Reviewer's report

Title: The variations of VP1 protein might be associated with nervous system symptoms caused by enterovirus 71 infection

Version: 1 Date: 22 August 2013

Reviewer: Yoke-Fun Chan

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The authors have utilized the publicly available sequences of EV71 to determine the association between VP1 sequences and neurological presentation in patients.

Major compulsory revisions

1. Pg4. Since AF135899 has been excluded from all the comparisons, the total sequences would be 186.

2. Supplementary table 1 should also include references of which the sequences were published. Most of the accession number pages do not reveal the clinical presentation.

3. Were all the VP1 sequences downloaded and looked at one by one? How thorough was the process and search? New sequences are available in Genbank every day, hence the date when sequences were accessed is important.

4. How the authors decide which C4 sequences to choose? There are really loads of them. Same goes to other subgenotypes, since they would be more HFMD sequences compared to others. Authors need to demonstrate that sequences were not selected to fit into the results.

5. Similarly, some genotypes may not be very well presented. The presence of mutations is very much subgenotype specific. More importantly, some EV71 subgenotypes are geographically distinct- C4 in China and Taiwan, and B4 and B5 in Malaysia. Can authors show or discuss how that can possibly skewed the correlation?

6. Discussion. Pg 7. 1st para. Most if not all the previous studies actually suggest that there is no correlation between EV71 subgenotype and neurovirulence. What’s probably different in this study is statistically methods were used to show the association.

Minor essential revisions

1. Pg 6. para 1. Change “To our surprising” to “to our surprise”

2. Discussion. Pg 8. Recently heparan sulfate has also been identified as the attachment receptor.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

'I declare that I have no competing interests'