Author's response to reviews

Title: A single nucleotide polymorphism in TRAF1/C5 locus is associated with rheumatoid arthritis in a Han Chinese population

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Author's response to reviews: see over
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Scott Edmunds, PhD
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Dear Dr. Edmunds,

We would like to thank you and the reviewers for the constructive comments regarding our manuscript entitled “A single nucleotide polymorphism at the TRAF1/C5 locus is associated with rheumatoid arthritis in a Han Chinese population” (MS: 169091871343735). We have addressed the comments of reviewer #1 point by point below, which we feel have significantly improved the manuscript.

Reviewer #1

Reviewer’s report:

The authors have improved their analysis of TRAF1/C5 SNP rs3761847 in RA. However, in addressing one earlier query, namely the direction of association at rs3761847 in their data compared to that in Caucasian, they have opened some important questions. Before suggesting some further work to further investigate the differing direction of association, I do note that identifying the differing direction of association should have been done by the authors in the original submission.

MAJOR

SNP rs3761847 was chosen based on association in one previous GWAS. However, other SNPs in TRAF1/C5 have been associated with RA in other populations, what is the linkage disequilibrium relationship between these and rs3761847? It is likely that the differing direction of association between Chinese and Caucasian could relate to differing frequency of risk haplotype. This would be clarified by typing either some tag SNPs or other associated SNPs. (To do further typing, I suggest using Taqman rather than the more laborious SnapShot).

Response: We completely agree with the reviewer’s point that rs3761847 may not be the causal genetic variant at TRAF1/C5 locus because the associations of this SNP with RA in Chinese and Caucasian populations are in opposite directions. It is more ideal to genotype more SNPs to identify the true causal genetic variant(s) at this locus as the reviewer suggested. However, this is out of the scope of this study; seeing as in this study, our aim was to examine if
TRAF1/C5 locus is associated with RA in the Chinese population studied. We concluded that the genetic variant (rs3761847) at TRAF1/C5 locus was significantly associated with RA in the Chinese population studied. We would like to do more experiments to identify the causal genetic variant(s) at this locus responsible for RA in future studies.

MINOR
1 Please put clinical data in Table 1.

Response: We have put more clinical data in Table 1.

2 Update RA gene list with new Stahl data (Nature Genetics May).

Response: We have updated RA gene list with new Stahl data (Nat Genet;42:508-14.) as the reviewer’s suggestion.

3 The final paragraph of the Discussion would be better in the Introduction.

Response: We have moved and modified the last paragraph of the Discussion to the Introduction of the manuscript as the reviewer’s suggestion.

We wish to again thank you and the reviewers for the helpful comments, and hope that our revisions have appropriately addressed the reviewer’s concerns and made the manuscript suitable for publication in the journal.

Sincerely,

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