

Dear:

Thank you for your thorough review and salient observations. We have carefully read and addressed the comments from reviewers in the revised manuscript. Please see the point-by-point responses. All the changes are highlighted and we hope the revised manuscript is suitable for publication.

Best regards,

Sincerely,

Duan-Yong Liu, Ph.D.

Jiangxi University of Chinese Medicine

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Email: liuduanyong@163.com

Reviewer:1

Specific Comments to Authors: Colitis is a common disease that seriously endangers human health and has a high incidence. The treatment effect of existing colitis drugs is not ideal. Therefore, it is of great significance to develop new colitis drugs with good curative effect and small side effects. Curcumin is a natural polyphenolic compound, which has been proved to have many pharmacological effects such as anti-oxidation, anti-tumor and anti-inflammation, and has little side effects. It is a promising drug for colitis treatment, but the mechanism of curcumin's anti-colitis action has not been revealed. This article entitled Curcumin alleviates DSS - induced experimental colitis by a potential mechanism involving the memory B cells and the In the paper of Bcl-6-SYk-BLNK Signal, the therapeutic effect of curcumin on DSS-induced colitis in mice and its effect on Bcl-6-SYk-BLNK signaling pathway in memory B cells were studied, and some valuable results were obtained, which laid a necessary foundation for the final elucidation of the mechanism of curcumin anti-colitis. This is an important and interesting study, but the paper needs to be revised and refined before it can be accepted. Some of the changes need to be made are as follows. 1. Line231: Please supplement the lot number of curcumin. 2. Line 249: pH = 7.2 can be directly written in the common form pH7.2. 3. Line251: Please provide the model of tissue slicer. 4. Line153:

Curcumin Cur should be written with the full name curcumin first and then with the short name Cur. 5. Line254: Please supplement the model of Leica microscope. 6. Line261, Cell Medium RPMI (Roswell Park Memorial Institute) 1640, which can be simplified to the generic medium name RPMI-1640. 7. Line288, please supplement the batch number of total protein detection kit and antibody and other reagents.

1. Line231: Please supplement the lot number of curcumin.

Response: Thank you very much for your review and guidance! Your suggestion will be the wheels of progress to our next work. Following your suggestions, we have added the batch number of curcumin. Please see the revised manuscript for further details. You can find it in the page 9, line 247-248.

2. Line 249: pH = 7.2 can be directly written in the common form pH7.2.

Response: Thank you very much for your review and guidance! We have modified it according to your suggestions. Please see the revised manuscript for further details. You can find it in the page 9, line 263.

3. Line251: Please provide the model of tissue slicer.

Response: Thank you very much for your review and guidance! We have supplemented according to your suggestions. Please see the revised manuscript for further details. You can find it in the page 9-10, line 265-266

4. Line153: Curcumin Cur should be written with the full name curcumin first and then with the short name Cur.

Response: Thank you very much for your review and guidance! We have revised it according to your suggestions. Please see the revised manuscript for further details. You can find it in the page 6, line 152-153.

5. Line254: Please supplement the model of Leica microscope.

Response: Thank you very much for your review and guidance! We have supplemented according to your suggestions. Please see the revised manuscript for

further details. You can find it in the page 10, line 268.

6. Line261, Cell Medium RPMI (Roswell Park Memorial Institute) 1640, which can be simplified to the generic medium name RPMI-1640.

Response: Thank you very much for your review and guidance! After verification, RPMI-1640 was not used in the experiment, so we have deleted this reagent in the article. Please see the revised manuscript for further details.

7. Line288, please supplement the batch number of total protein detection kit and antibody and other reagents.

Response: Thank you very much for your review and guidance! We have supplemented according to your suggestions. Please see the revised manuscript for further details. You can find it in the page 10-12, line 273-327.

