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July 1, 2021

Lian-Sheng Ma
Founder and Chief Executive Officer
Baishideng Publishing Group Inc

Dear Professor Ma,

I am submitting the revised review article "Newly discovered endocrine functions of the liver" to the World Journal of Hepatology. We have addressed all the issues raised by reviewers and editors. The revised texts are in red font. This article should be free of charge.

My ID is 00077678.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear authors I read your paper with great interest, and I think this review gives a comprehensive vision of the liver's pivotal endocrine role in the organism's homeostasis. Searching briefly in the literature, I found many papers focusing on a single or few aspects of this topic, but I didn't find an exhaustive and recent review like yours. I want to congratulate you on your work, and I would like to say that I understand the effort in summarizing such a big theme. Nevertheless, I would like to express some suggestion to improve the manuscript and facilitate its publication: - Even if the hormones, pathways, and physiopathological mechanisms are many, I suggest focusing on one of the two main aspects of the manuscript. It could be more interesting to develop a little more the discussion about the latest discovery in this field, giving less space (without completely removing) to the well-known hormones. Unfortunately, many pages might discourage the reading, while a more concise manuscript might be more eligible for a wider audience. - For better comprehension, I suggest assembling the physiological and pathological description of each hormone. I think that dividing the chapters like you made the

manuscript less fluent and a bit hard-reading. - I suggest developing more of the hepatokines paragraph. It could be interesting to explain their metabolic pathways, maybe using diagrams or images, and show their alterations in prevalent liver diseases as you did for the well-known hormones. - Some paragraphs are supported by the same sources. I suggest deepening the scout in the bibliography to give more relevance to this review. - In certain parts of the manuscript, the text might be hard-reading. I believe that an expert scientific editor should review the manuscript.

Authors response: We appreciate the positive comments and constructive critiques. We have now greatly reduced the first section (by 60%) and the corresponding references (by ~90 references). We now replace the original Table 1 with a new Table 1 summarizing the physiological and pathophysiological functions of the classic liver endocrine functions.

We respectfully wish to point out that our article intends to be a comprehensive review of all liver endocrine functions and we feel we have given the hepatokines appropriate attention.

We have re-edited the language.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This review is to summarize newly discovered endocrine function relevant or specific to liver organ. Generally the paper is well-written. Comments 1. The references are too many and redundant. For example, in page 12, "Androgens are predominantly secreted from Leudig cells in the testes in men[60] and from the ovaries and adrenal glands in woman[61]." Both references are review articles and not from the original discovery. Therefore, you should not individually cite 2 references just for men and women. Another example is in page 26, "Normally the number of islets is quite small, and the islets are mostly composed of beta cells [152]." Again, unless you cite the original discovery paper, you may cite a textbook in high school. Many examples like these should be examined carefully. 2. Some facts not relevant to liver can be reduced as much as possible. The focus of "newly discovered" evidence is diluted in the current format. 3. A summary table of "newly discovered" endocrine function +/- classical endocrine function is strongly encouraged to guide readers quickly. 4. A figure(s) illustration to provide relationship of these liver endocrine functions with other body parts is helpful.

Authors response: We appreciate the positive comments and constructive critiques

1. *We have greatly reduced the reference numbers (by ~90), including 2 specific references cited by the reviewer.*
2. *We have greatly reduced the first section (~60%)*
3. *We now revise Table 2 as requested*
4. *We add a new figure (Figure 2) as requested by the reviewer*

5 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript describes a Review of the Liver endocrine functions. The topic is within the scope of the WJH. (1) Classification: Grade B and Grade C; (2) Summary of the Peer-Review Report: this review gives a comprehensive vision. Authors should deepening the scout in the bibliography to give more relevance to this review. A figure(s) illustration will be helpful. The questions raised by the reviewers should be answered; (3) Format: There are 2 tables and 1 figure; (4) References: A total of 241 references are cited, including 51 references published in the last 3 years; (5) Self-cited references: There are 7 self-cited references; and (6) References recommendations (kindly remind): The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B and Grade B. The authors are native English speakers. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJH. 5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (2) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu

MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. 6
Recommendation: Conditional acceptance.

Authors response: We appreciate the positive comments and constructive critiques.

1. *We have removed redundant references and greatly reduced the reference numbers of the first section. We also reduced the first section by 60% to focus more on the second section. We now add a new Table (Table 1), revise a table (Table 2), and add a new figure (Figure 2).*
2. *We now provide original powerpoint figures (Figure 1 and Figure 2)*
3. *We now add the details of the documentation of a reused figure (Figure 1)*

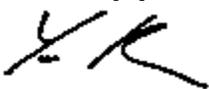
(2) Editorial office director:

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Authors response: We appreciate the positive comment from the Editor-in-Chief.

Thank you very much for your consideration.

Sincerely yours,



Run Yu, MD, PhD