Reviewer’s report

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

Version: 1 Date: 10 October 2011

Reviewer: Nikolaos G Frangogiannis

Reviewer’s report:

The study by Devaux and co-workers studies the predictive role of blood cell TGF-betaR1 (TbetaR1) expression and plasma TGF-beta in patients with acute myocardial infarction. The authors found that blood cell TbetaR1 was associated with LV dysfunction 4 months after STEMI; TbetaR1 added some value to the predictive potential of troponin T.

General comment:

This is an interesting study using a systems biology approach to identify biomarkers that may predict the development of adverse remodeling following infarction. Study of the circulating blood cell transcriptome is of interest as it provides information on inflammatory and reparative signals. Identification of TbetaR1 as a biomarker is novel. However, the following major concerns are raised:

Major comments:

1) The findings may reflect, for the most part, enhanced activation of TGF-beta/TbetaR1 in patients with larger infarcts, who are known to mount a more intense inflammatory response. Was the predictive value of TbetaR1 independent of the size of the infarct?

2) The animal study is weak and provides very limited new information:
   a. TGF-beta1 in the rat myocardium was studied at a single timepoint; because of the dynamic nature of the reparative response there are significant changes in TGF-beta levels as the infarct heals.
   b. Large amounts of latent TGF-beta is present in the myocardium; the levels assessed through ELISA in homogenized tissues do not reflect TGF-beta bioactivity in vivo.
   c. Immunohistochemical analysis of TbetaR1 expression does not identify the cells expressing the receptor. In any case, the receptor is present in all cells, but may be upregulated in reparative cells infiltrating the infarct.

The authors should recognize the many limitations of their animal study.

3) The findings would better reflect post-infarction remodeling had the authors excluded patients with a previous MI or underlying cardiomyopathy.

4) Relations between TbetaR1/TGF-beta and remodeling-associated parameters
should be studied and could provide important insights. These parameters could include chamber dimensions and the change in chamber dimensions/function during the remodeling period. Because the TGF-beta axis is also associated with cardiac hypertrophy relations with LV mass would be relevant.

5) The abstract needs to be revised to clarify important issues: a. “blood samples” does not accurately define the samples obtained; please indicate that mRNA extracted from whole blood cells was studied. b. Please define the patient population as individuals with STEMI who underwent primary PCI

Minor comments:
Please correct typos in reference 19, please update reference 27 (indicated as in press) and complete reference 43.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'