Dear Reviewers and Editors,

Please find our point-by-point responses (in blue) below along with reflected changes in the revised manuscript.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Though SC-RNA-Seq has developed prosperously in the recent years and intended to construct a real and objective correlation between genotype to phenotype. However, these techniques could not have issued the problems at all to date. So, the goal of this review is good. The shortages of the manuscript may be less enough of related contents about GI diseases, such as cancers. Overall, this is a good paper with high quality, I recommend to accept it. The shortages of the manuscript may be less enough of related contents about GI diseases, such as cancers. I suggest author could amend some important contents.

We thank the reviewer for their review and agree that GI cancers is an important topic of interest. Given the title of the invited minireview (Single cell Omics in IBD), we wanted to limit scope of the review to just IBD. However, we added into the text with references that scRNAseq has been used to better understand GI cancers and that these topics are equally important though beyond the scope of this minireview (please see text that was added to end of manuscript below).

"**Single-cell omics in other Gastrointestinal diseases**

Given the limited scope of this review, we have described these technologies only in the field of IBD and did not elaborate into its use in other GI disorders such as gastrointestinal cancers and other gastrointestinal diseases such as allergies of the gastrointestinal tract.

Spatial transcriptomics and various single-cell techniques have been successfully applied to colorectal cancers using the GI cancer tissue and resections allowing researchers to better understand the tumor microenvironment to deprive better chemotherapeutic targets [30-34]. Allergic disease of the GI tract such as eosinophilic esophagitis is also under interrogation using single-cell technologies [35]. The ability to study tissue level molecular changes across multiple disease is unparallel using single-cell technologies. "

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: In the study of inflammatory bowel disease (IBD), scRNA-seq is being used to identify novel cellular immune players in the pathogenesis of both ulcerative colitis and Crohn's disease. By analyzing individual cells from inflamed tissue, researchers can identify specific cell types that are involved in the immune response and determine how they contribute to disease progression. This information can then be used to develop more targeted therapies for IBD patients. Additionally, scRNA-seq may help detect signals of treatment response in IBD and tailor therapies to immune signatures present in the disease state. Overall, scRNA-seq has great potential to improve our understanding of IBD at a cellular level and lead to new treatments for this chronic autoimmune condition. This mini review discusses the emergence of single-cell technologies over the last decade and their published applications to GI disease, specifically IBD. The review also highlights how single-cell RNA sequencing can be used to better understand IBD at a cellular level and potentially lead to new treatments for this chronic autoimmune condition. However, while the review provides an overview of scRNA-seq and its potential applications in IBD research, it does not go into great detail about the technical aspects of the technique or how it compares to other transcriptomic approaches. Finally, the review is relatively brief and does not provide an in-depth

analysis of the current state of scRNA-seq research in IBD or its potential limitations. The authors had better add above two contents.

We thank the reviewer for their review. Given the scope of the minireview, we hope to keep the manuscript brief in nature.

(1) We have added in the introduction how single cell is different from previous sequencing techniques, namely bulk-sequencing (please see text that was added to the introduction of the manuscript below with appropriate references):

"The novelty of single-cell technologies versus previous technologies such as bulk-sequencing is the ability to detect rare subsets of cells that may be the aberrant drivers of disease[4]. The homogeneity of bulk-sequencing lacks the capacity to decipher cellular heterogeneity and loses dimmer signals in rare subsets that may be important in disease pathogenesis[4,5]. The inherent advantage of single-cell techniques has led to its continued popularity in research."

(2) We have also added a section at the end on limitations of these techniques, namely cost and integration of platforms (please see text that was added to the end of the manuscript below with appropriate reference):

"Limitations

The limitation to single-cell technologies is most importantly cost of reagents and cost of sequencing[38]. The ability to integrate multiple single-cell data across multiple platforms and techniques is also a challenge as there are many commercial products out in the market[38]."

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: This manuscript describes a review of Single-cell Omics in Inflammatory Bowel Disease. Although the title is very attractive, the content is too preliminary as a review of the World Journal of Gastroenterology. Furthermore, Fig. 1 does not show the impact of this research field. The authors should rewrite this manuscript for a variety of readers of the World Journal of Gastroenterology

We thank the reviewer for this review. We would like to point out that this was an invited manuscript and thus the author was granted with the choice of type of manuscript and this is a minireview.

Revision reviewer:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: I agree with the comment of the other editor and the authors.

We thank the reviewer for this review.

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:

The manuscript has been peer-reviewed, and it' s ready for the first decision.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, 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. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. 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.

We have included the powerpoint of the figure where the background (cell and cellular components) were made as one piece (using biorender.com online software subscription for publication purposes) and all the text is moveable/editable. This is an original figure and we have added the copyright information on the bottom righthand side.

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

Thank you we have done that and revised the manuscript as such.