Reviewer's report

Title: HLA-A and -B alleles and haplotypes in hemochromatosis probands with HFE C282Y homozygosity in central Alabama

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Version: 1 Date: 9 Sep 2002

Reviewer: Dr Maria de Sousa

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Accept after discretionary revisions

In the present paper, Acton and Barton review HLA A and B haplotypes in 118 Hemochromatosis probands and alleles in 139. All patients were homozygous for the C282Y HFE mutation. The corresponding numbers of controls include 605 for haplotypes and 1321 for the alleles. The controls are not HFE genotyped. Basically the results confirm in a large series the established association of HLA-A3 with the C282Y mutation in Hemochromatosis. The report includes a valuable review of the association of the C282Y mutation with HLA-A and -B haplotypes in additional published independent studies including an earlier report by the same group. another from Utah and others from 7 countries outside the US, namely, Germany, Denmark, Sweden, Brittany (France), Portugal, Italy and Australia. The present study uncovers new associations of the mutation with haplotypes HLA A2B39, A3B13 and A3B44 not previously reported. I could not find a reference to the frequencies upon which this conclusion is based; something the authors can easily add strengthening the validity of the statistical analysis (pag. 10). In the Materials Section the authors also overlooked to mentione the ethnic origin of the probands although it becomes apparent later that they are white. One flaw that perhaps can not be overcome is the use of different methods for HLA typing in probands (DNA based) and controls (serology). One of the interesting observations of the paper is the finding of an exceptionally high frequency (37.3%) of HLA haploidentical probands. In summary, although the general results of the present report are not new and the relevance of the new haplotypes should be better documented, the paper represents a valuable contribution to the field for two reasons: 1. the continuous importance of HLA typing in the disease, 2. the value of HLA for the understanding of the natural history of the HFE mutations.

Competing interests:

None declared.