Peer Review File

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Reviewer A

The authors studied the molecular mechanism of P. ternata using network pharmacology and in vitro methods. the study is very interesting and study design was well directed by the use of Network Pharmacology bioinformatics tool. I appreciate the authors for this interesting work. However, I have few minor observations-

1. The Figure F2 is not clear. Please improve the figure quality.

Reply 1: Thanks for your comment. We have modified the images as requested to provide higher quality images.

Change in the text: see Page 15, line 457.

2. The preparation of P. ternata should be explained in the methodology.

Reply 2: Thanks for your comment. And I've added that section to the text.

Change in the text: see Page 6, line 175-180.

3. In line 224, 13 compounds are mentioned for P. ternata but in line 241, it is 12. Please correct.

Reply 3: Thanks for your comment. One of the 13 compounds was untargeted, so only 12 compounds were used for follow-up studies.

Change in the text: see Page 8, line 236-238.

4. Please specify the control in Eca-109 migration and invasion assays.

Reply 4: Thanks for your comment. Saline was used in the control group in the migration and invasion experiment.

Change in the text: see Page 6, line 184.

5. How the KEGG pathway analysis is correlated with the studied Akt signaling pathway in this study?

Reply 5: Thanks for your comment. Among the signaling pathways enriched in the KEGG enrichment analysis the PI3K-AKT signaling pathway was significantly enriched. The KEGG enrichment only showed the top 20, and the PI3K-AKT signaling pathway was not actually shown.

6. The discussion part lacks previous similar study result comparison and how current findings are significant from other similar works.

Reply 6: Thanks for your comment. The section has been added.

Change in the text: Page 11-12, line 346-399.

Reviewer B

This study is very interesting because it combines bioinformatics techniques (networkpharmacology) and verification using in vitro tests. This research supports

thediscovery of new drugs, so it is very worthy of publication in JGO. But there are several critical things in the manuscript that need to be reviewed by the author.
Suggestions and comments are attached to the main text with yellow highlighting.
Reply: Thanks for your comment. I have replied in the yellow highlighted section and have made changes in the article as well.

Reviewer C

The manuscript contains fundamental errors. Many things are lacking in this paper. The conclusion is feeble, and it must be drawn appropriately based on the data presented. The soundness of the conclusion is lacking. I am concluding my few comments as follows:
1. In Table 1 names of target proteins are missing and only the number of targets is mentioned. Probably authors did not identify the targets. Also, are all the targeting proteins present in the targeted infection or not?
Reply 1: Thanks for your comment. I will add additional documentation to provide the target protein name. In a follow-up article we correlate raw *Pinellia ternata* target proteins with esophageal cancer disease-associated proteins whose intersections correlate with targeted infections.

2. The shortlisting of compounds is not justified. Add more promising parameters.
Reply 2: Thanks for your comment. However, I reviewed the relevant literature and found that most of the literature is screened by these two metrics Oral bioavailability (OB) and drug-like (DL), so it is feasible.

3. The TCMSP site is not opening. How did you work on it and how a reader will obtain information from it?
Reply 3: Thanks for your comment. I tried the URL for this site and it opens fine. Here is the URL: https://old.tcmsp-e.com/tcmsp.php

4. For more promising targets protein and compound analysis string analysis is not sufficient. You need to perform a docking analysis. It will improve your current results more accurately.
Reply 4: Yes, that's a great suggestion. In this paper, we have only conducted a preliminary study on whether raw *Pinellia ternata* can inhibit esophageal cancer cells, and its specific compounds of action need to be followed up with further research.

5. In the results section of lines 296 and 309, is it 10ng/ml or mg/ml?
Reply 5: The concentration of TNF-α was 10 ng/ml.
Change in the text: see Page 10, line 307.