

Dear Editors and reviewers,

Thank you for taking the time to review our manuscript and for providing insightful feedback. We appreciate the opportunity to clarify and enhance our study based on your valuable comments.

Reviewer #1:

1. Insufficient in-depth explanation of some mechanisms: Regarding the specific mechanisms by which immune cells, nutrition, and the microbiome regulate ISCs, only some cytokines and phenomena are listed, and the interaction network and key nodes are not explored in depth. It is recommended to deepen the research on mechanisms, supplement the molecular mechanisms by which immunity, nutrition, and the microbiome regulate ISCs, construct a complete regulatory network, and enhance readers' understanding.

Response: We acknowledge this important limitation and have substantially expanded our mechanistic discussion. We have added a comprehensive section detailing the molecular pathways governing ISC regulation, including:

1. Immune cells
2. Nutrition
3. Microbiome

The specific details can be found in the section titled “Other regulators of ISCs.”

2. Inadequate comparison in the treatment section: When introducing the treatment of IBD with hematopoietic stem cells, mesenchymal stem cells, and organoids, the comparison of the advantages and disadvantages of the three treatment methods is not detailed enough, making it difficult to highlight their respective characteristics. It is suggested to add tables or figures to compare the clinical data, application scopes, adverse reactions, etc. of hematopoietic stem cell, mesenchymal stem cell, and organoid therapies, facilitating readers' comparison.

Response: We have significantly enhanced the treatment comparison section as suggested. Specifically, we have:

- Added Table 1: A comprehensive comparison table detailing main source, primary mechanism, clinical stage, indications, and adverse effects for each therapeutic approach.

This enhanced comparison will enable readers to better understand the clinical positioning and selection criteria for each therapeutic approach.

3. Lack of innovation in research prospects. Attention can be paid to interdisciplinary fields, such as the combination of gene editing and stem cell therapy, and the use of artificial intelligence to assist in disease diagnosis and treatment monitoring, etc., to provide new ideas for research.

Response: We appreciate this forward-looking suggestion and have completely revised our research prospects section to incorporate cutting-edge interdisciplinary approaches. Further details can be found in the section titled “FUTURE PERSPECTIVES.”

Science Editor:

(1) **Country/Territory of origin:** China.

Response: We acknowledge that our manuscript originates from China. This information has been properly documented in our submission.

(2) The language classification is Grade B and Grade B. Please provide the latest Language certificate after Return the Manuscript to Author for Revision. Please visit the following website for the professional English language editing companies that we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response: We acknowledge the Grade B language classification and understand the need for professional English language editing. We will engage the professional English language editing companies and will submit the language certificate upon completion of the revision process.

(3) **Manuscript Title:**

The title should not start with ‘A’, ‘An’, or ‘The’.

Response: We have revised our manuscript title to comply with this requirement. The

title has been modified to remove the initial article and now reads: [Roles of intestinal stem cells in inflammatory bowel disease pathogenesis].

(4) **Authors and institution(s):** Author names should be written out first (as **first name, middle name initial (with no period) and family (sur)name**; with a hyphen included between the syllables of Chinese names) and typed in bold, followed by a comma and the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold. Examples for authors name and institutions are:

Yi-Fan Chang, Tao Liu, Chong-Qing Wei, Wei-Long Chang, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, China

Response: We have reformatted all author names and institutional affiliations according to the provided guidelines. Chinese author names now include appropriate hyphens between syllables, author names are bolded, and institutional information includes complete addresses with city, province, postcode, and country in non-bold format.

(5) Policy of allowing co-first authors and co-corresponding authors who made equal contribution to a manuscript (<https://www.wjgnet.com/bpg/GerInfo/310>).

Response: We have reviewed the policy regarding co-first and co-corresponding authors. Our manuscript complies with these guidelines, and appropriate notations have been added where applicable to indicate equal contributions.

(6) **Please add the “Audio Core Tip”.** In order to attract readers to read the full-text article, we request that the first author make an audio file describing the final core tip. This audio file will be published online, along with the article. **The author can invite English language editing company to assist in resolving the language issues of Audio Core Tip.**

Response: We will prepare the Audio Core Tip as requested. The first author will record an audio file describing the core findings of our study. We will ensure the audio quality meets publication standards and may engage professional language editing services if needed to optimize the audio content.

(7) **Reference numbers in the main text.**

The name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference. **Example:** Mandal *et al*[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

Please verify the order and total number of references cited to ensure that all references in the list are cited and in a correct numeric order.

Response: We have thoroughly reviewed the manuscript and corrected all in-text citations to ensure reference numbers appear immediately after author names when mentioned.

(8) There are issues with the references:

To ensure the accuracy of the references, please use "**Edit References by Auto-Analyser**" (<https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx>) to edit the references of the manuscript.

Response: We have utilized the recommended Auto-Analyser tool (<https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx>) to verify and correct all references. All references have been checked for accuracy, proper formatting, and sequential numbering. We have ensured that all cited references appear in the reference list and are numbered in the correct order of appearance in the text.

(9) Figures. Figures must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, *etc.*). All figures must have a detailed figure legend that provides a clear and comprehensive description of the information presented in the figure, so that the reader can understand without having to refer back to any other portion of the manuscript. Uniform presentation should be used for figures showing the same or similar contents; for example, "**Figure 1 Pathological changes of atrophic gastritis after treatment.** A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

Abbreviations must be defined upon first appearance in the **Figure Legends**. Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition.

Original figure documents. *In the meantime, authors should 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 upload it to the file destination of "Image File" in the F6Publishing system.*

Response: We have reorganized all figures to appear in sequential order (1, 2, 3, etc.) as they appear in the main text. Each figure legend has been enhanced to provide comprehensive descriptions that allow readers to understand the content without referring to other parts of the manuscript. We have standardized the presentation format for similar figures and defined all abbreviations upon their first appearance in figure legends. Original PowerPoint files with editable elements have been prepared for upload to the F6Publishing system.

(10) Please verify if all pictures (s) are original? 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 indicate 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.

Response: We have conducted a thorough review of all figures in our manuscript. The publication license required for the images has been provided in the supplementary file.