Reviewer's report

**Title:** Personalized medicine in psoriasis: developing a genomic classifier to predict response to Alefacept

**Version:** 4  **Date:** 14 August 2009

**Reviewer:** Claes Enk

**Reviewer's report:**

This work attempts to define genomic classifier genes to predict responsiveness to alephacept by analysis of peripheral leucocytes in psoriasis patients. Alephacept, being highly effective but only in a minority of patients, is indeed an ideal candidate for such an analysis as described in the introduction.

Major concerns

1. The analysis is based on tissue samples collected in connection with previously published work. This work dealt with immune mechanisms of alephacept, and the division between responders and non-responders was based on histological response, i.e. histological normalization of the individual psoriasis lesions. In clinical settings responders versus non-responders are usually defined by clinical scoring such as PASI. For genomic classifiers to have clinical impact, they should be able to predict which patients will respond to treatment and who will not. The authors appear to acknowledge the preliminary nature of the present work when they mention the need for "a prospective clinical trial". I would like the authors to elaborate on this issue and suggest that they add "histological" to the title: “Personalized medicine in psoriasis: developing a genomic classifier to predict histological response to Alephacept”

2. Confirmative PCR was not performed due to lack of RNA. This is a serious flaw that limits the validity of the findings as pointed out by the authors themselves in the cover letter. Would it be possible perform PCR on pooled samples?

3. Lacking confirmative PCR analyses, I suggest that a microarray analysis be carried out on an unrelated group of samples as a negative control to demonstrate the specificity of the genomic classifier for psoriasis

Minor concerns

4. Data on only 7 of the 10 non-responders are presented – what happened to the rest?

5. The abstract could be more detailed and specific on the findings

6. Page 7, line 9: At least in terms of expenses, treating a non-responder in vain appears more costly than abstaining from treating a potential responder

**Level of interest:** An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

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'