Reviewer's report

Title: Network Pharmacology Approach to Uncover the Mechanism Governing the Effect of Radix Achyranthis Bidentatae on Osteoarthritis

Version: 0 Date: 30 Nov 2019

Reviewer: Junguk Hur

Reviewer's report:

Laigen Zhang et al employed a network pharmacology approach to elucidate the potential mechanisms of Chinese herbal medicine, Radix Achyranthis Bidentatae (RAB), in the treatment of osteoarthritis (OA). Active components of RAB were collected along with their potential target proteins, which were compared against the genes that are potentially related to OA. The overlapping genes, OA-related RAB targets, were then examined in networks to identify critical targets and enriched biological pathways. Component-target pairs were evaluated for binding via molecular docking analysis. The study is straightforward but has much room for improvement.

Main comments:
1. The Introduction is very short. There is not enough background knowledge currently known about RAB other than it is the most frequently used than other herbs for treating OA. The authors need to provide more comprehensive background about the RAB, to the level of currently known in the literature. The authors claimed, "the mechanism of RAB in OA is still unclear."; however, the authors should also provide what's currently known or proposed in the published literatures about the potential mechanisms of RAB. The same thing applies to the "network pharmacology", for which more details are needed.
2. It is not clear how comprehensive and relevant to the collected genes from GeneCard and OMI with respect to OA. Besides, the scope of "OA-related" needs to be clearly defined. It is also not clear how they were actually collected. More details are needed, and a complete table (supplementary table) would be needed to list all the collected genes along with their detailed information, the method of collection, and the link to the source pages.
3. What was the rationale of selecting the top eight targets as the most important targets?
4. The authors claimed that the larger the degree, the more likely this target will become a key target for compounds. This statement needs to be justified. And there are other measures of node importance such as betweenness, closeness, eigen vector and etc. Why was only the network degree used in the study?
5. There is no statistical evaluation of the resulting network. How significant the constructed network is different from random networks? Like the significance of node significance needs to be evaluated using random models and compared against those from the constructed network.
6. Why was the docking analysis limited to certain compounds and targets? This needs to be extended to all pairs.
7. The writing needs to be substantially improved. Using a professional language editing service is highly recommended.
Minor comments:
1. The authors better not capitalize "Network Pharmacology".
2. I would recommend the authors to consider having a workflow (diagram) to illustrate the overall approach.
3. The definition of 'interaction' in this study needs to be clearly defined.
4. Acronyms must be defined before being used.
5. Table 2 Potential targets information of RAB for OA is not informative. Instead of just item numbers, including other information, such as protein name and IDs and OMIM ID, is highly recommended.
6. Term selection better be consistent throughout the manuscript. E.g. sides vs edges.
7. Most figures are missing legends and of low-quality. They are not readable.
8. References do not follow the style of BCAM.
9. Lines 242 - 244. It would be better to give the actual Figure number (network).
10. Multiple paragraphs include only one sentence.
11. It is not clearly justified why the Protein-Protein interaction networks among the targets are important.
12. The complete compound - target pair information needs to be provided as Supplementary Table.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
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