Author's response to reviews

Title: Molecular Identification of Adenovirus Causing Respiratory Tract Infection in Pediatric Patients at the University of Malaya Medical Centre

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Author's response to reviews: see over
Reviewer’s Report

Title: Molecular identification of adenovirus causing respiratory tract infection in pediatric patients at the University of Malaya Medical Centre

Version: 1   Date: 13 January 2010

Reviewer: David Schnurr

Reviewer’s report:

The manuscript describes the first study of the types of adenoviruses circulating in Malaysia. The number of isolates obtained and characterized is too few to base many conclusions on, other than that Ads were rare in this population or the culture method was not optimal. The observation of subclusters of Ad 5, 2 and 7 deserves to be followed up.

Comments

Major compulsory revisions
None

Minor Essential revisions
None

Discretionary revisions

Page 2 methods, not clear. Samples of what, cultured material?

Response: The Methods section under Abstract has been revised to include a more detailed description of the methods used in the present study.

Page 4 results:
Lines 3 – 5, describing results as percentage rather than as numbers is not clear. With such a small number of isolates the absolute numbers would be sufficient

Response: The Abstract has been revised to include both absolute numbers and percentage of samples to ensure clarity.

Page 3. Is HFM disease associated with Ad virus?

Response: No, HFMD is not generally associated with adenovirus infection. The virus, however, was isolated in a HFMD outbreak with high fatality in Sarawak, Malaysia in 1999 (Cardosa et al.).

Background: Lines 8 – 11. “Acute childhood mortality ranges..” what is the significance of these statistics? The number of children dying in 2000 does seem significant,

Response: The sentence “Acute childhood mortality rate…..” in the manuscript has been deleted
Line 8: that the virus imposes on (not to)

**Response:** The sentence which contains the phrase “imposes on” has been deleted.

Line 10: I would hesitate to mention future vaccination programs based on this data

**Response:** Any inference to future vaccination programs has been deleted from the manuscript.

Page 5 Methods: viral isolation

Line 8: what volume was inoculated into cell culture?

**Response:** For propagation of the virus, 200 µl of the processed nasopharyngeal secretion (NPS) suspension was used to inoculate into cell culture.

Page 8, line 14 – 15: the specimen that yielded Ad 41 came from a rectal swab, while Table 1 Sample AD07MY01, an Ad 41 came from a NPS? It seems unlikely that Ad 41 came from an NPS.

**Response:** It was a typing mistake. NPS in Table 1 has been changed to RS (rectal swab).

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

Quality of written English: Needs some language corrections before being published.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests
Reviewer's Report

Title: Molecular identification of adenovirus causing respiratory tract infection in pediatric patients at the University of Malaya Medical Centre

Version: 1 Date: 2 January 2010

Reviewer: Adriana Kajon

Major compulsory revisions

1. On page 2, in the background section of the Abstract, the authors state that human adenoviruses “comprise of different species, subgenus and serotypes…” The use of terminology is incorrect and a review of the ICTV website is recommended. The term “species” is now used INSTEAD of subgenus.

    Response: The sentence containing the above phrase has been deleted from the Background section of the Abstract

On page 2, in the Results paragraph, replacing “sequenced” by “types by sequencing of the hexon gene” is recommended for clarity.

    Response: The sentence containing the word “sequenced” has been deleted from the Results section of the Abstract

2. On page 3, first line, the term “species” is INCORRECTLY used. Type 3 WAS the most common SEROTYPE IDENTIFIED

    Response: The term “species” has been changed to “serotype” as suggested (page 3, line 3).

3. On page 9, the authors state that determining the serotype is important “for the determination of existing recombinant genotypes”. It is VERY important that this statement is revised because the approach used in the paper to identify and characterize Ad strains is very limited and will unlikely identify recombinants. In addition, the statement that “recombinant genotypes are usually associated with the more pathogenic strains of Ad” is incorrect.

