Reviewer’s report

Title: Multi-level transcriptome sequencing identifies COL1A1 as a candidate marker in human heart failure progression

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Reviewer: Honghuang Lin

Reviewer's report:

The current study compared the multi-level transcriptomic profiles of 21 HF patients and 9 healthy donors, and identified multiple differentially expressed genes. A further validation in 87 HF patients found that COL1A1 might be a biomarker for heart failure progression. Overall, the study is interesting and has the potential to contribute new knowledge to the field.

Following are some comments to be considered.

* Most HF patients included in the study seem to be quite young (mean age 34.6), which are much younger than the general patient population. Patients with early-onset HF could have familial history or quite different etiology comparing to those late-onset HF patients. Such limitation should be discussed.
* HFrEF and HFpEF patients could also have different disease mechanisms. Since 19 out of 21 patients were HFrEF patients, it would be useful to perform sensitivity analysis by excluding the two outliers and see if there is any difference.
* It is unclear how the tissue samples were collected. Were they from the discarded samples during heart transplantation? What about the 9 healthy controls?
* Were the fresh tissues or the frozen samples used in RNA extraction? How much RNA was obtained from each sample and what is the RIN value?
* Given that total RNA was used, was the ribosomal RNA depleted?
* In page 7, line 50, "it wound pick up a group of genes..." should be changed to "it would pick up a group of genes..."
* Was the plasma COL1A1 also measured in patients with tissue samples? If so, it would be interesting to see the correlation between plasma and heart tissue.
* Table 1 should include the clinical characteristics of both patients and healthy controls.
* Table 2 lists the summary statistics of sequencing data for all samples. However, it is unclear about the variation between samples in terms of sequencing coverage. Such information could be provided in a supplemental table.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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

Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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