Reviewer's report

Title: Lack of association between the chemokine receptor 5 polymorphism CCR5delta32 in rheumatoid arthritis and juvenile idiopathic arthritis

Version: 2 Date: 27 April 2007
Reviewer: tony merriman

Reviewer's report:

General

I have examined the responses of the authors to my (and the 2nd reviewers) comments. I am satisfied that my comments have been addressed (although there are still cases where genetic nomenclature is not italicized or non-italicised as appropriate, and there is still further proof-reading necessary eg 2nd sentence of the abstract). In my opinion the authors have also satisfactorily addressed the comments of the other reviewer. Regarding possible reasons why replication of CCR5?32 is inconsistent, a further reason the authors could cite is gene-gene interaction – the effect of CCR5?32 could depend on a biologically interacting molecule that could also exhibit a genetic effect on RA. See Moore “The ubiquitous nature of epistasis in determining susceptibility to common human diseases” Human Heredity 2003;56:73-82.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

I do have a few other comments, the most significant being the appropriateness of the final conclusion.

1. The concluding sentence should read “In conclusion, whether the CCR5 [non-italicised] gene is involved in RA or JIA susceptibility remains unclear, however, our study suggests that if a protective effect is exercised by CCR5?32, it is minor and less than predicted from the meta-analysis of previous publications [17].” This suggestion is to reflect that, because of power, even the authors largest individual study to date is still not the definitive ‘answer’ to the question of whether or not CCR5?32 is associated with RA and, if so, what the effect size is. This will be addressed by even larger studies in the future.

2. Add P values to the text added to the first paragraph of Results and Discussion that describes the new meta-analysis.

3. The modified sentence describing the LD between CCR5?32 and -1835T would be more accurate if it read: “No strong linkage disequilibrium between CCR5?32 and -1835T was evidence, which could suggest that these two alleles are present on a haplotype containing a true etiological variant of CCR5 in RA or JIA pathogenesis that is still unidentified.”

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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