Author’s response to reviews

Title: New variant identified in major susceptibility locus to Tuberculosis on chromosomal region 8q12-q13 in Moroccan population: a case control study

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Authors Response to Reviewers’ Comments

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The authors would like to thank the editor and the reviewers for their precious time and invaluable comments. We have carefully addressed all the comments. The corresponding changes and refinements made in the revised paper are summarized in our response below.

Reviewer #1: Pr. Raghupathy Anchala

Comment 1: Since most of the results are based on interpreting odds ratios. The methods section must include details on below mentioned essential revisions that are required:

1. Explain sample size calculations and power of study.

Our response:
The sample size used in our study is sufficient to do a genetic association according to the reference allele frequencies of each SNPs investigated using 95% as confidence interval (with 1.96 as level of confidence) and 5% of estimated error.

Comment 2: Controls should be twice the cases (preferably 1:4 or a minimum of 1:2). Every case should be matched with one hospital and one community control. Controls means absence of outcome. If we have defined cases abased on their sputum AFB status and or culture positive…then controls should be absent AFB and absent culture status. Healthy controls should be people without PTB. Please describe healthy control and justification.

Our response:

We have rewritten this paragraph to provide more clarification and justification.

Section: Methods, page 4, line 11-16.

“Healthy controls group consisted of healthy donors with no signs, symptoms or history of previous tuberculosis. They were tuberculin skin negative and remained in this immunological status during the two years after recruitment in a posterior telephonic check-contact”. The recruitment was done from the Regional Centers of Blood Transfusion (RCBT) of five different regions of Morocco (Oujda, Fez, Tangier, Rabat, and Marrakech)”.

Reviewer #2: Dr. Rika Yuliwulandari

Comment 1: The research is very interesting and the idea is very original. The authors reported for the first time the association between rs1050504, located in NSMAF gene, and PTB risk in Moroccan population. The discussion provided was very interesting to read and well-constructed with evidences. Below are my questions and suggestions for the authors:

I would like to know whether there is any previous study that discussed about the association of 3 selected SNPs with TB or other infectious diseases.

Our response:

We appreciate the positive feedback from the reviewer. In response to the reviewer's question, to the best of our knowledge, none of the three selected SNP were described in the context of tuberculosis or other infectious diseases.

Comment 2: In study design subsection, it would be nice for the readers if the author could include "HC" in the list of abbreviations.

Our response:

We followed the reviewer’s suggestion. The term “HC is included in the list of abbreviations.
Comment 3: In NSMAF genotyping subsection, how did you categorize the impaired samples?

Our response:

In the presence of samples did not generate fluorescence signals (FAM/VIC). We retest them to verify the result. If, no fluorescence signals are generated, this result is rejected and has not been accounted.

Comment 4: In the results section, haplotype analysis subsection, would you please confirm which SNP is correct, rs3808607 or rs380860?

Our response:

We have corrected the error in the revised version. The correct SNP is rs3808607.