Author’s response to reviews

Title: Correlation between Interleukin-17 Gene Polymorphism and Osteoarthritis Susceptibility in Han Chinese Population

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Reviewer reports:

Ingrid Meulenbelt (Reviewer 1):

This is a (old fashioned) genetic association study with a candidate gene IL17. IL17 may be hypothesized as being a candidate gene conferring risk to OA but none of the current comprehensive and powerful genetic association studies has highlighted this gene as potential candidate gene for OA. It must checked and addressed whether there is any signal for IL17 in any of the publicly available GWAs studies. The numbers of individuals is adequate the number of tests performed largely exceeds what is realistic with the dataset.

Response: I also check the GWAS database, can not find the reports about these two SNPs associated with osteoarthritis. Although there is no study about association between IL-17A rs2275913 and IL-17F rs763780 polymorphisms with osteoarthritis in GWAS study, the IL17
role in the pathogenesis of rheumatoid arthritis has already published in lots of documents, such as: Role of IL-17 in the Pathogenesis of Rheumatoid Arthritis, Curr Rheumatol Rep. 2009 Oct; 11(5): 365–370.


These documents are our hypothesis basis to start this current study.

For the second question, China has a 1.4 billion population, so it is not difficult to get 500 subjects to use in the current study.

Major comments:

The paper should be extensively shortened, just presenting a dose response association analyses with the IL17 SNPs. The sex stratification could stay but there is no power to perform haplotype analyses.

Response: thanks for your advice, I have deleted haplotype analysis.

Moreover, presenting the IL17 levels raises the question whether the SNP is associated to the IL17 levels that could add validity to the presented association.

Response: I have added serum concentration of IL-17A and F according to your suggestion, the detailed data was shown in new table 4 in the revised manuscript, and detailed serum concentration was grouped in different genotypes.

It must checked and addressed whether there is any signal for IL17 in any of the publicly available GWAs studies.

Response: thanks, I have checked GWAS database “GWAS Catalog”, and find no relative study about IL17 with OA, I have added this description in the “introduction’ part of the revised manuscript.
How and based on what criteria are the SNPs selected?

Response: actually, we have test six SNPs in our study, these six SNPs have been widely reported with several auto-immune disease, especially in Chinese population, that is criteria we select the SNPs. However, only these two get positive results with p value less than 0.05. I have added this description into the “introduction’’ part in the revised manuscript, and highlighted them.

Florin Burada (Reviewer 2): The manuscript „Correlation between Interleukin-17 Gene Polymorphism and Osteoarthritis Susceptibility in Han Chinese Population" examines the association of two IL-17 gene SNPs in a Chinese population.

Abstract. Purpose. The second phrase should be rewritten and the investigated SNPs should be included. Also, the same corrections should be done in the last sentence of Introduction.

Response: I have corrected them in the revised manuscript and highlight them.

Materials and Methods. Please include dominant and recessive models. Please specify which test was used for linkage disequilibrium. The results should be presented.

Response : based on the other reviewer’s advice, there is no enough power to conduct haplotype analysis, I have deleted linkage disequilibrium and haplotype in the revised manuscript.

Results. The phrases that include the frequency of genotypes should be removed (page 6 - rows 2-5, 22-30). The data is already shown in the Table 2. The relationship between IL-17 genotypes and serum levels should be presented.
Response: We have deleted the frequency of genotypes (page 6 - rows 2-5, 22-30) based on your suggestion. The relationship between IL-12 genotype and serum levels was shown in the new table 4.

Discussion. A subsection about other studies that investigated IL-17 SNPs should be included.

Response: I have added other study of IL-17 SNPs into the first paragraph in the discussion in the revised manuscript.

The entire manuscript should benefit from a careful evaluation for spelling and grammar checkers (e.g. a single format for investigated gene should be used - IL-17 or IL17).

Response: I have change IL17 to IL-17 through the whole manuscript.