Author's response to reviews

Title: Obesity-associated gene FTO rs9939609 polymorphism in relation to the risk of tuberculosis

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Author's response to reviews: see over
Dear editors and reviewers,

We thank the reviewers for their thorough review and constructive comments regarding our manuscript. We have carefully revised our manuscript according to the comments and suggestions. The following are the point-by-point responses to the reviewers’ questions.

**Reviewer: Adong Shen**

Discretionary Revisions

The author could do more discussion about the haplotype analysis in the Discussion section.

Reply: We have discussed the haplotype in the revised manuscript.

“In this study, a LD was found between rs9939609 and rs8050136. The haplotype rs9939609A-rs8050136C was related with an increased risk of tuberculosis. Previous studies have revealed that individuals who carry a particular SNP allele at one site often predictably carry specific alleles at other nearby sites. This correlation is known as LD and a particular combination of alleles along a chromosome is termed as the haplotype [47]. The relationship between causal mutations and the haplotypes have been regarded as a tool for genetic researches----first finding association to a haplotype, and then subsequently identifying the causal mutations that it carries [47].”

**Reviewer: Thorsten Thye**

1. **The authors did not explain sufficiently why SNP rs9939609 deviates substantially from Hardy Weinberg in the control group. The genotypes of this SNP should be analysed with a different platform to validate the previous results.**

Reply:

1) In fact, either the SNP rs9939609 or the SNP rs8050136 didn’t deviate from the Hardy-Weinberg equilibrium in the control group. Results of the H-W test are listed as the following:

rs9939609:

- TT 1250(80.91%)
- AT 275(17.86%)
- AA 19(1.23%)

HWE test: $\chi^2 = 0.768, P=0.381$
rs8050136:
CC 1250(80.91)
AC 282(18.31)
AA 12(0.78)
HWE test: $\chi^2 = 0.812$, $P = 0.368$

2) The genotypes of these two SNP validated by using gene sequence technique.
“We randomly selected samples with different genotypes for gene sequencing. The consistent rate was 100%.”

2. In addition, association analysis should be performed with people with no alcohol consumption to verify whether alcohol intake have an effect on the statistical results.
Reply: We further performed a stratification analysis by considering alcohol drinking history. Data were listed in the Table 5.
“Stratified analysis revealed that the effect of AA genotype of rs9939609 on tuberculosis was more evident among men, ever smokers and alcohol drinkers (Table 4 and 5). However, the heterogeneity wasn’t significant across the strata. A significant association between the polymorphisms of rs8050136 and tuberculosis was only observed among never drinkers. Compared with the wild type CC, the OR(95% CI) was 0.22(0.06-0.83) for rs8050136 AA genotype. However, it was not significant after the Bonferroni multiple comparison correction.”