Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: eview gdTC in liver disease REVISION.docx).

Title: The role of gamma-delta T cells in liver inflammation and fibrosis

Authors: Linda Hammerich and Frank Tacke

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 8147

The manuscript has been improved according to the suggestions of reviewers:
1) Answer to Reviewer 1:

The authors present a well-written review article about an important T-cell subtype.
It would significnatly improve the usefulness of the review if the authors could add information about mechanism (in various sections - such as viral infection, fibrosis etc.) through which this T-cell subtype contributes to either disease process or protection of the liver.

Response: Thank you very much for this helpful comment. We fully agree with the reviewer that the mechanisms by which gamma delta T cells either promote or protect from disease progression are of utmost interest. However, at this stage of research within the field, most of the disease-specific studies in humans are largely descriptive, while the studies in mouse models (e.g., Concanavalin A hepatitis or carbon tetrachloride induced fibrosis) provide mechanistic insights. In order to fully comply with the referee's valid comment we now modified the table, in which now all data with respect to the specific T cell receptor as well as the key cytokines identified are summarized. Although the current studies, especially in human disease, do not elucidate all potential mechanisms of action for the gamma delta T cell subsets, the key cytokines and TCR may provide valuable information about possible mechanisms of action. We have also modified the main text, as the referee suggested (for instance, we added a new paragraph on gamma-delta T cells in HBV infections and about possible mechanisms of action in hepatocellular carcinoma). Nevertheless, we believe that it is of utmost importance to further study gamma delta T cells and their subsets in acute and chronic liver inflammation and especially in different disease entities.

Also, if the authors could highlight the important references, that would benefit the reader immensely.

Response: We sincerely thank the reviewer for his/her comment. To facilitate comprehension for readers we included a table summarizing the 11 most important references on the different functions of gamma delta T cells in various liver diseases. By sorting these references according to disease etiology and species studied we hope to make it easy to find the desired publication.

Further, adding disease information to the figure too will add value to the manuscript.

Response: We thank the reviewer for this helpful comment. We have now incorporated a schematic depiction of the influence of different gamma delta T cell subtypes on disease progression into the revised figure. Specifically, the figure now illustrates how distinct mechanisms suggested for gamma delta T cells actions (e.g., apoptosis of hepatocytes vs stellate cells) are related to progression of inflammation, fibrosis or cancer.

2) We sincerely thank reviewer 2 for his/her favorable evaluation of our manuscript.

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

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