

We would like to first thank the editor and reviewers for their response to our work and their constructive comments. We have addressed the concerns that were raised through further editing of the manuscript and believe it has significantly improved as a consequence of this process. We greatly appreciate the opportunity to submit this revised review manuscript and hope it is now suitable for publication in World Journal of Gastroenterology.

### **Reviewer 1**

*1. As the title of the review suggests, the review should mainly introduce the application of transposon mouse models in the study of genetic mechanisms of HBV induced HCC. However, more than half of the review was about the background knowledge that are not relevant, including epidemiology of liver cancer, risk factors for HCC, ect. As a result, we recommend that authors introduce the background knowledge briefly and emphasize on the application of transposon mouse models.*

As suggested by the reviewer, we have deleted a substantial amount of irrelevant background information and two Figures (Fig. 1 and Fig. 6) to allow for more focus on the application of transposon mouse models for the study of genetic mechanisms of HBV-induced HCC. Some of the deleted parts are highlighted below:

Page 7 – Deleted “Risk factors for HCC”

Page 8 – Deleted irrelevant background information and made correction of minor spelling mistakes

Page 9 – Deleted general description of the HBV genome

Page 10 – Deleted irrelevant background information

Page 15 – Deleted “From HBV to HCC”

*2. The structure of the review needs to be reconsidered. There are too many subtitles in the review, the relationship of which, however, are sometimes not paralleled. For example, “HBV PreS1/S2/S ORF” and “X ORF” should be included in “HBV genome”.*

As suggested by the reviewer, the structure of the review article has been re-organized by deleting irrelevant background information and Figures. In addition, “HBV PreS1/S2/S ORF” and “X ORF” have been merged under “HBV Genome”.

3. A few minor typos, grammar hiccups should also be corrected, e.g., HVB in line 17, page 5.

As suggested by the reviewer, we have gone through the revised article and corrected minor typing mistakes and grammatical errors.

Page 7 - Corrected "HVB" to "HBV"

## **Reviewer 2**

*Chui et al. reported not only transposon mouse models to reveal carcinogenesis of the HBV related HCC but also genetic knowledge of the HBV infection itself. The review is very informative and well written. The only minor problem is the reference which does not follow the instruction. My question is the figs are really original? Thank you for submitting the review and very educational paper.*

As suggested by the reviewer, the referencing style has been changed to the World Journal of Gastroenterology format. These changes are found throughout the entire revised review manuscript.

The Figures are all original or designed using published information obtained from the cited journal references shown in the corresponding Figure Legends. We have made changes to original Figure 2 (now new Figure 1) to allow for better representation of the HBV genome.

### **Detailed additional changes (in track changes revised manuscript)**

- All pages - Changed all sub-titles into uppercase format
- Page 1 - Changed surname of running title due to our initial typing mistake
- Page 2 - Line spacing and conflict-of-interest statement edited
- Page 4 - Corrected minor spelling mistakes in Abstract
- Page 5 - Corrected minor grammatical mistakes in Core tips  
Added author abbreviation names and manuscript title as instructed
- Page 6 - Deleted irrelevant background information in the "Epidemiology of liver cancer" section  
Corrected minor grammatical mistake

- Page 7 - Deleted "Risk factors for HCC" section to focus on the application of transposon mouse models for the study of genetic mechanisms of HBV-induced HCC
- Corrected minor spelling and grammatical mistakes
- Page 8 - Deleted Figure 1 since it does not essential to the review paper
- Deleted irrelevant background information in the "HBV genotypes" section
- Corrected minor grammatical mistakes
- Page 9 - Changed Figure 2 to Figure 1 because the original Figure 1 has been deleted
- Added a sentence before the "HBV PreS1/S2/S ORF" section
- Deleted irrelevant background information in the "HBV genome" section
- Page 10 - Changed Figure 3 to Figure 2 because the original Figure 1 has been deleted
- Deleted irrelevant background information in the "HBV PreS1/S2/S ORF" section
- Page 12 - Corrected minor spelling mistake in the "X ORF" section
- Page 14 - Changed Figure 4 to Figure 3 because the original Figure 1 has been deleted
- Corrected minor spelling mistake in the "X ORF" section
- Page 15 - Corrected minor spelling and grammatical mistakes in the "X ORF" section
- Deleted "From HBV to HCC" section to focus on the application of transposon mouse models for the study of genetic mechanisms of HBV-induced HCC
- Deleted original Figure 6 to focus on the application of transposon mouse models for the study of genetic mechanisms of HBV-induced HCC

- Edited a sentence in the “Mechanisms of HBV-induced HCC” section
- Page 16 - Corrected minor spelling and grammatical mistakes
  - Page 17 - Added references that were previously left out in the original version
  - Page 18 - Corrected minor spelling mistake
  - Page 19 - Corrected minor spelling mistake
  - Added references that were previously left out in the original version
  - Page 20 - Corrected minor grammatical mistake
  - Page 21 - Corrected minor spelling mistakes
  - Page 23 - Changed Figure 7 to Figure 5 because the original Figure 1 and 6 have been deleted
  - Page 24 - Corrected minor spelling and grammatical mistakes
  - Page 25 - Changed Figure 8 to Figure 6 because the original Figure 1 and 6 have been deleted
  - Page 30 - Deleted original Figure 1 legend and changed all the Figure legend numbers appropriately
  - Made slight changes to Figure legend 3
  - Page 31 - Deleted original Figure 6 legend
  - Changed Figure legend numbers
  - Page 33 - Deleted original Figure 1 and replaced with new Figure 1
  - Page 34 - Deleted original Figure 2 and replaced with new Figure 2
  - Page 35 - Updated Figure number and replaced with new Figure 3
  - Page 36 - Deleted original Figure 6, updated Figure number and replaced with new Figure 4
  - Page 37 - Updated Figure number and replaced with new Figure 5
  - Page 38 - Updated Figure number and replaced with new Figure 6

Page 40 - Changed referencing style according to the manuscript format as instructed