Author’s response to reviews

Title: A Network Pharmacology-Based Study on Alzheimer disease prevention and treatment of Qiong Yu Gao

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Author’s response to reviews:

Dear Ka-Chun Wong,

Thanks very much for your email of March 10th, 2020, with regard to our manuscript “A network pharmacology-based study on Alzheimer disease prevention and treatment of Qiong Yu Gao” (BIDM-D-20-00011) together with the comments from associate editor and reviewers. According to the valuable comments, we have revised the relevant parts in the original manuscript. We also respond point by point to the comments as listed below, and the revised portions are marked with red color in the manuscript. I hope this will make it more acceptable for publication.
Thank you and all the reviewers for the kind advice.

Yours sincerely,

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Here below are our responses to the comments.

Comments to the Author

Associate Editor

Question 1:  
The study is based on network pharmacology in a theoretical manner. Therefore, statistical rigors such as p-values and FDRs have to be carefully measured and computed with well-grounded hypothesis.  
Answer:  
Thank you for your valuable comments. We strictly controlled the parameters and p-values of screening and assessment. For the collection of chemical ingredients in QYG, DL values ≥ 0.18, OB ≥ 30% and BBB ≥0.3 were considered; when examined the GO terms and KEGG pathway enrichment, the p valued were adjusted for multiple testing.

Question 2:  
Additional figure notations could be reader-friendly as most readers may find it difficult to read the complex network figures provided.  
Answer:  
Thank you for your reminder. We added additional figure notations in the figures.

Question 3:  
It is very interesting to see how herbal medicine (Qiong Yu Gao) is related to Alzheimer disease prevention. However, additional survey on Alzheimer disease prevention can add state-of-the-arts senses to the current study.  
Answer:  
Additional survey on Alzheimer disease prevention were added in the introduction and discussion part. Please see lines 97-101 on page 4 and lines 351-353 on page 14.
Reviewer 1

Question 1:
Grammatical and punctuation errors should be rectified. Authors are suggested to use smart tools like 1 checker, ginger, white smoke, etc.
Answer:
Thanks for your suggestions. We rectified grammatical and punctuation errors by using smart tools.

Question 2:
I think the writing language quality can be improved.
Answer:
We checked the manuscript again and again, and corrected some typos and improved the English expression all over the manuscript.

Question 3:
The figures are not clear well. They should be replaced by more good quality figures.
Answer:
We resubmitted more good quality figures.

Question 4:
Some of the references are not so relevance to the topic can be missed.
Answer:
We deleted the irrelevant references based on your comments.

Reviewer 2

Question 1:
Because of the theoretical nature of the study, it would be more welcomed by the readers if the authors can demonstrate how Alzhiemer's cell models behave after QYG treatment (eg., cytotoxicity using SH-SY5Y cells or any relevant models).
Answer:
Thanks for your valuable suggestion. In the last paragraph of the “Discussion part”, we mentioned the limitation of this study that “The potential advantage of ‘network targets, multi-component’ strategy of network pharmacology is obvious, but it is generally as a guided theoretical science, which is also the limitation of this study. Therefore, the demonstration in the gene and protein levels of QYG treated Alzheimer disease will be provided in the future”. We will further demonstrate how Alzhiemer's cell models behave after QYG treatment.
Question 2:
Further, discussion of safety and side effects of the concoction would add more strength to the study.
Answer:
We added the safety and side effects of QYG in the discussion part based on your comments. “All the ingredients of QYG belongs to medicinal and edible plant or diet, and they have a history of safe use.” Please see lines 358-359 on page 14.

Question 3:
Content overlap in the figures has to be avoided (eg; fig 5)
Answer:
Thanks for your reminder. We deleted the repetitive content in the figure 5.

Question 4:
Inclusion of a figure with the major ingredients of 4 herbs in QYG would be beneficial to the readers.
Answer:
Thanks for your suggestion. Actually, the putative major chemical ingredients and ADME parameters in QYG were provided in the Table S2 in detail. We think the table may be more beneficial to the readers.