Reviewer's report

Title: Detecting 22q11.2 deletion in Chinese children with conotruncal heart defects and detection of single nucleotide polymorphisms in the haploid TBX1 locus in cases of 22q11.2 deletion

Version: 2 Date: 28 July 2011

Reviewer: Dana Crawford

Reviewer's report:

In this revised manuscript, Xu and colleagues have addressed many (not all) of the concerns voiced by Reviewers 1 and 2. Unfortunately, this revised manuscript is no clearer than the original submission. Below are suggestions meant to help the readers understand the data the authors are trying to describe.

1. Table 1. What is “N” in the column labeled “TBX1 Sequence”? That is, what does “normal” mean in this context?

2. Tables 3-5 can be consolidated into one table. Each row of the consolidated table could be the SNP (rs number). And, the different groups (various case and control groups) and their respective allele frequencies can be listed in different columns.

3. For statistical tests (such as those in Table 3), why isn’t Fisher’s exact being used for situations were counts are less than 5? The authors mention this test, but it’s not obvious that they used it for the appropriate situations. Perhaps the authors could put an asterisk next the p-values that were calculated using Fisher’s exact in these Tables.

4. For Table 3, there’s a typo for rs5748418 (comma instead decimal for chi-statistic). And, for Table 4, one of the p-values is 0.000. Why not use scientific notation for small p-values (2.0E-4)?

5. Tables 6 and 7 can be consolidated. And, a Fisher’s exact test must be performed for rs41298838.

6. The text along the x-axis for Figure 3 is still too small to read.

7. There are numerous spacing typos throughout the manuscript. It seems the authors used track-changes and accepted the changes without ensure the text is free of typos.

8. In the text, the authors state that the eight SNPs examined in their cohort were similar in frequency compared with the Han Chinese from HapMap. This statement was added in response to the Reviewer. However, the authors do not show these data. These data could be easily added to the consolidated table described in point #2. The authors could add a column with the HapMap data and do formal comparisons between HapMap and their cohort.

9. In the Discussion section on page 16, the authors state that nonsynonymous rs41298838 is a known mutation (but they fail to provide a reference) and that
“interestingly, no allele A was found in the locus of the haploid 22q11.2 in the del22q11 patients examined.” Was the A allele really expected in this small sample size? That is, given the frequency known for A, what are the chances of observing one copy of A among this cohort? This Reviewer doubts the absence of A is interesting given the small sample size.

10. In the final statement of the Discussion section, the authors overreach. That is, the statement “The differences suggest the involvement of these SNPs in the pathogenesis of CTDs.” The data presented in this manuscript do not support that statement. A form of this statement is also repeated in “Conclusion”. This should be revised.

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

**Quality of written English:** Not suitable for publication unless extensively edited

**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.