Reviewer's report

Title: XPD Codon 312 and 751 Polymorphisms, and AFB1 Exposure, and Hepatocellular Carcinoma Risk

Version: 1 Date: 15 June 2009

Reviewer: Pierre Hainaut

Reviewer's report:

This study reports on the analysis of two polymorphisms in the XPD gene involved in nucleotide excision repair in 618 HCC cases and 712 controls from Guangxi, China, a population in which the main risk factors for HCC are hepatitis B and C infection and exposure to Aflatoxin.

The results show a significant association between the risk of HCC and the G allele of codon 751. This is to my knowledge the first report of such an association. Furthermore, there is an interesting combined effect with the duration of aflatoxin exposure.

Major revisions

1. The tables giving actual data must be integrated in the manuscript and not given as supplementary material. At least tables 1, 3 and 5 should be given in text, with the possibility of keeping the other tables as suppl. In contrast, Fig 1, which is included in the text, may be placed in the suppl. data file.

2. I do not understand the rationale for some of the analyses. In particular, HBV and HCV status as well as sex were matching variables between cases and controls. Therefore, differences between cases and controls may reflect imperfect matching rather than biologically significant effects. In my opinion these analyses cannot be performed in the present study design.

3. The association with duration of aflatoxin exposure should be better explained. Is the association with the total number of years of suspected exposure, or with the time at which exposure occurred? Patterns of exposure to aflatoxin have dramatically changed over the past twenty years. There is evidence that food contamination with aflatoxin has strongly decreased. Therefore, the association observed here may identify a higher risk with patients who have been exposed at a time when food contamination by aflatoxin was high.

Level of interest: An article of importance in its field

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I declare that I have no competing interests