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

Authors:

Qiuyue Wu (475626760@qq.com)
Jing Zhang (jingjasmine@126.com)
Peiran Zhu (980346785@qq.com)
Weijun Jiang (jiangweijun0524@163.com)
Shuaimei Liu (719305071@qq.com)
Mengxia Ni (949299259@qq.com)
Mingchao Zhang (zmchj99@163.com)
Weiwei Li (eeeeet@sina.com)
Yingxia Cui (cuiyingxia55@126.com)
Qing Zhou (863840726@qq.com)
xinyi Xia (xixynju@163.com)

Version: 2 Date: 01 Jun 2017

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For your convenience, we now provide our point-by-point responses to all the concerns as detailed below.

Answers to Editor:

Comments 1. The grammar and wording still needs some work. Please see detailed comments in the attached marked-up manuscript for some needed changes /comments. Note that not all needed changes might be denoted in the marked-up manuscript - please proofread carefully for clarity and grammar issues.
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. For the meta-analysis, remove SNPs with HWE < 0.05 from any analyses and remove the stratified analysis by HWE p < 0.05 and p > 0.05 (only present results for SNPs / studies with HWE p > 0.05).

Responses 2: According to your request, we have already removed it in the text of MS.

Comments 3. Only present meta-analysis results for Caucasian and Asian populations (remove "other" group).

Responses 3: In our meta-analysis, there was only one study collected from the Brazilian population, which indicated in “other” group. Maybe, we could use "Brazilian population" instead of "other group".

Comments 4. Only present results from recessive (RR vs WR+WW, 1 df test), dominant (RR + WR vs WW, 1 df test), additive (0, 1, 2 coding in terms of minor alleles, 1 df test) and co-dominant (WW vs WR vs RR, 2 df test) genetic models. Remove all other comparisons. For example, remove RR vs WW comparisons mentioned on page 9.

Responses 4: Thank you for your comprehensive analyses of our manuscript. According to your request, we have searched some literature carefully and found four genetic models, including the rare allele homozygote (RR) vs wild-type homozygote (WW), the heterozygous (WR) vs WW, RR vs WW+WR and RR+WR vs WW, exited in the meta-analysis. In our this study, significant differences were observed for the model RR vs. WW in SNPs rs6165 and rs6166(Table 5). Therefore, we think it is necessary to save it.

Comments 5. Present association of genotype with clinical features on table 1 as might go to "function". For example, is the genotype for a SNP associated with sperm concentration?

Responses 5: Exactly, we collected the clinical features to verify the potential effects of the polymorphisms associated with male fertility. But the failure in the LIS system, we only obtained the part of data from the patients, which were presented in Table 1. And using existing data, we found that the FSH and LH levels in the infertile patients were significantly higher than that in the fertile men (P <0.05). And fertile men had higher sperm concentration and sperm motility compared with the infertile patients.

However, we could not further evaluate the potential interactions between clinical reproductive parameters and gene SNPs, which might affect the male infertility.