Reviewer's report

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

Version: Date: 5 October 2004

Reviewer: Donna M Martin

Reviewer's report:

General

This is an important study in which the authors test for PITX2 mutations in patients with transposition of the great arteries. The hypothesis that PITX2 mutations may contribute to TGA is sound, and the authors carry out a detailed analysis of PITX2 for testing their hypothesis. The text is well written and the data are nicely and logically presented.

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

The authors claim to have analyzed all exons for PITX2 mutations, and provide a list of primers used for PCR in Table 1. They neglected to mention that their analysis omitted exon 1, the 5' most exon of human PITX2 that encodes for the amino termini of both the a and b isoforms of PITX2. Prior PITX2 mutational analyses by other investigators uniformly included this exon, and it is unclear why the authors chose to ignore it here. The authors neglected to comment on why they did not analyze exon 1 for mutations, and this is a major flaw in their paper. Without a detailed analysis of exon 1 in this patient population, it is not possible to draw definitive conclusions about the contribution of PITX2 to the etiology of TGA.

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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. There are inconsistencies in the paper with respect to italicizing and capitalizing gene or protein names, especially for Pitx2. Standard rules of genetic nomenclature such as at www.jax.org would help the authors be consistent about this.

2. Pitx2 null mice survive up to e15, not e14, as suggested on p. 4 (see refs. 17-20)

3. CHD in the abstract needs to be spelled out.

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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:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

None