

Dear Editor,

We greatly appreciate the reviewers' comments and suggestions. We have revised the manuscript to provide a more scientifically sound article and have answered their questions here.

Reviewer #1

Q1: They used bioinformatics tools to analyze 2 publicly available microarray datasets (GSE92415, GSE87466) for core genes involved in UC and verified in vivo via DSS-colitis mouse model. Major concerns: 1) The author should clearly describe how they analyzed the microarray data. By using GSE92415, the authors stated that there were 162 UC samples. However, those samples were from both TNF- α inhibitor-treated and placebo-treated UC patients. Moreover, the response of the patients also varies. In the manuscript, it seems all those samples were combined and re-analyzed as "UC". In this case, the result did not correctly reflect UC vs. healthy conditions.

A: We are grateful to the reviewer for this question. Because of the current shortage of microarrays with samples from patients with UC using the same platforms, we chose the GSE92415 microarray dataset including patients with UC who were treated with a TNF- α inhibitor and placebo that may have resulted in an inaccurate depiction of the detailed scientific features of UC. I added this explanation to the discussion (paragraph 7, lines 8-11). However, we are currently conducting a multi-center, randomized, double-blind, controlled trial of 630 patients with active UC, and we believe it will help us obtain additional information about the features of UC. We will be glad to share our achievements with the journal and readers in the future.

Q2: The authors stated in the 'Methods' portion that they used 3.5% DSS to establish the colitis model, while in the discussion the DSS concentration was 4%. They need to be consistent.

A: Thank you very much for your comment. We apologize for our carelessness that caused this error. We used 3.5% DSS to establish this model, and I have changed the DSS concentration to 3.5% in the discussion.

Q3: The authors stated that they verified the transcription levels of CXCL13, NYP1R, and CXCR2 by qPCR using mouse colon tissues, rather than mucosa tissues which were used in the published microarray datasets. The mouse colon tissues contain submucosa, the muscle layer, and subserosa. The authors need to make it clear in their manuscript.

A: Indeed, we had not noticed this issue in the original version. You are correct that the

microarray data were obtained from human colonic mucosa, while RT-PCR analyzed mouse colon tissues, which contained the mucosa, submucosa, muscle layer, and subserosa. Thus, the bioinformatics results and results of the in vivo analysis produced a difference; this explanation has been added to the discussion (paragraph 7, lines 5-8). We will try to scrape the mucosa lightly and use the mucosal layer as much as possible in subsequent studies to solve this problem.

Q4: Please provide the full name of the abbreviations while they appear for the first time in the manuscript such as BP, CC, and MF.

A: Thank you very much for your comment. We apologize for our carelessness that led to this error. The full names of these abbreviations are provided in the introduction (paragraph 5, lines 4-5) and the full name of the 17 core genes are provided in the results section of the abstract, lines 3-8.

Q5: The authors cited Figure 5 in the text but the figure 5 was missing.

A: We apologize for the error. The manuscript includes 4 figures, and we included the data from Figure 5 in Figure 4.

Q6: In Abstract, AIM: “To identify by bioinformatics analysis and in vivo verification” should be corrected as “To identify by bioinformatics analysis and in vivo verification of”. -. In Abstract, CONCLUSION: “these reactions are core pathogeneses in UC” should be corrected as “these reactions are core features of UC pathogenesis”. -. And other grammatical errors throughout the text.

A: We are very sorry that the reviewer was not satisfied with the English language in the paper. We and editors at AJE have revised the language, including grammar, words, sentences and logic, throughout the article based on the suggestions.

Reviewer #2

Q1: This Ms is potentially informative and helpful for the management of UC. I have a few comments about it. #According to the text, the paper should have ‘Figure 5’. But according to the Ms file I have downloaded, it is nowhere found. I wonder if this is really missing or this is only a careless mistake. If this Ms is to be published, ‘Figure 5’ should be placed in the right place.

A: We apologize for the error. The manuscript includes 4 figures and the data from Figure 5 have been incorporated in Figure 4.

Q2: Figure 3, HE: The HE photos of higher magnification need to be shown for both blank and

colitis mice to clearly show the absence/presence of neutrophilic infiltration, cryptitis, and/or crypt abscess.

A: We are grateful for this tip. We will supply the original figures at a larger size, which may solve the fuzziness and facilitate editing. The photos cannot be uploaded now because the instruments have recently been moved to a new campus.

Q3: Tables 2, 3, 4, 5 'P-value': In the columns of 'P-value', there are many descriptions like '#E-#'. In understand that this kind of 'P-value' is just what the computer or software shows on the screen. But I guess, for most of the readers, this kind of descriptions of 'P-value' makes no sense. As long as these tables are about the genes tagged with $P < 0.05$, these columns of 'P-value' can be omitted.

A: Thank you very much for your comment. Columns listing the '*P*-values' in Tables 2 to 5 have been deleted for clarity.

Q4: The last sentence of the DISCUSSION, 'However...future': This sentence makes no sense, which is just a useless excuse. This should be erased.

A: Thank you for your great suggestion. We have deleted this sentence, and other useless statements like this were edited at the same time.

Q5: There are a number of grammatical errors or clumsy, 'difficult-to-understand' sentences throughout the text. Please check the Ms again and have it proofread by professionals. Ex #Abstract > background > line 1; a kind of inflammatory bowel disease > a kind of inflammatory bowel diseases #Abstract > background > line 4: unsatisfactory specificity > an unsatisfactory specificity? #Abstract > background > line 4: bioinformatics analysis > a bioinformatics analysis? #AIM: To identify by bioinformatics analysis and in vivo verification UC-related > To identify, by bioinformatics analysis and in vivo verification, UC-related? #INTRODUCTION, line 4-6, 'Because...Organization': This sentence is structurally wrong and cannot be understood. # INTRODUCTION, line 22-23, 'however...ignored': This sentence is hard to understand in this context. #etc, etc, etc...

A: We are very sorry that the reviewer was not satisfied with the English language in the paper. We and editors from AJE have revised the language, including grammar, words, sentences and logic, throughout the article based on the suggestions.