Reviewer’s report

Title: Association study of the HLA-DRB1 locus reveals the first evidence for the association of HLA-DRB1*15 and DRB1*09 with leprosy and the impact of DRB1*09 on the onset of disease in Chinese population

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Reviewer: Milton O Moraes

Reviewer’s report:

The paper entitled “Association study of the HLA-DRB1 locus reveals the first evidence for the association of HLA-DRB1*15 and DRB1*09 with leprosy and the impact of DRB1*09 on the onset of disease in Chinese population” by Zhang et al describes the frequency of HLA-DRB1 alleles in leprosy patients and healthy volunteers also investigating association according to age of onset. The paper is interesting, but some issues need clarification.

Patients and controls: general characteristics of patients and controls should be described in detail. Authors should consider the inclusion of a table with total counts and frequency of each sex, ethnicity, etc. Clinical forms should be listed according to the Ridley-Jopling classification, and not only WHO (MB vs. PB). The age of patients and controls should be represented at least as mean and standard deviation for both groups (also the numbers for patients and controls after stratification for age in each class needs to be provided). In addition, it is not clear if patients and controls were selected from the same geographic area, although authors claim that “control samples, collected from the Shandong Blood Center, were matched to the patients regarding to ethnic origin, age and the male/female ratio”. A better description of patients and controls is crucial to define if patients and controls were adequate for this kind of analysis.

Statistical Analysis: results of the age dependent effect should be interpreted carefully. The same control group was used in both comparisons (early-onset vs controls and late-onset vs controls) in a way that Bonferroni correction should be performed by multiplying each p-value by 26, instead of 13.

Nevertheless, I do not think this is the best way to access the effect of HLA in the age of leprosy onset. A fundamental point in this case is the age of the controls, which has to be in the same range as the patient ages. More specifically, the controls should be stratified in the same two classes defined for patients in a way that patients with early-onset disease would be compared to controls with similar ages (<16). Authors declared in the methods section that controls were obtained from a Blood Bank, which suggests that the control group has few or no individuals under 18 years old and, so, they could not be used as controls to patients with early-onset disease. In this case, authors should consider the use of multivariate models to include age as a covariate to adjust the model.

Minor revisions
Authors should revise English.

Materials and methods section:
The sentences “Of the 305 patients...” (Patients and controls section), and “Power calculations carried out...” (Statistical analysis section) are really confused and should be rewritten.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
'I declare that I have no competing interests'