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Reviewer A:

Comment #1: please describe in the method or results section, how many animals were used

Reply #1: We have added descriptions on the number of experimental animals by noting "n=3" for each group (see Line 115 in Methods section, and column titles of Table S2 and Table 1).

Changes in the text:

"Male C57/BL6 mice of SPF level rendered by Experimental Animal Center of Guangzhou University of Chinese Medicine (No.44005800003866), were randomly divided into two groups: the HF group (n=3) and the Sham group (n=3), which were matched by age, weight and health state."

Table S2 Ratio of heart weight/body weight in different groups（x±SD）

Parameter	Sham Group (n=3)	HF Group (n=3)
BW (g)	24.73±1.96	24.03±1.63
HW (mg)	105.33±13.99	203.07±10.21*
HW/BW (mg/g)	4.25±0.23	8.5±1.03*

*, $p < 0.05$ vs. Sham group; BW, body weight; HW, heart weight; HW/BW, heart weight/body weight ratio; HF, heart failure.

Table 1 Echocardiography data in each group (x±SD)

Parameter	Sham Group (n=3)	HF Group (n=3)
LVEDD (mm)	3.36±0.17	4.29±0.16*
LVESD (mm)	2.33±0.27	3.48±0.23*
EF (%)	59.08±6.92	39.22±4.13*
FS (%)	30.60±4.66	18.87±2.23*
HR (bpm)	549.10±40.48	585.00±60.53

*, $p< 0.05$ v.s. Sham Group; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; EF, ejection fraction; FS, fractional shortening; HR (bpm), heart rate (beats per minute); HF, heart failure.

Reviewer B:

The study identified a total of 3830 DElncRNAs, 13 DEmiRNAs and 1139 DEmRNAs, which could be involved in the pathogenesis or progression of heart failure.

The method is appropriated and the paper is well written but some points should be better clarified.

- Identified RNA biomarkers are not related with pathophysiologic correlates, clinical phenotypes and heart failure progression.

Reply: We mentioned some already-reported RNAs which participate in heart failure processes in the Introduction and Discussion sections, such as miR-208 (a pro-hypertrophic miRNA), lncRNA CHRF (cardiac hypertrophy-related factor) and CARL (cardiac apoptosis-related lncRNA). Some RNAs do have associations with heart failure, which is widely accepted. In our study, hierarchical clustering of 1139 DEmRNAs showed that DEmRNAs could basically differentiate HF group from Sham group, which implied a potential association between these RNA biomarkers and heart failure. It is a further research direction to select several detailed RNAs based on our results and test their correlations with cardiac functions.

Changes in the text: No changes in the text for this reply.

- In the discussion section, the translational aspects on human patients should be better discussed.

Reply: We have added a paragraph discussing the promising future of turning RNA biomarkers into diagnostic and therapeutic practice in the Discussion section (see Line 314-323). Actually, there is still a huge gap between identified RNA biomarkers and their clinical application, before which in vitro and in vivo validation experiments are required. Our study focused on the screening phase of RNA targets and biomarkers, so we did not discuss much in terms of their translational issues.

Changes in the text: Line 314-323

"To date, RNA therapy is seeing a bright future. There are a considerable number of drugs targeting RNAs to treat specific diseases, which are based on their regulatory effect. For instance, Mipomersen, brand-named Kynamro, was approved to use in familial hypercholesterolemia, which decreases cholesterol level by targeting ApoB mRNA and inducing its degradation by RNase H (33). In addition, there are others under clinical trial, such as Miravirsen targeting miR-122 to treat Hepatitis C and MRG-106 targeting miR-155 used in lymphomas (34). Similarly, RNA diagnosis is evolving as a growing number of RNAs are showing high diagnostic efficiency (35, 36). Our study filtrating hopeful targets and RNA biomarkers of heart failure were expected to add more to current researches."

- Transaortic arch constriction is an experimental model which can not reflect pathophysiology of most of the human heart failure pathophysiologic background. This is another limitation of the study.

Reply: We agree with this, and have revised a paragraph in Discussion section to denote this limitation (see Line 325-330). Interestingly, to literatures and our knowledge, heart failure can be caused by different etiologies of different pathophysiologic background, but it still has some common pathophysiological processes, such as cardiac fibrosis, apoptosis of cardiomyocyte and energy metabolic disorders. Some differentially expressed mRNAs of our study were predicted participating in these common pathophysiological processes, so this TAC model, to our point of view, is still of good help to study the mechanism underlying heart failure.

Changes in the text: Line 325-330

"The expression profiles of RNAs and their interactions shown in our study were only a screening process based on experimental data using bioinformatics analyses. The TAC model of HF based on pressure overload, can not cover all subtypes of heart failure, such as volume overload and tachycardia induced heart failure, et al, which is a limitation of this study. Thus, to explore more comprehensive and deeper insights, different HF models and more HF samples are required. Validation experiments are also needed to perform both in vivo and in vitro to verify our findings."

We have had our manuscript proofread by a native English speaker. We hope the revised manuscript will meet your standard.