Reviewer’s report

Title: The presence of KIR2DS4 full-length gene decreases a chance of rheumatoid arthritis patients to respond to methotrexate treatment

Version: 2  
Date: 16 February 2014

Reviewer: Tony Bjourson

Reviewer’s report:

1. Is the question posed by the authors well defined?

The paper is interesting and timely – markers of response to therapy are urgently required if the objectives of stratified medicine are to be realised. There is a general unmet clinical need for reliable markers that have the ability to identify rheumatoid arthritis (RA) patients that are likely to respond or not respond to the diversity of therapeutic drugs available. Methotrexate is the most widely used disease-modifying antirheumatic drug (DMARD) for the treatment of RA.

Discretionary revision

It has been reported that there is a lack of response to methotrexate in 30-40% of treated patients and that there is a scarcity of clinically reliable markers of response to methotrexate. The authors clearly state that they aim to examine the association of carriership of specific KIR genes with response to methotrexate. However, if this paper aims to address this unmet clinical they should state this in the introduction section and state how their work meets this need in the conclusion section.

2. Are the methods appropriate and well described?

The methods seem to be reliable although I cannot authoritatively comment on the appropriateness of the statistical analyses undertaken.

3. Are the data sound?

The data appears to be sound - in this report the response and non-response to methotrexate was approximately 57.3% and 42.6% respectively, in general agreement with previous studies, this could also be stated.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes – and ethical approval for the study has been clarified.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

Discretionary revision

6. Are limitations of the work clearly stated?
No limitations of the work were addressed (Discretionary Revision)

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes, the authors have quoted the appropriate literature. Discretionary revision - state the percentage of rheumatoid arthritis patients that are methotrexate responders and non-responders generally and how that compares with their findings.

8. Do the title and abstract accurately convey what has been found?
Yes, an appropriate title that adequately reflects the aims of the research and the content of the paper.

Minor Essential Revisions

9. Is the writing acceptable?
Yes - the writing is generally good. There are a number of grammatical errors throughout that should be corrected prior to publication.

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: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

The reviewer was cited as a co-inventor on a filed patent application (US2010323358) for “the use of KIR genes for predicting response to anti-TNF-a therapy”. The reviewer has undertaken a commercial project relating to biomarkers of response to anti-TNF therapy with Randox Laboratories Ltd.