Reviewer’s report

Title: A new 500kb haplotype associated with high CD8+ T-lymphocyte numbers predicts a less severe expression of hereditary hemochromatosis

Version: 1 Date: 11 August 2008

Reviewer: Lawrie Powell

Reviewer’s report:

This is a very interesting paper which addresses the question of the variable phenotypic expression in the genetic disease hereditary hemochromatosis. The essential finding is that a highly conserved ancestral haplotype (designated by the authors A-A-T) was found to be associated with both abnormally low CD8+ T-lymphocyte numbers and the development of more severe clinical expression of the disease. In contrast some patients were found with another conserved haplotype (designated G-G-G) which was found to associate with high CD8+ T-lymphocyte numbers and a milder clinical expression. Of particular interest is the fact that the two conserved haplotypes defined in Portuguese patients were also observed in the Canadian patients, i.e., a different geographical and ethnic group. In this population the conserved haplotypes also predicted the CD8+ T lymphocyte numbers and severity of disease.

The finding is of particular interest because of the current controversy over the variable expression of the disease.

- Major Compulsory Revisions

I have no major compulsory revisions.

- Minor Essential Revisions

I have no minor essential revisions and I think the paper warrants publication in its present form.

- Discretionary Revisions

No comment here.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
No competing interest.