Author's response to reviews

Title: Screening of potential target genes for cataract by analyzing mRNA expression profile of mouse Hsf4-null lens

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Author's response to reviews: see over
Dear Ms Erica Cruz,

Thank you very much for your letter and for the reviewers’ comments concerning our manuscript entitled “Screening of potential target genes for cataract by analyzing mRNA expression profile of mouse Hsf4-null lens” (Manuscript ID, 5922350301596375). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches.

We have studied the comments carefully and have made corrections which we hope meet with approval. Revised portions are highlighted by track changes mode in MS word in the paper for easy editing purpose. The point-by-point responses to the reviewers’ comments are listed below.

We are looking forward to getting your approval for its publication. If you have any additional questions, please contact us without hesitation.

Sincerely yours,

Jinghai Li

Our response to comments

Reviewer(s)' and Editor's Comments to Author:

Reviewer: 1
Comments to the Corresponding Author

1. Please give some detail on the genetic background of the Hsf4-null mice in this work.

   Answer: Thank you for your kind suggestion. We have added a reference in the section of “Microarray data and data preprocessing” as “The total microarray contains 6 chips of mouse tissue samples from Hsf4-null and wild-type lenses, which were described as a previous study [6]”.

2. For functional analysis, besides the general analysis by DAVID, if it is possible for the authors to combine the lens differentiation or cataract development data for further comparison?

   Answer: Thank you for your kind suggestion. Your suggestion is very helpful to our further studies. However, in the present study, the functional analysis by DAVID is significative to understand the roles of Hsf4 mutations in cataract development. The the genes (Ubc, Ptgs2, Egr1 and Fos) associated with DNA damage which were dicussed in this study were related to cataract development. These results were very meaningful to further studies. In our further studies, we will consider your technical suggestion. Thank you!

3. Generally, after microarray analysis, it is very necessary to confirm the findings by realtime PCR, there is no such data in this manuscript.

   Answer: Thank you for your technical suggestion. You are right that the predictions in this study should be validated by assays. However, this manuscript aimed to re-analyze the published microarray expression data by using bioinformatics methods
to further investigate the molecular mechanisms of how mouse Hsf4 (mHsf4) mutations influence lens development and lead to cataract. The significance of this research has been mentioned in the conclusions. Therefore, although there are no additional confirmatory experiments, this study is significant for further studies.

Reviewer: 2

1. In line 155, the authors state “cataracts may be caused primarily by damage to DNA”. They should discuss more about relationship between cataract and DNA damage and should cite references.

Answer: Thank you for your technical suggestion. We have added some discussion about relationship between cataract and DNA damage as follows:

Cataracts may be caused primarily by damage to the DNA damage, such as oxidized purines [33] and DNA single strand breaks [34]. Study has found that oxidative DNA damage is significantly high in the lens epithelial cells (LECs) of cataract patients [35, 36]. Besides, loss-of-function mutations in TBC1D20 cause cataracts in blind sterile mice [37]...

2. In line 159, the reference 6 is not correct. They should at least refer Fujimoto et al, EMBO J. 23, 4297-306, 2004.

Answer: Thank you for your technical suggestion. We have corrected the reference as “Fujimoto et al, EMBO J. 23, 4297-306, 2004”.

Editor's Additional Request:

1. Please provide the Source of Funding in the Acknowledgement section.

Answer: No funding supported this study.
2. Requesting for Copy-Edit

- We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service.

Answer: Thank you for your technical suggestion. We have asked a native English speaker to improve the language of this manuscript.

3. Please provide email address of each co-authors in the Title page of the manuscript PDF file.

Answer: We have added the email address of each co-authors in the Title page. Thank you.