Peer Review File
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Reviewer A

Title: 'SNHG 12 and hsa-miR-140-5P may play an important role in the ceRNA network related to hypertrophic cardiomyopathy' doesn't accurately reflex the data presented. Multiple factors have been identified as central to the ceRNA network, not just the two in the title. Additionally, the importance of these factors has not been proven. A more accurate title would be about the construction of a HCM ceRNA network.

Key findings box: 'we discovered a ceRNA network' should be changed to 'we constructed a potential ceRNA network'
Reply : We have modified it.

L74 'perfect' should be changed
Reply : There really is no perfect medication by now.

L84 The authors claim, 'some recent research has shown susceptibility modules and genes in HCM, but the whole ceRNA network has not been established (7).' However, the paper cited in reference 7 does indeed generate a ceRNA network. This should be commented on and the differences between that study and the present one should be highlighted.
Reply: On that paper, it's only represent a signal pathway of HCM ,not the whole ceRNA network.

L101 The 'data downloading' section lists the number of HCM and control samples in each of the data sets. It would be helpful to include these sample number on workflow figure 1 or at least in the legend of this figure.
Reply: This has been described in the text.

L180 states 'As shown in Figure 2A,2B, 93 DEGs (77 up-regulated and 16 down-regulated), 163 DEMs (91 up-regulated and 72 down-regulated), and 432 DEGs were screened. They are used in the subsequent analysis.' The '93 DEGs' is a typo and should be changed to '93 DELs'. This should also be done in line 414 in the figure legend.
Reply: Thank you, it's revised.

L250 ‘useful’ should be changed. Suggest ‘disease-associated’
Reply: Thank you, it’s revised.

L286 ‘The role of IGFBP5 in HCM has not been previously reported’. IGFBP5 was also identified in the ceRNA network generated by references 7 and therefore this overlap should be mentioned.
Reply: In citation 7, IGFBP5 is only speculated to be involved in HCM development, and there are no experiments to confirm this hypothesis

L295 ‘In our study, most of the hub genes were regulated by hsa-miR-140-5P, whereas all of them were related to SNHG12 (lncRNA).’ It should also be noted that SNHG12 is a snoRNA host gene and snoRNAs have recently been identified as potential HCM signalling candidates- this interesting observation should be commented upon https://doi.org/10.1089/scd.2021.0202
Reply: Thank you I‘ve add this information on Line 306.

Figures
Full lists of the 93 DEGs, 163DEMs and 432DEGs with directional changes should be included as supplementary tables.
Reply: We can provide this as an attachment, but it doesn't fit inside the text.

Figure 2B does not show overlapping DEMs- include these.
Figure 5B and 5E- quality of figure is unreadable and needs improving.
Reply: We uploaded the picture again.

Reviewer B

Authors collected 353 RNA-analysis data of HCMs from GEO database. The differential expression of lncRNAs, miRNAs, and mRNAs between the HCMs and controls were analyzed. Further, WGCNA, GO, KEGG analysis, and TF prediction of miRNAs were performed to further explore the pathological significance of the data. The GO terms, KEGG pathway terms, PPI network, and Pearson correlation network of the mRNAs were visualized with the STRING database and Pearson analysis. No similar study is found so far. The authors applied bio-informatic analysis platforms to deeply analyze the data and conclude that SNHG12, hsa-miR-140-5p, hsa-miR-217, TFRC, HDAC4, TJP1, IGFBP5, and CREB5 may form an important network involved in the pathology of HCM. The research ideas are ingenious. The method is reasonable.

All results are theoretical speculation. The results provide a directional clue for further studies. Some other questions concerning this manuscript are indicated below:

1.Your findings indicated that SNHG12, hsa-miR-140-5p, hsa-miR-217, TFRC, HDAC4, TJP1, IGFBP5, and CREB5 may form an important network involved in the pathology of HCM. However, your title is: SNHG 12 and hsa-miR-140-5P may play an important role in the ceRNA network related to hypertrophic cardiomyopathy. Can you explain why?

Relpy: As the title of the article, I have selected two genes that I consider the most critical, which can be seen in the discussion. The remaining genes are also important, but I don't think it's appropriate to listed all of them in the title.

2.The beginning of line 110 should not has a space.

Reply: Thank you I've revised that.

3.In 34 lines of the abstract, the abbreviations of differentially expressed mRNAs are both DEmRNAs and DEGs. However , the abbreviation of differential expression mRNAs in the text of lines 87-89 is DEmRNAs. The abbreviation of differential expressed gene is DEGs. What is the difference between the two interpretations?

