Reviewer's report

Title: TRAIL receptor I (DR4) polymorphisms C626G und A638C are associated with an increased risk for hepatocellular carcinoma (HCC) in HCV-infected patients

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Reviewer: Saumitra Das

Reviewer's report:

The paper describes the influence of DR4 gene polymorphism on the development of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV) infected patients. Specifically, they have analyzed the C626G and A638C and tried to establish correlation with the occurrence of HCC in patients chronically infected with HCV.

The question is well defined but the study largely reconfirms the previous observations by other groups and provides only an incremental advance to our knowledge on the influence of variations in DR4 gene in triggering carcinoma.

The experiment design, data quality and representation are appropriate. However, the manuscript is difficult to follow due to the style of writing and several spelling, grammar and typographical errors in the text.

Following are the specific comments on the manuscript.

1. What is the significance that these genetic variants (C626G, A683C) matched Hardy-Weinberg equilibrium?
2. The authors didn’t attempt to address whether C626G and A638C polymorphism is specific for HCV induced HCC or true for even Hepatitis B virus induced HCC.
3. It is not clear that distribution of A683C is identical in healthy control and HCV infected patient without HCC. However, HCV virus load tend to increase in case of A683C and considered as risk factor-why?
4. Also, it is not clear whether the C626G transition happens with the gradual progress towards HCC in the HCV infected patients.
5. It appears from the results that presence of both the variations (C626G, A683C) together is significant for developing HCC-this should be clarified further.

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'