Reviewer's report

Title: PITX2 mutations are not a common cause for transposition of the great arteries (dTGA)

Version: 1 Date: 28 September 2004

Reviewer: Diego Franco

Reviewer's report:

General

This paper describes the absence of significant mutations in the PITX2 gene in patients with transposition of the great arteries (TGA). TGA is a common congenital malformation that has been related to be a left/right developmental disorder. PITX2 is a gene involved in left/right signalling in the gastrulating embryo and also within the developing heart. Altered expression of PITX2 in the mouse has been correlated with other major congenital cardiac malformations such as double outlet right ventricle (DORV) and null mutants of Pitx2 display DORV and TGA. Thus, the results presented in this paper are very interesting.

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

The authors have analyzed the putative mutations in three out four PITX2 isoforms. They do report that they did not analyzed PITX2d since this isoform does not bind DNA. However, it is rather likely that mutations in this isoform can affect expression levels of other isoforms or the transcriptional potential of these. Thus, to confirm that no mutations of PITX2 are found in patients with TGA, sequencing of the four PITX2d isoform is fully required.

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

The title should be change, adding in the new version that only the coding sequence was analysed. As the authors report in their paper, the promoter and some intronic sequences were not analysed. Thus, it is formally possible that mutations in the intron/exon boundaries can affect PITX2 gene expression and certainly true that mutations in the promoter sequences can alter any of the PITX2 isoform expression and/or function.

Discretionary Revisions (which the author can choose to ignore)

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 importance in its field

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

None