Author’s response to reviews

Title: The susceptibility of FSHB -211G>T and FSHR G-29A, 919A>G, 2039A>G polymorphisms to men infertility: an association study and meta-analysis

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Answers to reviewer “Yiran Guo, Ph.D.”

Major issues:

Comments 1: Double check grammatical errors throughout the manuscript.

Responses 1: With the help of professional English editor, we have already made some corrections about the typographical and grammatical errors. And we have tried our best to improve our English.

Comments 2: Table 5 is very hard to read. Please only include the most important information and move others to supplementary material.
Responses 2: Table 5 showed that stratification analyses of genetic susceptibility of FSHR gene polymorphisms to male infertility, including the rs6165, rs6166, and rs1394205. It indicated that statistically significant results and text of heterogeneity and sensitivity analysis with different symbol as a mark. Although a large space occupied in MS, it is still important information that can not be moved.

Minor issues:

Comments 1: Title: why do the authors use G-211T instead of -211G>T?

Responses 1: Learning from the application of FSHR G-29A in other reported study, we used G-211T instead of -211G>T in FSHB gene. However, searching related literatures about FSHB, it has not been used yet, which could be corrected by -211G>T.

Comments 2: Were sample sizes reflected in forest plots (figure 2)?

Responses 2: I am sorry that sample sizes was not displayed in forest plots (Figure 2), which automatically generated by software STATA 12.0. And it was seen in the Table 5.

Answers to reviewer “Prabhakar Chalise”

Major comments

Comments 1: The language of the manuscript must be clear, correct and unambiguous to meet the standard of the journal. There are numerous errors and it is difficult to understand at some places about what the authors mean. The manuscript must be extensively edited. A few examples of errors are:

i. Page 3, line 5/6, "15% age-couples" should be "15% couples"

ii. Page 3, line 7/8, "causing" should be "caused"

iii. There should be space between word and parentheses throughout the manuscript. e.g. page 3, line 15 "syndrome(KS)", should be "syndrome (KS)"

iv. Page 3, line 56/57, the word "recessive" has been used incorrectly. Recessive is noun or adjective but not verb.

v. A few words appear together, page 4, line 31/32, "thepromoter" should be "the promoter"

Responses 1: We have already modified above typographical errors and grammatical errors in the text.
Comments 2: In page 8, line 17/18, authors state that chi-square test was used to assess the differences in baseline clinical characteristics between case and control groups and the results are presented in Table 1. All of the characteristics presented in the Table 1 are continuous variables. How did the authors use chi-square test? T-test or Wilcoxon rank sum test are the appropriate tests to assess the differences in continuous characteristics between the two groups. But, if the authors had categorized the variables before using chi-square test, they should mention the details in the manuscript.

Responses 2: It’s awfully sorry that ‘chi-square test’ was a clerical error. We used T-test to assess the differences in the distributions of clinical characteristics.

Comments 3: Explain the logistic regression model in more detail clarifying what was the response variable used, how the SNPs were coded etc. Based on the results presented in Table 2, it seems that infertility status was regressed with each SNP at a time with SNPs coded as three categories: AA (reference), AG and GG. Then, it is not clear to me why AG/GG (seems like sum of AG and GG) was used as separate covariate. Moreover, I don't see the rationale behind computing the frequencies of A allele and G allele separately and adding in the model as a covariate without any explanation in the text. Probably, this table can be shortened by including only the results for AA, AG and GG.

Responses 3: In the “Analysis of genetic data of Methods”, we have already explained the logistic regression model in more detail, which showed that “The difference of FSHR rs1394205, rs6165 and rs6166 polymorphism and FSHB rs10835638 polymorphism between the infertile and fertile groups was calculated using a logistic regression model, SNPs coded as three categories: wild-type homozygote (WW, reference), the heterozygous (WR) and rare allele homozygote (RR), which yielded a p value and odds ratio (OR) with the corresponding 95% confidence interval (CI), using SPSS for Windows 14.0 (SPSS, Inc, Chicago, Illinois)”. And at the same time, the table has been shortened, which the frequencies of AG/GG, A allele and G allele were deleted.

Minor comments:

Comments 1: Resolution of Figure 2 and 3 should be increased. It is hard to read the way it appears now.

Responses 1: According to the request, we have already increased the resolution of Figure 2 and 3.