Reviewer:2

Specific Comments to Authors: In the present basic science article Wei et al showed that curcumin may improve DSS-induced colitis in a murine model by activating memory B-lymphocytes and modulating some proteins involved in Bcl6-Syk-BLNK pathway. Overall, this is a very good study and I have only few minor objections: 1) Lines 319-330: this is not a result, it should be moved in the Introduction. 2) I do not understand why, in “Flow cytometry” paragraph, Authors affirm that spleen was homogenized while in figures 4-7 “peripheral blood” was mentioned. Please explain. 3) A mention about proapoptotic effect of curcumin is necessary, especially in colorectal cancer.

1. Lines 319-330: this is not a result, it should be moved in the Introduction.

Response: Thank you very much for your review and guidance! But I'm sorry, I don't understand the specific meaning of this question. Because the introduction section is in the line 147-206, or not in the line 319-330, which is the results section. Maybe, I think, you should think that the texts in the line 319-330 are not a result. So we had revised it. You can find it in the page 12, line 344-349.

2. I do not understand why, in “Flow cytometry” paragraph, Authors affirm that spleen was homogenized while in figures 4-7 “peripheral blood” was mentioned. Please explain.

Response: Thank you very much for your review and guidance! Beg your pardon, I am sorry, this is a clerical error. After verification and confirmation, the samples used in the flow experiment are mouse peripheral blood, not mouse spleen. So we had revised it. Please see the revised manuscript for further details. You can find it in the page 10, line 273-276.

3. A mention about proapoptotic effect of curcumin is necessary, especially in colorectal cancer.

Response: Thank you very much for your review and guidance! According to your suggestions, we have discussed the anti-apoptotic effect of curcumin in colorectal cancer in the article. Please see the revised manuscript for further details. You can find it in the page 6, line 163-172 and the page 7-8, line 204-211.

Reviewer:3

Specific Comments to Authors: In this paper the effect of curcumin on in an experimental, murine model of ulcerative colitis (SDD) was investigated. Authors concluded that curcumin has anti-inflammatory properties since it may decrease colonoc pro-inflammatory cytokine levels and may modulate the memory B cell response. It is an excellent paper, I have only few minor points to be addressed. 1) Please discuss the effect of curcumin in inflammation-related colorectal cancer. 2) Do Authors think that Bcl-6-Syk-BLNK signal is modulated in colonic lymphocytes or in central, peripheric ones? 3) Numbers of cited articles in bibliography is missing.

1. Please discuss the effect of curcumin in inflammation-related colorectal cancer.

Response: Thank you very much for your review and guidance! According to your

suggestions, we have discussed the anti-apoptotic effect of curcumin in colorectal cancer in the article. Please see the revised manuscript for further details. You can find it in the page 6, line 163-172 and the page 7-8, line 204-211.

2. Do Authors think that Bcl-6-Syk-BLNK signal is modulated in colonic lymphocytes or in central, peripheric ones?

Response: Thank you very much for your review and guidance! The present experiment showed that the Bcl-6-Syk-BLNK signal was regulated in peripheral lymphocytes in colonic tissue. Bcl-6-Syk-BLNK signal is a very important role in the development of B cells, which will be cycled in local tissue and peripheral blood by lymph-vessel or blood vessel or tissue space. So the change of B cell in the peripheral blood and the colonic tissues should be synchronously affected by Bcl-6-Syk-BLNK signal. In the future, we will analyze the Bcl-6-Syk-BLNK signal activation in B cell which be separated from the peripheral blood and colonic tissues. I think, these evidences will be more and more direct in the next work.

3. Numbers of cited articles in bibliography is missing.

Response: Thank you very much for your review and guidance! We have checked and supplemented the number of the references. You can find them in the Reference section.

Dear:

Thank you for your thorough review and salient observations. We have carefully read and addressed the comments from reviewers in the revised manuscript. Please see the point-by-point responses. All the changes are highlighted and we hope the revised manuscript is suitable for publication.

Best regards,

Sincerely,

Duan-Yong Liu, Ph.D.

Jiangxi University of Chinese Medicine

Nanchang, 330004, Jiangxi, China

Email: liuduanyong@163.com

We are very pleased to receive your revised manuscript (No. 78544). However, there are some questions that need to be addressed.

