Reviewer's report

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

Version: 3 Date: 27 April 2010

Reviewer: Rogelio J Palomino-Morales

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In this work Zhu et al. examine the possible role of the rs3761847 SNP in TRAF1/C5 locus and rs2476601 SNP in PTPN22 gene in the genetic susceptibility to RA in a Han Chinese cohort. This is the first time that an association of the rs3761847 SNP in TRAF1/C5 locus with RA has been reported in this population. The study is of relevance in the field, the technology is adequate, and the results are presented in a concise and effective way. Nevertheless there are some points that, in my opinion, must to be addressed:

Major comments:

1. The rs2476601 SNP in PTPN22 has been reported to be not polymorphic in Asian populations. Moreover, several authors reported a lack of association with rs3761847 SNP in Asian and stated others polymorphisms in this locus with a most important role. What criteria did the authors take to select the polymorphisms under study? A more detailed SNP selection must be present in the manuscript.

2. As comment above, the role of rs3761847 SNP in susceptibility to RA in Asian is not clear since this SNP is not associated in Korean and in Japanese the susceptibility allele seem to be the opposite. This issue should be discussed in the manuscript.

3. Since the importance of these loci in RA is well known and the relevance of this work is the new genetic background, more detailed Clinical information of patients should be included in order to see whether these data could be extrapolated to other populations and cohorts. This information is especially important since rs3761847 polymorphism has been reported to be associated with severity of RA.

4. Although the sample size is enough for the case control study, authors do not have power enough in the anti-CCP and RF stratification study to fully exclude differences: “Our results further confirmed that rs3761847 in TRAF1/C5 was associated with RA in Han Chinese Asians, and this association does not depend on the concentrations of anti-CCP antibodies nor RF”. The lack of power in the stratification should be addressed.

5. PTPN22, TRAF1 and C5 are very important genes in autoimmunity. Therefore, a concise explanation of the role and whether the polymorphism studied could
change its function should be important.

Minor comments:
1. Typo error in page 8 second paragraph: “TSTAT4” should be STAT4.
2. Gene names must to be in italic.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.