

Answering Reviewers

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Title: " Therapeutic interventions targeting the NLRP3 inflammasome in ulcerative colitis: A comprehensive study "

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We would like to thank the editors and the reviewers for their precious time and thoughtful review of the manuscript. They raise important issues, and their inputs are very helpful for improving the manuscript. We agree with almost all their comments, and we have carefully modified the manuscript accordingly, and the detailed corrections are listed below point by point. (The reviewer comments were made in *Italic*)

Reviewer #1:

1. *There are a few grammatical, alignment and typographical errors are noted in the revised manuscript, and it should be carried throughout the manuscript. For example, the words "because of" may be as "because"; "Panax" as "the Panax"; "in ischemic" as "ischemic"; "immuno regulating" as "immune-regulating"; "and others" as "others"; "damp-heat" as "the damp-heat"; "in DSS" as "in the DSS"; "TWHF demonstrate" as "TWHF demonstrates"; "activity mediated" as "activity was mediated"; "such TNF- α " as "such as TNF- α "; ", antioxidant [305" as ", and antioxidant [305"; "NLRP3 pathway" as "the NLRP3 pathway"; "NLRP3-inflammasome" as "NLRP3 inflammasome"; "in in a" as "in a"; "in inflammation" as "inflammation".*

Response: The manuscript was deeply revised, and the errors were corrected as recommended.

2. *Check the abbreviations throughout the manuscript and introduce the abbreviation when the full word appears the first time in the abstract and the remaining for the text and then use only the abbreviation (For example, Ulcerative colitis (UC), Inflammatory bowel diseases (IBD), GIT, IL-1 β , IL-18, etc.). Make a word abbreviated in the article that is repeated at least three times in the text, not all words need to be abbreviated.*

Response: The abbreviations were carefully revised and were provided as recommended.

3. *The literature search should be described in detail. The authors are encouraged to include the database, search engines (like PubMed, ScienceDirect, Google scholar etc.), the keywords used etc., which may be included in the introduction section or separately in the materials heading since it is a review article. How many articles obtained from each of the search engines? What is the inclusion and exclusion criteria? What is the type of article included in this manuscript? How many articles are included for this manuscript? A diagram depicted the literature search should be included for better understanding and outcome.*

Response: Our review is a comprehensive review since most studies were carried out on experimental rodent models as well as in vitro cells and not on the patient such that systemic review and meta analysis require the mention of the database, search engines, the type of article included in this manuscript, the inclusion and exclusion criteria and others.

4. *In the introduction, the authors have cited upto 2019 for the prevalence of disease chosen and it may be updated with recent references.*

Response: Based on the raised comment, the last study contains statistical data about the prevalence of ulcerative colitis was issued in 2019. Therefore, this reference is considered the most recent source.

5. *The full form of the species should be given when the first time appears in both the abstract and in the remaining part of the manuscript and it should be followed by only the first letter of the genus (e.g., Dendrobium officinale / Schisandra chinensis when the first time appears and followed by D. officinale / S. chinensis,*

Response: The full form of the species was deeply revised in the whole manuscript and corrected as recommended.

6. *The figure legends should be improved and a proper footnote should be given. All legends should have enough description for a reader to understand the figure without having to refer back to the main text of the manuscript. For example, the necessary expansion may be given for abbreviations use.*

Response: Figure legends were improved and a footnote was added as the reviewer recommended

Reviewer #2

This manuscript comprehensively reviewed the mechanisms of NLRP3 inflammasome activation by various signals and its regulation and impact on UC, indicating that targeting NLRP3 inflammatory body signals may be a potential candidate drug for treating UC problems. The manuscript is well organized and its presentation is good. The references are complete and the whole article is logical. However, some parts of the manuscript need further modification.

1. The authors tried to list all the phytochemicals and plant extracts, probiotics, synthetic drugs for the treatment of ulcerative colitis targeting NLRP3 inflammatory body signal, which was impossible and would make the manuscript appear too much. The authors should further summarize and simplify this part.

Response: Based on the raised comment, the manuscript was carefully revised and simplified as the reviewer recommended.

2. I think the discussion parts should be strengthened.

Response: Based on the raised comment, this manuscript does not contain a discussion section