Author's response to reviews

Title: Clinical Features and Phylogenetic Analysis of Coxsackievirus A9 in Northern Taiwan in 2011

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Author's response to reviews: see over
Clinical Features and Phylogenetic Analysis of Coxsackievirus A9 in Northern Taiwan in 2011, Yi-Chuan Huang, Ying-Hsia Chu, Ting-Yun Yen, Wen-Chan Huang, Ai-Ling Cheng, Hurng-Yi Wang, Li-Min Huang and Luan-Yin Chang

Dear Editor

We address the comments in the revised manuscript and provide this cover letter giving a point-by-point response to the comments of the Reviewer.

Thank you very much for your consideration.

Sincerely yours,

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Response to the comments of reviewer
Reviewer's report
CLINICAL FEATURES AND PHYLOGENETIC ANALYSIS OF COXSACKIEVIRUS A9 IN NORTHERN TAIWAN IN 2011 written by Yi-Chuan Huang and co-authors describes the clinical presentation of Coxsackie A9 (CV-A9) infections in order to upgrade the differential diagnosis of those infection from other diseases caused by non-polio enteroviruses and provides an inside into molecular epidemiology of CV-A9.

The paper needs to be improved with some major and couple minor modifications to meet the journal criteria before being accepted for publication.

Major Compulsory Revisions
1. Indicate in the text, how many isolates from current study was used to build the phylogenetic tree? Selection criteria, if it’s any?
   Response: We randomly selected 13 isolates from current study to build the phylogenetic tree. We indicated it in the text and the accession numbers were also provided (Page 8, the last ine).

2. Also provide the GenBank accession numbers for each sequences from your current study (Taiwan, 2011) used for phylogenetic tree construction. They must be deposited in the GenBank, because study is on phylogenetic analysis.
   Response: the GenBank accession numbers (KC286622, KC286623, KC286624, KC286625, KC286626, KC286627, KC286628, KC286629, KC286630, KC286631, KC286632, KC286633, KC286634) for each sequences from current study (Taiwan, 2011) used for phylogenetic tree construction were provided (P9, Lines 2-4).

3. METHODS section needs to be renamed as MATERIALS and METHODS
   Response: it was revised accordingly (P6).

4. In RESULTS section: “All the current CA9 strains from 2011 epidemic were within the same lineage and closest to the CA9 isolate 27-YN-2008 GeneBank accession number HQ844647) which was isolated from one child near the border of Yunnan province, Mainland China and Myanmar in 2008. “
   This need to be corrected to “….from healthy child near the border of Yunnan province…. “ all over the text, based on the information for CA9-HQ844647 in GenBank: Tian,B.J., Zhang,J., Tang,J,J., Chang,S.S. and Wen,H.M. “Virological investigation of enteroviruses from healthy children in the border
areas of Yunnan province with Myanmar”, 2008 (unpublished)

Response: It was corrected according to your suggestion (P13; P17, Lines 6-8).

Minor Essential Revisions:
1. In ABSTRACT section correct “…(CA9) was one of the most prevalent serotype…”
Response: It was corrected according to your suggestion (P3).

2. In ABSTRACT section for results correct: “…among whom, 6 cases…”
Complicated cases included: aseptic meningitis (n=8), bronchopneumonia (n=6), etc. n=” (IN DISCUSSION the same correction for same data presentation needed).
“Phylogenetic analysis for our current CA9 strains…”
Response: It was revised according to your suggestion (P3, the last 2 lines; P4, the first line; P11, Lines 16-17; P16, Lines 3-4).

3. In INTRODUCTION section suggestion change the scientific language:
“We also constructed a phylogenetic tree in order to understand the molecular epidemiology of CA9 infections in Northern Taiwan.”
Response: It was revised according to your suggestion (P6, the last 2 lines).

4. In METHODS in “Case definitions” correct “Throat swabs were taken…”
Response: It was corrected accordingly (P6, Line 4).

5. In METHODS correct “Viral identification, typing….”, because it’s a molecular typing. Correct: “The partial VP1 gene was amplified by RT-PCR…” Correct: “…nucleotide position from 97 to 412 based on the CA9 GenBank…”
Response: It was corrected accordingly (P6, the 2nd paragraph, Lines 6-8).

6. In METHODS correct: With a newly obtained sequences n=13 (Accession numbers: …)“….we constructed a phylogenetic tree based on the 280 bp of VP1 region in MEGA…”
Check and correct the accession numbers in the GenBank for No. FJ868, GU142 (wrong numbers) and make the correction in the Figure 3 also.
Remove repeat listing of CA16 reference from context.
Response: Thank you for your careful checkup. Some of the numbers were
missing and were corrected. We remove repeat listing of CA16 reference from context (P9, Lines 7-8).

7. In RESULTS in “Seasonal distribution and Demography” section correct: “were aged from 2 to 8…”, “The eldest patient…”
   **Response:** It was corrected accordingly (P10, Lines 6-7).

8. In RESULTS at Characteristics of skin rash paragraph correct 61% to Sixty one percent. 3% to Three percent.
   **Response:** It was corrected accordingly (P11, Lines 3 and 12).

9. In DISCUSSION correct: “The most common presentation on the skin was hand-foot and mouth disease (HFMD)”.
   Correct: “In 2011 sixty one (61%) from 100 children infected with …..”
   Correct: “The genome of enteroviruses encodes 11 proteins, including VP1 to VP4, 2A to 2C, and 3A to 3D. Among these genes, VP1 ….”
   **Response:** It was corrected accordingly (P14, Line 16; P14, the 2nd paragraph, Lines 3-4; P16, the last line).

10. FIGURE LEGENDS: Figure 1. Correct: Typical skin rash observed in patients with CA9 infection.
    **Response:** It was corrected accordingly (P25).

    Figure 3. Correct all the text: Phylogenetic tree of Coxsacie A9 (CV9), based on partial VP1 gene. In bracket CA9 isolate 27-YN-2008 isolated near the border of Yunnan province, Mainland China and Myanmar in 2008.
    **Response:** It was corrected accordingly (P25).

11. Figure 3. The word “gene” should be omitted from strains name, to make them consistent. Use Taiwan, 2011 in phylogenetic tree instead of “Current strains”. Does “rc” have meaning after the year in Taiwanese strains name?
    **Response:** the VP1 or Vp1 gene was omitted and we made all the strain names consistent (Figure 3).