Reviewer’s report

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

Version: 0 Date: 01 Jul 2019

Reviewer: Peter Van Der Meer

Reviewer's report:

Hua and colleagues report transcriptomic data from 21 failing hearts and compared these to 9 healthy donor hearts. They focus in their analysis on fibrosis. Eventually they identify COL1A1 as a novel marker to predict outcome in patients with HF.

I have several comments:

- From the manuscript it is unclear what the etiology of HF is? DCM? ischemic HF? Myocarditis? Furthermore it is unclear how the authors identified the 21 HF patients from their pathology archives/database.

- How were areas chosen for fibrosis assessment? Was scar tissue excluded?

- Mechanistic insights are lacking how col1A1 eventually leads to fibrosis and whether this is a causal factor.

- In itself it is interesting to validate their findings as a serum biomarker in a larger HF cohort. However, in the manuscript it is unclear in which cohort this was tested, apparently 87 patients were recruited, but unclear how they were included, what in and exclusion criteria were used, what kind of MV modeling was done. Due to the small numbers HR are extremely large (27 [95% CI 7-100]... The authors should either leave this out and focus on a more mechanistic approach or include many more HF patients with adequate follow up. Current biomarker study is too small to draw any meaningful conclusions.
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?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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