Reviewer's report

Title: HLA HAPLOTYPES ASSOCIATED WITH HEMOCHROMATOSIS MUTATIONS IN THE SPANISH POPULATION

Version: 2 Date: 16 August 2004

Reviewer: Ronald Acton

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Although the authors indicated that in the revised manuscript HFE was in italics this has not been done. HFE is not in italics throughout the manuscript.

In the background section first paragraph lines 11 and 12 amino acid should be two words not as one word (aminoacid). In line 13 of this paragraph, "the risk of disease in heterozygous", ahould be risk of disease in persons heterozygous.

Under methods first paragraph the authors indicate that, "a presumptive diagnosis of hemochromatosis using an elevated saturation criterion". The diagnosis of hemochromatosis is usually based on elevated transferrin saturation greater than 60% on at least 2 occasions in the absence of other known causes of elevated transferrin saturation, or other clinical criteria (Witte, DL, Clinica Chimica Acta 245:139-200, 1996).

The title of Table 1 would be clearer if, "the C282Y group" was changed to the C282Y homozygous group. In addition the Table columns labelled, "C282Y Haplotypes" would be clearer if changed to C282Y Homozygotes.

Under the results section, first paragraph, line 5, change, "haplotypes in comparison" to haplotypes in the homozygous group in comparison.

Table 3 is out of order and should be Table 2. As presented now the authors jump from data on HLA antigens in the C282Y homozygous group to haplotypes and then back to data on HLA antigens in the H63D homozygous group.

The title in the present table 3 should be changed to ...in the H63D homozygous group... and the columns from H63D Haplotypes to H63D Homozygotes.

In the second paragraph under the results, line 1, the authors refer to H63D carriers. However, they state in the methods section that the subjects are H63D homozygous. This need to be clarified.

Under the Discussion section, second paragraph, line 2, the following sentence is confusing. "This finding supports the founder hypothesis of Simon et al [5]: the ancestral haplotype where the C282Y mutation occurred was HLA-A3/B7....." The sentence might be clearer if changed to: ...where the C282Y mutation occurred on the ancestral haplotype HLA-A3/B7...

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the
author can be trusted to correct)
Although the authors indicated that the manuscript had been checked to correct English and improve readability, it still needs additional polishing.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

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

**Statistical review:** No

**Declaration of competing interests:**

None