Author’s response to reviews

Title: Novel compound heterozygous mutations in OCA2 gene associated with Non-syndromic Oculocutaneous Albinism in a Chinese Han patient: a case report

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Author’s response to reviews:

Dear Dr. Kannabiran,

Please check the revised version of our manuscript “Novel compound heterozygous mutations in OCA2 gene associated with Non-syndromic Oculocutaneous albinism in a Chinese Han patient: a case report” in the attachment, which we would like to resubmit for publication as a case report in BMC Medical Genetics.

We are thankful to the editor and reviewers for pointing out several important modifications needed in this report. We have thoughtfully taken into account these comments. The explanation of what we have revised in response to the reviewers’ concerns is given point by point in the following pages.

We also have checked and corrected the grammar and spelling errors. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in BMC Medical Genetics.

We shall look forward to hearing from you at your earliest convenience.
Yours sincerely,

Jing Wang

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Responses to the comments of Reviewer #1

1. This manuscript describes a single patient with OCA2. The patient has two novel mutations: one missense and one gross deletion encompassing part of the OCA2 gene.

These data are not significant to be published on their own.

In comparison, there are many papers available describing large series of patients with different forms of albinism. There are more than 300 OCA2 mutations published in HGMD for instance.

Response: We agreed that this is just a single case, however, it reported two novel compound heterozygous mutations in OCA2 gene, which has never been reported before. It can expand the mutation spectrums of OCA2 gene and assist the genetic counselling, carrier screening and personalized healthcare of the disease.

2. In addition, the bibliography is far from being up to date, and some references are inappropriate.

Response: Thanks for the reviewer’s suggestion. We have checked the bibliography, updated and corrected the citations.

Responses to the comments of Reviewer #1

1. The manuscript described a case report to identify genetic defects causing OCA in a patient. The study is straight forward and complete with respect to the question asked. In my opinion the manuscript requires a thorough check for the language and grammatical correction.

Response: Thanks for the reviewer’s suggestion. We have reviewed the original manuscript, checked and corrected the grammatical errors and spelling mistakes.

2. TITLE:

No need to mention the extent of deletion in the title. If it is done then the novel mutation should also be defined.
Response: We have revised title name “Novel compound heterozygous mutations in OCA2 gene associated with Non-syndromic Oculocutaneous albinism in a Chinese Han patient: a case report. (Title section, line 1, page 1).

3. ABSTRACT

Background:

Why say "...suspected oculocutaneous albinism (OCA)"? Phenotype in an OCA patient is obvious. It is the subtype that is being characterized by identifying the gene containing the mutations causing the disease.

Response: Thanks for the reviewer’s suggestion. We have deleted the word “suspected”. (Background section in ABSTRACT, line 3, page 2).

4. Case Presentation:

(a) What was the rationale of using panel of 54 inherited eye diseases instead of the known candidate genes for OCA?

Response: The panel of 54 inherited eye diseases used in this study contains the most frequently non-syndromic OCA candidate genes (TYR: OCA1; OCA2: OCA2; TYRP1: OCA3; SLC45A2: OCA4) and nine syndromic OCA candidate genes (HPS1, AP3B1, HPS3, HPS4, HPS5, HPS6, DTNB1P1, BLOC1S3, BLOC1S6) already.

5. (b)"The mutations in the OCA2 gene were the cause of the proband." It is cause of the disease not the "proband".

Response: Thanks for the reviewer’s suggestion. We have deleted this sentence. (Case presentation section in ABSTRACT, the last line, page 2).

6. (c) "It extends the genotype phenotype spectrum of OCA2." The genotype has not been correlated specifically with OCA2 phenotype among different subtypes of OCA. Therefore, this statement is not justified and its deletion is recommended.

Response: Thanks for the reviewer’s recommendation. We have replaced this sentence with “It expands the mutation spectrum of OCA2 gene”. (Conclusions section in ABSTRACT, line2-3, page 2).
7. Conclusion: "It is necessary to screen for large deletions with targeted NGS protocol in monogenic disease." It is helpful but not "necessary". Enough large deletions have been identified in various genes causing different diseases much before use of NGS.

Response: Thanks for the reviewer’s recommendation. We have changed “necessary” to “helpful”. (Conclusions section in ABSTRACT, line 3, page 2).

8. BACKGROUND

"Oculocutaneous albinism (OCA) is a group of rare heterogeneous clinically and genetically autosomal recessive disorders with the deficiency in melanin synthesis." The disease is not also clinically "autosomal recessive disorder". This is one of many examples showing desperate need to work on the language of the manuscript.

Response: We have deleted “clinically and” (BACKGROUND section, line 1, page 3), checked and corrected the grammatical errors and spelling mistakes of the manuscript.

9. DISCUSSION AND CONCLUSION

The last sentence of this section, "Copy number analysis is important for routine genetic diagnostics with targeted NGS in monogenic disorder, given the complexity of the genetic lesion", is not of much relevance with the content of the study and discussion presented in the manuscript. Existence of the identified deletion does not remove the entire gene. So, I think that the statement may be removed from the text.

Response: Thanks for the reviewer’s suggestion. We have removed this sentence from the text. (DISCUSSION AND CONCLUSION section, last line, page 7).