Author's response to reviews

Title: Overexpression of eIF-5A2 in mice causes accelerated organismal aging by increasing chromosome instability

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Author's response to reviews: see over
Aug. 18, 2010

Dr. Pulivathi Rao,

BMC cancer Editorial Office,

Dear Dr Rao,

RE: MS: 1149143646400892
Title: Overexpression of eIF-5A2 in mice causes accelerated organismal aging by increasing chromosome instability

Thank you for reviewing the above-referenced manuscript submitted earlier to your office. We would like to take this chance to express our appreciation to you and Reviewers. In accord with the Editor’s and Reviewers’ comments and suggestions, the manuscript has been revised accordingly. We feel that this revised manuscript has been strengthened by the Editor’s and Reviewers’ comments and suggestions. A point-by-point response to the Reviewers’ comments and suggestions has been prepared and follows this cover letter.

I hope the changes and explanations satisfy the requirements of the Editorial Board. I thank you again for reviewing the manuscript and look forward to hearing your favorable reply soon.

Sincerely yours,

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A point-by-point response to Reviewers’ comments and suggestions

Reviewer 1:
No major compulsory revisions are required.

Minor essential revisions:
1. According to Reviewer’s comment, we delete “such as errors in cell dividing during metaphase and anaphase” from the “Abstract” section in the revised manuscript.
2. According to Reviewer’s suggestion, we changed “The transgene was mapped to chromosome 10 in line 11” to “The transgene was mapped to one chromosome site in line 11” in the revised manuscript (the 3rd paragraph in page 10).
3. Reviewer is correct. It should be “phenotypes”, not “genotypes” in page 12. We have corrected it in the revised manuscript.

Discretionary revision:
We appreciate with Reviewer’s suggestion. We want to keep the karyotype and SKY data in this manuscript although they are relatively weak. We checked again and found the Reviewer is correct. The right panels of Figure 7A should be reversed DAPI stain rather than C-bands. This error has been corrected in the revised manuscript (Figure 7A legend).

Reviewer 2:
Specific comments that requires Major Compulsory Revision:

1. Since eIF-5A2 is a new gene and its function is mainly revealed in cancer, the physiological role of eIF-5A2 remains unclear.
2. According to Reviewer’s suggestion, Figure 1A has been deleted from the revised manuscript. Figure 1C, the metaphase spread was prepared from bone marrow lymphocyte. Figure 1D, One mouse without eIF-5A2 transgene (No. 9) was used as negative control. Figure 1E, No endogenous expression of eIF-5A2 was detected. The posttranslational modification is hypusination at the lysine-50 residue. All these changes have been made in the revised manuscript in Figure 1 legend.
3. We have deleted lung and heart in the text (page 11) in the revised manuscript. The purpose of this study was to investigate if eIF-5A2 plays any role in mouse development. However, no difference was observed between transgenic and wild-type mice.
4. As mentioned in reply 3, the purpose of this study was trying to the effect of eIF-5A2 on mouse development. Since the results were negative, we only showed the data from liver and heart as representatives in Figure 3.
5. To avoid the potential difference of body weight between male and female mice, only male mice were included in the experiment. According to Reviewer’s suggestion, statistical analysis was used to determine whether the differences were significant (see revised Figure 4 and 2nd paragraph in page 12).
6. “…liver lysates from transgenic…” should be “…lysates from transgenic…”. We have modified it in the revised manuscript (Figure 6B legend).
7. According to Reviewer’s suggestion, the quantification of metaphase spread data, including the bone marrow of the adult, has been included in the revised manuscript (the 1st paragraph in page 16).

Discretionary revision:
Thank the Reviewer’s comment and we plan to do that experiment in our future work.