

**Yuan Qi,
Science Editor,
World Journal of Gastroenterology**

February 22, 2017

Resubmission of Manuscript: NO. 32280

Dear Sir,

Enclosed please find the revised manuscript entitled “Indoleamine 2, 3-dioxygenase: a prognostic marker and immunotherapeutic target for hepatocellular carcinoma” (Manuscript: NO. 32280) and our responses to the reviewers and editor comments. We appreciate the time and details provided by each reviewer and by you, which enabled us to improve the manuscript.

We hope the revised manuscript is now acceptable for publication in *World Journal of Gastroenterology*. All amendments in the text are marked in blue.

We appreciate your consideration of our manuscript.

Yours sincerely

Kashif Asghar

Point-by-point response

Editor's suggestions:

Q1: Please provide language certificate by professional English language editing companies.

Ans: We are exempted from the language certificate (as per our email correspondence).

Q2: This file must be signed by the corresponding author and provided in a PDF format, and the statement must also be mentioned as a footnote in the manuscript text.

Ans: Statement is attached now.

Q3: Telephone and fax should consist of +, country number, district number and telephone or fax number, e.g. Telephone:

Ans: The required details are provided now.

Q4: Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

Ans: We have added the summary in the main text.

Q5: Audio Core Tip

Ans: Audio file is attached now.

Q6: Please provide the grant application forms. If you can't provide it, please delete this part.

Ans: This part is deleted.

Q7: Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

Ans: We have changed the reference style as you suggested. These references have no PMID and DOI (Ref: 6, 13, 28 and 66). These references have only PMID, but no DOI (Ref: 15, 34, 35 and 53).

Q8: Please provide the decomposable figure of Figures, whose parts are movable and can be edited. So please put the original picture as word or ppt or excel format so that I can edit them easily.

Ans: Please find attached the figure in .ai format compatible with Adobe Illustrator CS5; it can be edited in this format. The image was not created in .ppt, .doc or excel file. A .png file is also attached to maintain the high resolution of the image.

Reviewer: 1

Q1: Introduction is too long and contains specific statements regarding IDO in the pathogenesis of hepatitis B and C or hepatocellular carcinoma, which should be described in an independent chapter.

Ans: Introduction has been divided into four subsections, (see page no. 4-5).

- i. Hepatocellular carcinoma (HCC)
- ii. HCV induced HCC
- iii. HBV induced HCC
- iv. Indoleamine 2, 3-dioxygenase (IDO)

Q2: The title states that IDO is a prognostic marker, but there are few data or descriptions to support that point.

Ans: IDO is involved in the onset of immune exhaustion and poor prognosis that eventually leads to HCC (53, 62). IDO might have potential to be used as prognostic marker in HCC (46). Therefore we proposed to evaluate its potential as prognostic marker. Keeping in view the reviewer's valuable suggestion we made an amendment in the title "Indoleamine 2, 3-dioxygenase: as a potential prognostic marker and immunotherapeutic target for hepatocellular carcinoma".

Reviewers: 2

Q1: Author have mentioned about the role of occult HBV and I think they can also speak about the role of occult HCV infection in the HCC as this form of HCV cannot be diagnosed easily with usual laboratory approaches

Ans: Occult HCV infection part is now included, (see page no. 4,5).

Q2: I think authors should briefly mention their methods (data resources and search strategy) for performing this review and they can bring it in a separate paragraph in the manuscript.

Ans: As per reviewer's suggestion, we have included it (see page no. 4).