions

1. Line 165: Real time-PCR generally picks up 10- to 100-fold more viruses, compared to plaque assay. This may possibly be due to the detection of the viral genome of non-viable viruses during PCR and/or the clumping of viral particles during plaque assay. The authors may wish to justify here their preference of real-time PCR over plaque assay.

2. Lines 167-173: The authors may wish to elaborate on the antigen-antibody complex dissociation process, which was not mentioned in the Methods section.

3. The results have been rather confusing. With 705 DENV-4 cases in the beginning, the total number of samples tested has not been consistent for real time-PCR, detection of anti-DENV IgM in both acute and convalescent samples, and detection of NS1 with or without antigen-antibody complex dissociation. Again, the total number of males and females (Line 204), immune response characterization in primary or secondary infections (Line 207), and disease severity characterization (Line 210) did not add up to 705. The authors may wish to elaborate on the differences. One suggestion may be for the authors to include a flow chart to explain how and why certain samples were "dropped out" at each stage of their characterization.

4. Lines 216-219: The authors made an observation on abdominal pain in DWAS and severe Dengue cases. What is the significance statistically and clinically?
5. Line 224: It was mentioned in the Methods section that a total of 20 samples were quantitated for viremia (Line 164), instead of the 16 samples mentioned here. Please clarify. Also, the authors may wish to elaborate on the statistical reasoning behind choosing 16 or 20 samples to represent a 705-subject cohort.

6. Lines 229-231: This section is hard to comprehend. Please rephrase and elaborate.

7. Line 238: Again, the authors may wish to elaborate on the statistical reasoning behind sequencing 12 samples to represent a 705-subject cohort.

8. Lines 259-261: This sentence is hard to comprehend. Please rephrase the sentence and briefly elaborate on it where possible.

9. Lines 273-276: Are these 2 percentages tabulated in any of the tables? If so, please include the table number.

10. Lines 278-279: The 2 percentages here differ from what was mentioned in the Results section (Line 212). Please clarify.

Minor Revisions
1. Line 148: Replace "preM" with "prM".

2. Line 195: Insert "(Table 2)" after "... only one sample".

3. The authors may wish to ensure that all their table numbers in the prose are correct.

4. The authors may wish to replace "dengue cases" throughout the prose with "DwoWS" as they have already introduced the abbreviation in Line 113.

5. Line 267: Please elaborate briefly on what was previously described in Ref 9.

6. Table 1: This table does not seem to be referred to in the prose. If this is indeed the case, the authors may wish to consider shifting it under Supplementary Materials.

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? 
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I am able to assess the statistics

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