Reviewer's report

Title: Meta-analysis of tumor necrosis factor alpha -308 polymorphism and knee osteoarthritis risk

Version: 2  Date: 16 July 2014

Reviewer: John Loughlin

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Major Compulsory Revisions
1. Perform an allelic meta-analysis - A allele versus G allele.
2. Clarify to the reader how the ORs reported here relate to the ORs in the original seven manuscripts from which this data has been extracted. Are they comparable.
3. Expand on why you chose to do an AA versus GG comparison and a GA versus GG comparison. What were the genetic models being tested here?
4. The controls in the Moos et al study were not in HWE but were included in the analyses. Why?
5. The Han et al study is an outlier, as the authors note; 34 of the cases from this study were AA whereas none of the controls had this genotype. This is clearly a concern. The authors need to provide the reader with detailed justification for the inclusion of this study.
6. Why are some of the studies excluded in some of the comparisons (i.e. 3A) and why is the reader not made aware of this in the text?

Minor Essential Revisions
1. Provide much more detail in the legends to the tables and figures, thus making them easier to understand.
2. Figure 1 is redundant, as it adds nothing to what is already written in the text. It should be removed.
3. Provide the reader with more details about what Fig 4 is actually showing.
4. The data in Table 3 should also be presented as a figure.
5. There have been several relatively recent OA GWAS reports in Asians and Europeans. The authors comment on an Asian one. Have any of the European ones highlighted evidence of association of the region harbouring the TNF gene with OA? Please comment.
6. Check that all tables are accurate. For example, in Table 1 the number of cases in the Sezgin study is listed as 146, but when broken down into their genotype groups the number is 151 (121, 26 and 4).

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.

**Declaration of competing interests:**

I declare that I have no competing interests