Reviewer’s report

Title: Association between HLA-DRB1 alleles polymorphism and hepatocellular carcinoma: A Meta-analysis

Version: 5 Date: 12 August 2010

Reviewer: Adriana Rojas-Villarraga

Reviewer’s report:

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- Page 4, Methods section, Search Strategy:
Specify if terms in addition to HLA such as MHC or HLA-DRB1 were used to search for the studies.

- Page 4, Methods section, inclusive selection criteria:
Specify detailed study characteristics including the criteria that the diagnosis of patients with HCC was based on and give the age range of patients that were included. Move the information that is in the results section (Page 7) “The diagnosis of HCC was based on at least one of the following criteria: classical histological characteristics or a serum a-fetoprotein (AFP) level higher than 500µg/ml together with radiological findings (ultrasound and/or CT) consistent with HCC” to the inclusive selection criteria part of the methods section.
In addition, specify if the criteria for HCC diagnosis are author based or if they are based on specific reported guidelines. If so, include the specific reference.

- Page 6, Statistical analysis, first paragraph:
State if I2 was used as an additional method for heterogeneity because it is shown in the author’s attached forest plots. Furthermore, it is important to state if Tau squared was used to evaluate heterogeneity because it is also reported on the forest plots.

- Page 6, Statistical analysis:
Clarify if the crude number of patients and controls was used to calculate ORs and if specific allele frequencies were not used. Indicate what the reason was for not doing it. Specify that heterozygosity and homozygosity (allelic dosage) were not taken into account for these calculations.

- Page 7, Results section, Association between HLA-DRB1 alleles with HCC:
Clarify if the results by random effect model were the same as the results from the fixed effect model in the article in the case of HLA-DRB1*07 where I2 shows some heterogeneity other than the Q statistics results (54%).

- Page 8, results section, last paragraph:
Specify that fixed effect model was used for the results reported for HLA-DRB1*15 in Asians.

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

-Page 3 and 4, Methods section, selection criteria:
  As stated in the author guidelines, authors are requested to make use of the PRISMA checklist (http://www.prisma-statement.org/) when reporting systematic review and meta-analysis. Authors have to refer to this in the methods section and be sure they fit the minimum set of items for reporting in systematic reviews and meta-analyses included there.

-Page 8, Discussion section:
  It is important that the authors explain why the DRB1*07 and DRB1*12 could be of interest in HCC. Do these two groups/alleles share some pocket specificities? Are these groups/alleles described in association with specific viral hepatic infections? Do these groups/alleles have a similar preference for specific types of amino acids? Do the authors have a specific hypothesis regarding why these groups/alleles confer susceptibility to HCC?
  All of the information in the discussion section is of essential importance for understanding functional and biological aspects of HCC and HLA.

**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:**

I declare that I have no competing interests