Author's response to reviews

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

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Author's response to reviews: see over
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Editor of
*BMC Medical Genetics*

Dear Editor,

We appreciate all of the enlightening and helpful comments from the reviewers. The manuscript has been revised accordingly, and the modified parts are highlighted in blue. We have also responded to each reviewer’s comments point-by-point as listed below.

Thank you very much for your consideration of our manuscript.

Best regards

Yours sincerely,

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Response to reviewer’s comments:

**Reviewer: Dana Crawford**

**Comments to the Author**

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

**Author’s response:**
Thank you for pointing this out. We have made changes accordingly in the revised manuscript. Please see Table 1.

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.

**Author’s response:**
Thank you very much for the suggestion. We have made changes accordingly in the revised manuscript. Please see Table 3.

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.

Author's response:
Thank you for the suggestions. We have added the asterisk and explanation in the revised manuscript. Please see the 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)?

Author’s response:
Thank you for pointing this out. We have made changes accordingly in the revised manuscript. Please see Table 3.

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

Author's response:
We have performed Fisher's exact test in Table 5 (Table 7 in last manuscript) and added HWE_P of rs5748417 and rs5748418 in Table 4 (Table 6 in last manuscript) in the revised manuscript. We did not consolidate Tables 4 (Table 6 in last manuscript) and 5, because the former shows genotype frequency, while the latter shows allelic frequency.

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

Author's response:
Thank you for pointing this out. We have made changes accordingly in the revised manuscript. Please see Figure 3.

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.

Author’s response:
We have corrected these errors in the revised manuscript. Thank you very much.

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.

Author's response:
We have added the allelic frequency in dbSNP into Table 3. Due to lack of the accurate number of the dbSNP cohort, we could not perform comparisons between dbSNP and our 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.

**Author's response:**
We have added the reference and deleted the sentence in the revised manuscript.

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.

**Author's response:**
We have made changes accordingly in the revised manuscript. Please see the final statement of the Discussion section and the “Conclusion”. Thank you very much.