Reviewer's report

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

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Reviewer: tony merriman

Reviewer's report:

General

This paper describes testing the CCR5d32 polymorphism for association with RA and JIA in Norwegian cohorts. No evidence for association was found between the variant and either disorder.

In the case of JIA, the previous evidence for association of CCR5d32 with disease, was equivocal, to say the least, and the lack of evidence of association with JIA in the Norwegian cohort adds to the literature.

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

In the case of RA, there was more existing evidence supporting a role for CCR5d32 in disease aetiology. Whilst I found the study to be well carried out and presented, I do not agree with the primary conclusion of the manuscript (see Abstract): “Our data do not support an association between the CCR5d32 polymorphism and RA.” There have been five studies previously published testing for association between CCR5d32 and RA in Caucasian, which were combined in a meta-analysis by Prahalad last year. The meta-analysis provided reasonable evidence for association (OR = 0.65, P<0.0001) in a total of 1,790 cases and 2,717 controls. Here, Lindner and co-authors test a significantly smaller cohort (853 patients and 658 controls) of reduced power (63% using the Prahalad OR estimate) and do not find evidence for association. I felt the authors did a good job in considering possible reasons why they did not detect association in the main text, but this is not reflected in the Conclusion. To rectify this I suggest that a revised meta-analysis is presented formally in the Results (rather than mentioned as part of the Discussion) and the primary conclusion modified along the lines of: “We did not detect significant association of CCR5d32 with RA in our Norwegian cohort, although by meta-analysis there is still evidence for a role for CCR5d32 in RA.” It is evident that the authors do understand the power issues inherent in replicating weak genetic associations, thus the individual result from the moderately-powered Norwegian cohort should not be over-interpreted.

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

Other comments:

1. Gene and polymorphism names should be italicized when mention in isolation eg “Taken together with the published studies of RA and CCR5d32, our results…” should be in italics, whereas “Our data do not support an association between the CCR5d32 polymorphism…” should not be in italics. This convention should be adhered to throughout the manuscript.

2. Pg 5, the http://calculators.stat.ucla.edu/powercalc URL did not work for me.

3. Pg 5, para 2. Why was the Zapico et al. OR estimate of 0.56 chosen for the power a priori power calculation? The power calculation for RA should be based on the meta-analysis estimate presented by Prahalad (0.65) (a power calculation based on this estimate was presented in the Discussion – this should be in the Methods).

4. A formal meta-analysis of association of CCR5d32 in JIA should also be presented in the paper.

5. pg 8, para 1, last sentence. The point the authors are trying to make here is unclear to me.
6. There are a number of typographical and grammatical errors in the manuscript that need correcting.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory 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.