Reviewer's report

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

Version: 1 Date: 1 December 2003

Reviewer: Josef M Penninger

Reviewer's report:

General

Clark and colleagues report that ACE2 mRNA is upregulated in IDC and ICM patients using quantitative reverse PCR. Ace2 is a new ACE homologue and has generated enormous interest. In that sense the paper is very timely and important. The data that ACE2 is upregulated is also convincing.

As stated by the authors this study only makes a correlation using RNA and it would be of interest to see whether Ace2 protein is also upregulated using Western blots (since anti-ACE2 Abs have been published already). Moreover, since ACE is also upregulated to a similar extent one wonders whether this indeed alters tissue AngII level which would be the "real functional" correlate. I of course realize that the determination of AngII levels in tissues requires a significant amount of material.

The numbers of samples in each group are quite small. Could sex and/or age biases contribute to the alterations. Moreover, all patients had previous treatment - how can one exclude that these treatments have affected ACE2 mRNA expression?

Discretionary Revisions (which the author can choose to ignore)

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

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

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes
Declaration of competing interests:

We applied for an ACE2 patent to activate ACE2 in heart failure.