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): The rational to study IL17 assumes that OA is an autoimmune disease which it is not. Furthermore, the results do not match the conclusions that are drawn. Additional revisions are necessary.

Please add page numbers in addition to the line counts in this way it is very difficult for me to indicate the section/sentence I am referring to. Better use consecutive line numbers throughout the manuscript.

Response: thanks, I have added line number through the whole manuscript according to your suggestion.

Osteoarthritis per definition is not an autoimmune disease. This suggestion should be removed from introduction and first paragraph of the discussion. Please address here how the immune system could come into play in OA. Is IL17 expressed in bone, cartilage and/or synovial tissues?
Response: thanks for correcting my wrong concept, and I have deleted wrong description from introduction and first paragraph of the discussion.

I also added the role of immune system and OL17 in OA in the revised introduction part. Based on literature, IL17 is expressed in synovial tissues. I also add five new reference to confirm the IL17 distribution in synovial tissues and role in OA in the revised manuscript.

I highlight the correction content in the revised manuscript.

Please remove the sentence in the discussion indicating that IL-17 serum level may be greatly related to the risk of knee OA. Since the SNPs do not affect the IL-17 serum levels the observed association of increased IL-17 serum levels among OA patients could only mean that IL-17 serum could be a marker of ongoing OA disease process. Per definition the results of a cross sectional study design of a level with a disease can not provide information on underlying the disease process.

Response: thanks, I have deleted this description in the revised manuscript.

In the discussion please remove the section "CD4+ Th17 cells…. Until …modulate the susceptibility to OA". It is unclear how the statement refers to any of the results in the paper other than that the 2 SNPs that were investigated do not affect the IL-17 levels in serum and as such it could not explain the association observed with the SNPs and OA.

Response: thanks for your advice, I have removed this section in the revised manuscript.

The results of the serum IL-17 association among OA patients does not justify the statement (final sentence discussion) that serum IL-17 may facilitate in predicting the risk of developing OA. The association of serum IL-17 with OA could just be a marker of ongoing OA disease process. Actually, the fact that the SNPs do not show association to the level indicates that the SNP does not affect the serum IL-17 levels. Instead the authors need to hypothesize in which way the IL-17 SNPs could contribute to OA if not via levels?

Response: thanks for your advice, just like the limitations which I mentioned in the discussion part, the serum IL17 is an inflammatory index of systemic immune reflection, and the real IL17 which plays an important role in OA is the one which expressed in the knee articular cavity and
synovial tissues. So we hypothesize that it is possible that SNPs of IL-17 might cause alteration of the IL-17 concentration in knee joint microenvironment, including knee articular cavity and synovial tissues, further influence the risk of OA development.

I have highlighted them in the revised manuscript.

The option of a false positive result should be added to the discussion

Response: thanks, but I am not sure that I get your point. You mean the statistical method could have bias to produce the false positive result? If it is, I have addressed this limitation in the revised manuscript.

The added content is “More importantly, population stratification—allele frequency differences between cases and controls due to systematic ancestry differences—can cause spurious associations in disease studies, and possible false positive results [35]. Therefore, more detailed statistical analysis is need to done to make results more accurately.”.

Florin Burada (Reviewer 2): Abstract.Methods. The haplotype analysis should be excluded

A reference for the sentence "By a pilot study with small population, IL-17A rs2275913 and IL-17F rs763780 shows more potential risk factor in OA in our recruited subjects." should be included

Response: thanks, I have corrected them in the revised manuscript based on your suggestion.