Author’s response to reviews

Title: Streptococcal toxic shock syndrome caused by the dissemination of an invasive emm3/ST15 strain of Streptococcus pyogenes

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Author’s response to reviews:
November 8, 2017

Dear Yi-Tsung Lin, MD, PhD

Editor, BMC Infectious Diseases case report,

RE2: INFD-D-17-01180

Streptococcal toxic shock syndrome caused by the global dissemination of an invasive emm3/ST15 strain of Streptococcus pyogenes

Dear Dr. Lin,

We wish to resubmit our manuscript entitled “Streptococcal toxic shock syndrome caused by the global dissemination of an invasive emm3/ST15 strain of Streptococcus pyogenes” (RE2: INFD-D-17-01180) for publication as a Case Report in BMC Infectious Diseases.

The manuscript had been revised in accordance with the suggestions made by the Reviewers and the additional editor. All revisions are highlighted to the manuscript are highlighted in yellow (RE1) and green (RE2). We appreciate the helpful suggestions offered by the reviewers.

I trust that you will now find the manuscript suitable for publication.

I look forward to your final decision.

Sincerely,

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Reviewer reports:

Chuan Chiang-Ni (Reviewer 1): Do I miss something in Fig. 2? If this strain (KS030) is the first emm3 GAS strain with complete genome sequencing in Japan, how can you conclude that the KS030 "was not similar to other ST15 isolates identified in Japan" (Page 4, Line 112-113) (Page 1, Line 31)? Did the isolates showed in the additional-file1 (5 isolates from Japan) have complete genome sequencing results? In addition, I only found KS030 but not other Japan isolates in Fig. 2. I suggest the information about 5 Japan isolates should be shown (at least should be described in the text).

Reply to query:

The sentences " rather than other ST15 isolates identified in Japan" in line 31 and "but was not similar to other ST15 isolates identified in Japan" in line 111 were overstated, because recent isolates similar to our isolate KS030 might be uncovered by whole genome sequencing. Thus, the sentence has been removed in the abstract and the main text. Relatively old Japanese ST15 isolates in 1990s were highlighted in Fig 2, in order to easily find the distinct genetic phylogeny among Japanese isolates.

The sentence of conclusions in Page 1 (Line 32) should be revised.

Reply to query:

The conclusions in line 32 has been revised, and we expect it to meet the reviewer’s request.

Page 4, Line 123-125, the rocA and emm3 should be italic.

Reply to query:

As suggested, these genes have been revised as italic.

In Reference: the Streptococcus pyogenes and emm3 should be italic.

Reply to query:

As suggested, bacteria species and the gene have been revised as italic.
Claire Turner (Reviewer 2): Thank you for the revision. The authors have answered all my comments appropriately. I have three more comments though on the revisions made.

Line 105. Where the prophage regions also excluded? if not then this cannot be described as the 'core' genome.

Reply to query:

We appreciate the appropriate suggestion. KS030 carries six prophages, and the sentence has been revised as follows.

“After excluding repeated regions and six prophage sequences throughout the whole genome sequence, 80.3% of the region was assigned as the core genome sequence among 484 GAS strains,”

Line 112. This sentence needs further clarification. The KS030 strain carries the 1bp deletion in rocA that is common to all emm3 isolates sequenced (please provide a reference for this). Aside from this, there are no more genetic features described in the supplementary table therefore the last part of the sentence should be removed.

Reply to query:

We have checked all tested whole genome sequences, and found to be 1-bp deletion in the rocA gene at all strains. Please see the revised additional file 1.

Line 123. rocA and emm genes need to be in italics. The deletion in rocA does not lead to an absence of CovR/S activity. This should be described as an absence of RocA activity on the CovR/S resulting in the de-repression of more than a dozen....

Reply to query:

As suggested, these genes have been revised as italic.

And the sentence has been revised as the reviewer suggested.