Reply: It's a fault on line 34, and has been revised.

4.Are all HCM's RNA data detected from myocardial tissue samples? Dose it also include the data from blood or other sample sources?

Reply: They are just tissue samples.

5.Some other abbreviations should be addressed with full names. Such as GEO2R, BP, CC, MF, etc.

Reply: I've added them in the legend of Figure 4.

6.In lines 152-159, what RNAs (DEMs or DEGs?) were screened for Hub genes and Pearson correlation analysis?

Reply: The hub gene were present in line 217-222.

7.In lines 411-415 (Fig2), 163DEMs (91up; 72down) in the text description are not found in the pictures of Fig2B.

Reply: This content cannot be placed in the picture.

8. Some words in the figures are too small to see.

Reply: We uploaded the picture again.

9.What does red (or green) means in Fig. 5?
Reply: Red nodes represent upregulated lncRNAs/miRNAs/mRNAs in HCM, and green nodes represent downregulated lncRNAs/miRNAs/mRNAs in HCM. It's in the legend of figure 5.

Reviewer C

The manuscript "SNHG 12 and hsa-miR-140-5P may play an important role in the ceRNA network related to hypertrophic cardiomyopathy" found that SNHG12 and miR-140-5P were potential players in HCM. Before considering its acceptance, several issues should be resolved.

1. The major concern was, just as illustrated in limitation part, the two molecules were not verified in HCM samples. Could the authors add this data, to make the two palyers more confidential in HCM.
Reply: Due to time constraints, we will supplement this content in future research.

2. Several similar researches were reported, using these datasets（PMID: 34497835, PMID: 31180540, PMID: 35990977 etc.）.Part of the conclusions could be added and discussed, to further show the novelty of this study.
Reply: Our references are abundant enough, so there is no need to add these articles.

3. Too many datasets were included in this study, please added characteristics of these datasets in a table, such as number of patients, platform. This was important for readers to evaluate datasets.
Reply: This has been described in the text.
4. Why the WGCNA was only performed in GSE36946 dataset?
Reply: As I've show on line 112-114, miRNA are only enrolled on GSE36946, WGCNA is used for miRNAs.

5. What is the clinical expection of the conclusion? biomarkers or intervention targets for HCM?
Reply: Thank you for your advice, and I've put this on the conclusion section.(line 329-330).

6.The language can further be polished.
Reply: We have improved this opinion.

Review Comments-reviewer D

The paper titled "SNHG 12 and hsa-miR-140-5P may play an important role in the ceRNA network related to hypertrophic cardiomyopathy" is interesting. The novel ceRNA network that we have demonstrated will provide new research points about molecular mechanisms of HCM. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) It may be more meaningful to add functional research on key ceRNAs.

Reply: It's on the discussion ,P9 274-294

2) It is suggested to increase the analysis of the relationship between clinical features and related ceRNAs, which may make the research more complete.

Reply: Thank you for your suggestion. Our team has discussed your suggestions and think that your suggestions are very good. However, it is difficult to supplement this part of the experiment due to time and funding reasons. We will combine other detection methods in the follow-up study.

3) It is suggested to add weighted correlation network analysis to identify key module, which may make the whole study more complete.

Reply: It's in WGCNA and functional enrichment analysis of miRNAs, P6-7,184-193

4) This study is based on bioinformatics analysis. It is recommended to increase in vivo and in vitro experimental studies, which may be more meaningful.

Reply: Thank you for your suggestion. Our team has discussed your suggestions and think that your suggestions are very good. However, it is difficult to supplement this part of the experiment due to time and funding reasons. We will combine other detection methods in the follow-up study.

5) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Competing endogenous RNA network analysis reveals pivotal ceRNAs in bladder urothelial carcinoma, PMID: 33718081", "Soluble ST2, Galectin-3 and clinical prognosis of patients with hypertrophic cardiomyopathy undergoing ventricular septal myectomy: a correlation analysis, PMID: 32420094". It is recommended to quote this article.

These two documents have different themes from our article, so it is unnecessary to quote them.

6) How to provide candidate targets for the treatment of hypertrophic cardiomyopathy based on the results of this study? It is recommended to include relevant descriptions in the discussion.

Reply: Thank you for your suggestion. Due to time constraints, we will supplement these in the follow-up study.