Reviewer's report

Title: Mutations in the 3'-untranslated region of GATA4 as molecular hotspots for congenital heart disease (CHD)

Version: 1 Date: 22 November 2006

Reviewer: Vidu Garg

Reviewer's report:

General
For my part, the authors have addressed all the major comments and concerns. I have attached some additional minor comments but I think the paper could be accepted for publication.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) Consider commenting on the significance of finding the c.+119A>T variation in an unaffected individual. The two possibilities of incomplete penetrance versus no causal association should be clearly stated.
2) The authors may consider expanding the discussion to comment more on the relevance of the haplotypes. According to the authors' response, the presence of multiple haplotypes may be the result of chromosomal duplications and/or rearrangements in a subpopulation of cardiomyocytes near the diseased tissue. This implies multiple levels of DNA damage (point mutations to chromosomal rearrangements) to the diseased cardiac tissue and calls into question if the genetic abnormalities are causal versus an artifact of DNA damage from tissue processing. The authors should comment upon this finding in the discussion.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential 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