

We were most delighted to learn that our manuscript (64365) has been permitted to be revised for publication in the *World Journal of Gastroenterology*. All revised parts in the previous manuscript are highlighted in yellow. We have carefully considered the valuable comments provided by the reviewer and made efforts to improve the manuscript accordingly. We hope that the revised version of this manuscript will meet the standards required for publication.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes. 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes. 3 Key words. Do the key words reflect the focus of the manuscript? Yes. 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes.

→ Thank you for these comments. There is no question to answer, as I known.

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? NO. The suggestion is that the clinical significance of *Fusobacterium nucleatum* should be verified using patients' samples.

→ Thank you for this comment. We have a plan to verify these results using patients' samples.

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes. The authors provided a novel hypothesis that "a high abundance of *F. nucleatum* in the gastrointestinal tract could cause reduced NK cell activity". It is interesting to explore the underlying mechanism of *Fusobacterium nucleatum* in gastrointestinal tract and their potential relationship with the occurrence and development of colorectal cancers.

→ Thank you for your kindly comment on our study.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes. Yes. Yes.

→ Thank you for these comments. There is no question to answer, as I known.

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Yes.

→ Thank you for this comment. There is no question to answer, as I known.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes. 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes. 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? Yes. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes.

→ Thank you for these comments. There is no question to answer, as I known.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: In this study, Kim et al. demonstrated that high abundance of *Fusobacterium nucleatum* (fn) plays a critical role in gastrointestinal tract which reduces the host NK cells activity, and affects the pro-inflammatory cytokines in circulating levels, including IL-1b and TNF-A. These outcomes suggesting that Fn in colon could be a factor disrupting the immune system in the experimental mice. The authors also provided all the essential documents in terms of ethics approval and biostatistics reviews. Here are the comments/questions for the authors,

(1) Many studies confirmed that Fn can be found in colonic tissues. Could the authors also give a try in the detection of Fn colonic tissue by using qPCR approach?

→ Thank you for this comment. Unfortunately, we did not try to detect Fn in the colonic tissue using qPCR. This is a good suggestion, we will try to examine on next study according to your suggestion.

(2) Do IFN, IL-1b, and TNFa also higher in NK92 cells treated with Fn and the colonic tissues from the experimental mice, either mRNA or protein expression level?

→ Thank you for these comments. We did not check the IFN, IL-ab, and TNF-a in NK92 cells or colonic tissues treated with Fn. These could be limitations of our study.

(3) In Figure 3A, the authors should also provide the error bar of each point of the measurement groups. If can't, please mention it in the figure legend. The length of the colon from each measurement could also provide as a bar chart in Figure 3.

→ Thank you for these comments. We added the error bar in Figure 3A and 3B

(4) Could the author propose a mechanism in a combination of your finding and the existing literature in your discussion? Giving a graph could be better for the explanation, if possible.

→ Thank you for these comments. We added a potential mechanism in discussion and added a figure for an easier explanation (Figure 7).

(5) The authors could consider redrawing the graphs in color instead of black and white.

→ Thank you for this comment. We redrew the graphs in color (Figure 3,4,5,6) as your recommendation.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Comments In this article, the authors report the impact of *Fusobacterium nucleatum* in GI tract on NK cells. Abstract: Written well. Introduction and methods written well. The authors target the role of *Fusobacterium* excess and change in NK cell activity. Description about the role of *Fusobacterium* in CRC given. It is highly suggested to the role of NK cell activity in IBD, NASH with autoimmunity. As authors noted, the NK cells play a major role in tumor microenvironment with constant interactions with tumor progression. Reshaping the gut microenvironment is an area of intense interest to provide potential therapeutics in the future cancer prevention. The figures and graphs are appropriately noted. Please provide limitations of this study.

→ Thank you for this comment. We added the limitations of this study in Discussion.

Reviewer #4:

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The overall quality of this study is well. The experimental methods and results are described clearly. But the possible signaling pathways involved should be discussed.

→ Thank you for this comment. We added a potential mechanism in discussion (summary).

4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

→ [We rechecked our revised manuscript by a native-English speaker.](#)

5 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: 1 Scientific quality: The manuscript describes a basic study of the impact of *fusobacterium nucleatum* in gastrointestinal tract on natural killer cells. The topic is within the scope of the WJG. (1) Classification: Two Grades B, Grade C and Grade D; (2) Summary of the Peer-Review Report: The overall quality of this study is well. The experimental methods and results are described clearly. The questions raised by the reviewers should be answered; (3) Format: There are 6 figures; (4) References: A total of 33 references are cited, including no references published in the last 3 years; (5) Self-cited references: There is no self-cited reference; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A, two Grades B and Grade C. A language editing certificate issued by World Editing was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate. The Institutional Animal Care and Use Committee Approval Form is not provided. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by National Research Foundation of Korea grant funded by the Korea government. The topic has not previously been published in the WJG.

5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

→ [We uploaded the approved grant application form.](#)

(2) The authors did not provide original pictures. Please 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

→ [We uploaded original figures using PowerPoint.](#)

(3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

→ [We added the article highlights section.](#)

6 Recommendation: Conditional acceptance.

(2) Editorial office director:

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, 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. Before its final acceptance, please upload the primary version (PDF) of the Institutional Review Board's official approval in official language of the authors' country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

→ Thank you for this comment. We previously uploaded the Institutional animal care and use committee statement. In our study, no human experiments were conducted or no human samples were used. Therefore, we did not acquire the approval of IRB. We added this sentence in the manuscript.