    Response: Any mention or inference made on existing recombinant genotypes has been deleted from the Discussion section. The phrase “recombinant genotypes are usually associated with the more pathogenic strains of Ad” has also been deleted from the Discussion section

4. In the last sentence of the third paragraph, the wording is confusing. The hexon gene DOES NOT play a significant role in typing. It is the SEQUENCING of the hexon gene!
Response: Agreed. The Discussion section has been restructured and any inference made on the hexon gene playing a significant role in typing HAdV has been deleted.

5. On page 11, there are 2 different literature citation systems used in the first paragraph and this needs to be corrected. The sentence starting with “Ad-B type 3 and 7” is poorly written.

Response: The citation system has been standardized throughout the manuscript. The sentence containing the phrase “Ad-B type 3 and 7…” has also been deleted.

6. As mentioned above, the study provides a benchmark for future studies of adenovirus infections in the country, NOT classification!

Response: Agreed. Correction from “classification” to “infection” has been made in Conclusions (page 10, line 8)

7. On table 2, the word University is incorrectly spelled in the title

Response: Correction of spelling of the word “university” has been made on Table 2.

8. The 2 figures show redundant data. Figure 2 is more informative and suffices to display the findings.

Response: Agreed. Figure 1 has been deleted from the manuscript

Minor essential revisions

1. The authors should clarify what they mean by “common” RTI

Response: The term “common RTI” has been changed to “mild infection” (page 9, line 19) and has been removed from page 10, line 6.

2. In the last line of the Conclusions paragraph on page 3, the future studies proposed are NOT of Ad classification but of Ad identification and molecular characterization.

Response: The phrase “Ad classification” in the last sentence of the Conclusions section has been deleted and replaced with “HAdV infection” (page 10, line 8)

3. On page 4, first line the words “common infection” should be deleted.

Response: The phrase “common infection” has been removed and the whole sentence has been revised to “Respiratory tract infection (RTI) is common in adults and children worldwide” (page 4, line 2).

4. On page 5, line 6, rewording the sentence to read “determination of the partial sequence of the hexon gene” is recommended for clarity

Response: The sentence has been reworded to “determination of the partial hexon gene sequence” as suggested (page 5, line 3-4)
5. On page 5, line 11, the sentence should be reworded to read “Nasal aspirates from infants and children.....”

   **Response**: The sentence “Nasal aspirates from infant and children...” has been deleted from the Virus section of Methods. The whole paragraph has been revised for clarity.

6. On page 7, in the last paragraph, deletion of the word “isolated” is needed.

   **Response**: The word “isolated” in the phrase “....HAdV isolates from UMMC were determined” has been deleted (page 7, line 14).

7. On page 8, the Genbank accession # for the Guangzhou, Ad3 strain or the published paper need to be referenced.

   **Response**: The accession # for the Guangzhou isolate has been included (page 8, line 1).

8. On page 10, third paragraph, it is not clear what the authors mean by “The two proteins showed their EVOLUTIONARY roles”

   **Response**: The Discussion has been thoroughly revised for clarity and the sentence mentioning the above phrase has been deleted.

**Discretionary revisions**

1. On page 6, line 2, the use of “cytopathic” instead of cytopathologic is recommended.

   **Response**: Revision has been made (page 5, line 20).

2. On page 10, first paragraph, the authors state that the higher percentage of Ad-C isolation is a reflection of Ad-C endemicity. What does this mean? It may be a good idea to discuss that the Ad-C serotypes also cause persistent infections and that this may be also a possible reason for an increased isolation from the upper respiratory tract.

   **Response**: We have substituted the term “endemicity” to “persistent infection” (page 9, line 18-19).

3. On table 1, what does “viral fever” mean?

   **Response**: “Viral fever” was the written diagnosis given by the consulting clinician and that was printed on the laboratory record. Since we do not have access to the patient’s record, a clear indication of “viral fever” cannot be given in the present study.

4. In the last line, on page 10, it is redundant to mention the endemicity of the Ad-C again.

   **Response**: Agreed. The sentence has been deleted from the manuscript.
Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published.

Statistical review: No, the manuscript does not need to be seen by a statistician

Declaration of competing interests: I have no competing interests