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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Major Compulsory Revisions

1. The fact that the frequencies of HLA-DRB1*04, -DRB1*12 and –DQB1*0303 in ILD show differences with controls but not patients who do not develop ILD is of concern. ILD is a complication of PM/DM. The primary level of genetic selection in these patients therefore is for genes which confer susceptibility to IIM. Within the patients who develop IIM there is further genetic selection for genes which confer susceptibility or resistance to ILD. It stands to reason therefore that if there are HLA genes which confer ILD susceptibility or protection these should be identified by comparing ILD patients with non ILD patients. The fact that differences cannot be seen when performing this analysis but can be observed when comparing with controls suggests this is a statistical quirk of the small numbers in some categories. This point should at least be acknowledged in the manuscript.

2. The second last para of page 9 requires a change in the wording. It refers to DRB1*07 being a risk factor for DM while the same allele on another haplotype is a protective allele in Caucasians and African Americans suggesting it is a shared susceptibility allele across ethnic groups. It is not a shared susceptibility allele but rather shows opposing effects in different ethnic groups. The possible explanation for this effect needs to be discussed in the MS.

3. I still have concerns re the combined PM/DM group. It is claimed in the MS that PM and DM are distinct diseases with different genetic backgrounds yet the combined analysis is included on the basis that other groups have presented the data this way. None of the studied alleles were significantly increased or decreased in this group in table 2. In table 1 a comparison is made between PM and DM with respect to the occurrence of ILD There is a significant difference between the groups yet they are combined into a single group with an expected frequency somewhere in between PM and DM. This provides no additional information, and in fact is not supported by any rationale. I would suggest that the PM/DM group be deleted with an explanation included in the MS.

Discretionary Revisions

4. The functional unit of the DQA1 and DQB1 alleles is the DQ dimeric molecule. The authors do not wish to analyse the data with respect to DQA1,DQB1 combinations on the basis that their data suggests that DQA1 is involved in PM/DM susceptibility, while DQB1 is involved with ILD. Despite this analysing for
combinations of these DQA1 and DQB1 alleles may enhance some of the associations and is more relevant to function.

5. The comment is made on page 10 that DM is likely to be induced by a humoral response while PM is more likely cell mediated. This statement needs to be discussed in the context of the greater frequency of autoantibodies in the PM group.

Minor Essential Revisions
6. In the conclusion section The “D” has been left out of the DRB1 designation.
7. To be consistent the word “putative” should be inserted in the heading to table 3.

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 have no competing interests