-----1. You need to provide the grant application form(s) or certificate of funding agency for every grant, or we will delete the part of "Supported by the National Natural Science Foundation of China (No. 81760808, 81803988, 82060799, and 82060838), Natural Science Foundation of Jiangxi Province (No. 20192ACB20015, 20192BAB215050 and 20202ACBL206026), and Jiangxi University of Chinese Medicine Science and Technology Innovation Team Development Program (No. CXTD22008)." –

Response: Thank you very much for your review and guidance! we provide the certificate of the National Natural Science Foundation of China (No. 81760808) and Jiangxi University of Chinese Medicine Science and Technology Innovation Team Development Program (No. CXTD22008). While other projects were deleted. You can find them in the second attachment (2. 78544--certificate of funding agency).

----2. We request that the first author make an audio file describing your final core tip. Acceptable file formats: .mp3, .wav, or .aiff. Maximum file size: 10 MB.

Response: Thank you very much for your review and guidance! we had made the audio file which you can find it in the third attachment (3. 78544-Audio Core Tip).

-----3. Any article describing a study (basic research and clinical research) involving human and/or animal subjects is required to have the institutional review board (IRB) name, whether institutional (part of the author(s)' academic/medical institution, such as the Oak Grove Children's Hospital Institutional Review Board) or commercial/independent/private (contracted for-profit organizations, such as the ClinicCare Coalition for Human Rights Institutional Review Board), stated explicitly

on the title page (it should be in native language).

Response: Thank you very much for your review and guidance! we had the certificate of Jiangxi university of Chinese Medicine Formula-pattern Research Centre (4. 78544-Institutional Review Board Approval Form or Document).

-----4. Further language polishing is required in order to meet the publication requirement (Grade A). Now, you are requested to send the revised manuscript to a professional English language editing company or a native English-speaking expert to polish the language further. When you submit the subsequent polished manuscript to us, you must provide a new language certificate along with it.

Response: Thank you very much for your review and guidance! we had invited the native English speakers from the MedSci language editing company to polish the whole manuscript. while the medsci had supplied the certificate of English editing. You can find it in the fifth attachment (5. 78544-Certificate of English editing)

-----5. Please download and complete the ‘The-ARRIVE-Guidelines’, Authors must state on the title page of the manuscript that the guidelines of the The-ARRIVE-Guidelines have been adopted (see attachment). Authors must upload the PDF version of the completed checklist to the system.

Response: Thank you very much for your review and guidance! according to the guidelines of The -ARRIVE-Guidelines, we had checked the whole text and made the new checklist of the manuscript. You can find it in the sixth attachment (6. 78544-The-ARRIVE-Guidelines checklist)

-----6. Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as “Manuscript No. -Figures.ppt” on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.

Response: Thank you very much for your review and guidance! we had provided all of the decomposable figure of figures in the PowerPoint file. You can find it in the 7th attachment (7. 78544---Figures)

-----7. Before final acceptance, 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: ...”. Please add secondary title to your figure legends in order to explain the figures more clearly.

Response: Thank you very much for your review and guidance! we had added the secondary title in the figure legend. You can find them in the figure legends part.(8 . 78544 the revised manuscript ---Auto Edited)

-----8. Your manuscript has been checked by CrossCheck. Please read the attached CrossCheck report for details. Our editorial policy states the overall similarity should be less than 30%, the overlapped section should be less than 5% in single papers, including author's own work.

Response: Thank you very much for your review and guidance! according the CrossCheck report, we revised the whole manuscript again. You can find it in the 9th and 10th attachment. (9 .78544 the revised trace of manuscript ----Auto Edited)(10 .78544 The CrossCheck report)

-----Please revise in the attached file "78544_Auto_edited" and reply within two weeks, thank you!

Response: Thank you very much for your review and guidance! We had revised and polished our manuscript in the file "78544_Auto_edited"