Reviewer’s report

Title: ALDH1A2 (RALDH2) genetic variation in human congenital heart disease

Version: 2 Date: 26 August 2009

Reviewer: Judith Goodship

Reviewer’s report:

Minor essential revisions

Abstract:

TOF patients displayed other ALDH1A2 variants that map to exonic sequences such as the silent Ala151Ala polymorphism, previously associated to spina bifida. We determined that exon 4 rs16939660 does not impact splicing.

It is not immediately obvious to the reader of the abstract that ‘the silent Ala151Ala’ is rs16939660

It would be better to state
We determined that the SNP rs16939660, previously associated with spina bifida and observed in patients with TOF, does not affect splicing.

Abstract

In summary, our screen indicates that ALDH1A2 genetic variation is present in TOF patients, suggesting a possible causal role for this gene in rare cases of human CHD, but do not support the hypothesis that variation at the ALDH1A2 locus is a significant modifier of the risk for CHD in humans.

Should read ‘but does not support ….

Results section for tetralogy of Fallot mutations

A “T” to “C” transition (p.Ile157Thr) changed a non-polar isoleucine residue to a polar threonine and a “G” to “T” transversion changed a non-polar alanine to a polar serine (p.Ala151Ser) (Figures 1A and 1B).

Should change to
A c.T470C transition was identified which changes a non-polar isoleucine residue to a polar threonine (p.Ile157Thr) and a c.G451T transversion ….. i.e. use HGVS
nomenclature to describe the nucleotide change.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests