Reviewer's report

Title: Transforming growth factor beta receptor 1 is a new candidate prognostic biomarker after acute myocardial infarction

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Reviewer: Chrishan Samuel

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This paper utilised blood samples from patients with acute MI, a rat model for MI, microarrays, qPCR and ELISA kits to demonstrate that TGFBR1 is a potentially novel prognostic biomarker for acute myocardial infarction in humans and rats. Furthermore, the increase in TGFBR1 expression correlated well to known biomarkers of myocardial injury and/or improved the prediction of adverse outcomes. Although this study is of interest and the conclusions drawn fairly well supported by the findings obtained, there are a few queries the authors should address and/or clarify, as detailed below:

Major Compulsory Revisions:

1. The authors ‘introduce’ this study (on page 3) by saying that “A rapid and accurate prediction of the development of HF after MI would be a major breakthrough….”

-However, only one-time point is investigated from both human blood cells and rats post-MI; which appears to be a limitation of this study. Understandably, it would be difficult to study additional time points in humans, but why was only 2-months post-MI chosen as a time point of study in rats? This is a time point of chronic MI, where limited angiogenesis would be occurring in the border region of the LV…..the authors should additionally demonstrate what happens to TGFBR1 and TGFB1 at earlier time points (ie 2-, 4- and 6-weeks post-MI; when angiogenesis would clearly be expected to occur) or at the very least, better explain why this one time-point was chosen for the experimental studies included.

2. In Table 1, 81-85% of the acute heart failure patients included (in the test and validation cohorts) were men - were the limited female patients included sufficient enough to demonstrate whether gender was a contributing factor to TGFBR1 being a good prognostic marker of acute MI?

3. In Table 2, the TGFBR1, TGFBR2 and CLU genes were consistently found in all subsets of angiogenic genes associated with LV function. The authors report that the TGFBR2 gene was not detected in their microarrays – but what about the CLU gene? In the logistic regression models used, how did the CLU gene alone or in combination with TGFBR1 classify patients with low/high EF (compared to the combinations outlined in Table 3)?

4. On page 7, the authors state that the 3 genes that best classified patients with
low/high EF were the TGFBR1, PTK2 and ITK genes – yet only show data for the TGFBR1 gene. A comparison of how better the TGFBR1 gene was correlated to LV function, compared to the other two genes should be included.

5. Do the authors have access to cardiac biopsy tissue from the patients studied – to correlate their findings from blood cells to – to further validate their findings?

Minor Essential Revisions:
6. The authors should include the coefficient of intrassay (and interassay if appropriate) for the TGF-beta1 ELISA.

7. On page 5, the authors should define GSEA before using it as an abbreviation; and on page 15, they should add “...Gene Set Enrichment Analysis (GSEA) software.”

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests