Reviewer's report

Title: HLA class II allele polymorphism may influence susceptibility to adult dermatomyositis and polymyositis in a Han Chinese population

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Reviewer: Brian Tait

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This is a well presented manuscript which is easy to read and comprehend. However many of the HLA associations described are weak and this is partly the result of relatively small numbers in some of the groups, for example polymyositis, which only consists of a patient cohort of 20. The numbers are my main concern and they need to be expanded to give confidence in the findings. There are difficulties with this as idiopathic inflammatory myopathies are not conditions with a high incidence. However multicentre studies have been of benefit in the past when required in the study of these conditions.

I include some specific comments in the form of suggested revisions which should be considered.

1. The use of the type 1 correction error is very conservative and has in fact rendered all the associations described statistically insignificant. So strictly speaking using the criteria outlined this manuscript has demonstrated no statistically significant HLA associations with PM or DM. However an argument could be put that since PM and DM have demonstrated HLA associations in other studies there is an a priori reason for looking at HLA alleles in PM and DM particularly alleles such as DRB1*07 which has been implicated in other studies.

2. The functional unit of the DQA1 and DQB1 genes is the dimeric DQ molecule. When analysing the effect of DQA and DQB alleles on disease susceptibility the combination of genes should also be considered in both cis and trans confirmation. This data should be included in table 2. Consideration should be given to just including alleles at all loci showing statistically significant differences between the groups studied to shorten the size of the table and focus on the relevant alleles.

3. On page 7 it is stated that DQB1*0303 is lower in frequency in ILD than controls. In fact the frequency is similarly low in the PM group but is not significant due to the small number. However this can impact on the number in the ILD group since they are drawn from both the PM and DM groups. It might be preferable to compare frequencies of alleles in those with ILD with patients without ILD to confirm this finding.

4. Another example of a statistical quirk is the report that DRB1*4 and DRB1*12 are associated with ILD. The frequency of these two alleles in ILD are really no higher in this group than the frequencies found in the other groups (especially for DR12) except for the control group which has the lowest frequency. This leaves
open the possibility that these alleles (particularly DR12) are primarily associated with PM and DM.

5. The statement is made on page 9 that “HLA-DQA1*0301 and HLA-DRB1*03 may provide protection from PM and DM respectively” This is misleading as in table 2 DRB1*03 is shown as being protective for the development of DM while DQA1*0301 is shown as being protective for the combined PM/DM group yet the frequency in this group is higher than that seen in the PM group alone. Again is this just a reflection of small numbers in the PM group or a mistake in the table?

6. I would suggest that the combined PM/DM group is deleted from the tables as PM and DM appear to have different genetic profiles and it again creates doubt due to the small numbers in the PM group. For example in table 3 the DR7 haplotype is shown to be increased in the DM group yet the frequency in the combined group is approximately the same as the DM group. Again this is due to the small contribution of the PM group and the increase in the PM/DM ILD group may be just a reflection of the increased frequency in the DM group.

7. DQA1*0103 is mentioned in the conclusions as being “likely” associated with an increased risk of DM and PM. This allele is not shown in table 2 as being associated and no mention is made of this is made in the result section. DRB1*03 is also stated as being associated with lung complications in DM but again this is not shown in table 2 nor is it mentioned in the result section.

Minor Points

1. Page 5 – SSA and SSB require definition n the text before the acronyms are used.

2. The word haplotype should only be used when the cis configuration of a group of alleles at neighbouring loci has been demonstrated. What is actually shown in table 3 are co-occurring alleles which are designated haplotypes based on population studies. They should be referred to as putative haplotypes particularly in disease studies where linkage disequilibrium seen in the normal population can be perturbed.

3. The paper from Han et al Chinese Journal of Microbiology and Immunology 23(3) p225;2003 which reported on DRB1 alleles in PM/DM in Northern Chinese should be recognized and quoted in the manuscript.

4. The “R” has been left out of DRB1 twice on page 7.

5. Heading to table 1- “e” has been left out of the word “features” in heading

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

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