

## Peer Review File

Article information: <https://dx.doi.org/10.21037/tp-23-111>

### Reviewer A

Traditional Chinese medicine (TCM) believes that central precocious puberty (CPP) is affected by the imbalance of kidney Yin and Yang. Dabuyin pill is a recipe for nourishing Yin and lowering fire. In the manuscript “Analysis of the efficacy of Dabuyin pill combined with gonadotropin-releasing hormone analogue in the treatment of central precocious puberty girls based on network pharmacology”, authors used network pharmacology method to analyze the active components, action targets, and molecular pathways of Dabuyin pill in the treatment of CPP.

Couple questions are required to be answered before it will be accepted.

(1) What were the correlations between kidney Yin and Yang and sex hormones? Please state in the introduction.

Reply 1. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 3/Line 25-30.

(2) In the introduction, it was proposed to add related reference (DOI: 10.21037/tp-21-352) about the central precocious puberty.

Reply 2. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 12/Line 28-30.

(3) What were the main causes leading to central precocious puberty? Please state in the introduction.

Reply 3. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 5/Line 2-10.

(4) Nowadays, whether the Dabuyin pill has been applied for central precocious puberty in clinical? Please state in the introduction.

Reply 4. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 5/Line 10-18.

(5) In the figure 4-6, please mark the number of images.

Reply 5. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 9/Line 11, Page 9/Line 19 and Page 9/Line 31.

(6) Missing experimental data was the biggest short board in the study. It was better to validate the functions and expressions of target genes of Dabuyin pill in the study.

Reply 6. Thank you very much for your suggestion. Due to the lack of experimental equipment and relevant experimental conditions, the experimental verification cannot be carried out.

(7) In the results, the inflammation was involved in the biological functions of Dabuyin pill? What were the roles of inflammation in the central precocious puberty? Please state in the discussion.

Reply 7. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 10/Line 19-22.

(8) What were the effects of GnRHa on secretion of sex hormones? Please state in the discussion.

Reply 8. Thank you very much for your suggestion. We have revised the content of the manuscript according to your requirements. Page 11/Line 19-24.

### Reviewer B

1. Please indicate the online link for STRING database.

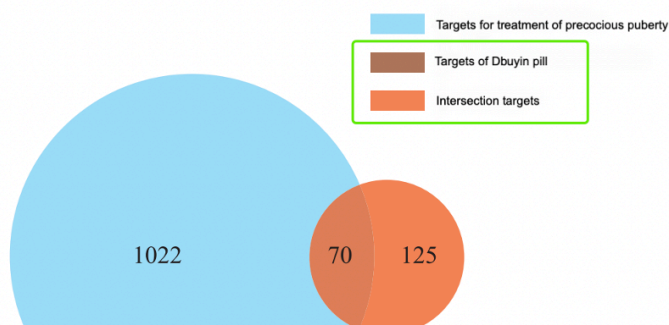
22    ##Target interaction network↵

23        To explore the interaction of Dabuyin pill components on CPP disease targets, the  
24    Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database was  
25    used to construct a protein-protein interaction (PPI) network relationship table. The

Reply 1: We have added the online link in the manuscript. Page 6, line 25.

2. Figure 2:

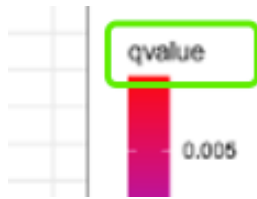
Your Figure labels are wrong. The dark orange should be intersection targets, and light orange should be targets of Dabuyin pill.



Reply 2: We have revised. See the attached files.

3. Figure 5:

1) Please revise all “qvalue” to “**q value**”.



Reply 3.1: We have revised.

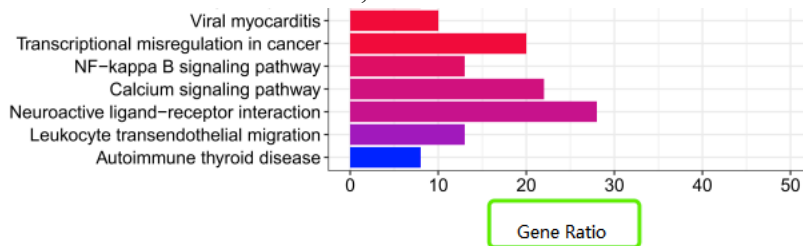
2) Please revise all “GeneRatio” to “**Gene Ratio**”.



Reply 3.2: We have revised.

3) Figure 5A:

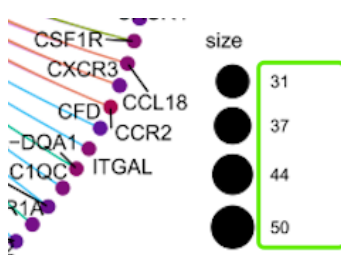
Should the x-axis be “**Counts**”, not “Gene Ratio”? Please revise.



Reply 3.3: We have revised.

4) Figure 5C:

Please check whether the numbers of size are correct.



Reply 3.4: We confirmed that it was right.

5) Please mark the letters "A", "B", "C" parts in your Figure 5 and combine the three parts in one image.

Reply 3.5: We have revised.

4. Figure 4:

1) Figure 4 has the same issues with Figure 5. Please revise.

2) Please explain BP, CC, and MF in the legend.

Reply 6: We have revised the figure 4 accordingly.