Reviewer’s report

Title: ACE2 Gene Expression is Up-regulated in the Human Failing Heart

Version: 1 Date: 17 November 2003

Reviewer: Chris Tikellis

Reviewer’s report:

General

This is a well conducted study with sound methodology. The authors have examined and determined ACE2 mRNA expression levels in human failing heart. The number of samples is adequate and the data are clearly presented. This manuscript is well written and the discussion addresses the data and some of the limitations of this study well. This manuscript adds to the concept, from other studies, that ACE2 is important for normal cardiac function and that it may have a role in tissue repair.

Discretionary Revisions (which the author can choose to ignore)

The scale on the y-axis (Figure 1) should be changed to a log scale.

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

As the authors note it is interesting that ACE2 mRNA was more highly expressed in non-failing ventricle than ACE. This is puzzling as most studies show that ACE mRNA is more highly expressed than ACE mRNA. It would be adequate if the authors could address this observation in a more detailed manner in the discussion.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The major limitation, as identified by the authors, is that only mRNA levels were examined. Obviously there may be some limitations as to the techniques that can be performed on the tissue (due to the amount starting tissue obtained). If possible the authors should attempt immunocytochemistry on at least some of the samples they have collected. Commercial antibodies for ACE and ACE2 are available and they would greatly improve the manuscript as they will assist in identifying the cell type(s) which express ACE and ACE2 in failing heart. This technique will also indicate whether ACE and ACE2 protein is upregulated in failing heart.

In the discussion the authors discuss that ACE2 cleaves AngII to A1-7 which has opposing effects to AngII. As they have shown upregulation in ACE2 mRNA in failing heart they should also follow through with this theory by measuring levels of A1-7 receptor mRNA which has been identified as Mas 1 (Santos et al 2003, Proc Natl Acad Sci U S A).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None