

Dear Editor of World Journal of Clinical Cases

Authors would like to thank reviewers for their careful review of our manuscript (No.51430) and providing us with their comments and suggestions to improve the quality of the manuscript. We have carefully considered these comments and revised the manuscript accordingly. We hope that the manuscript has now been improved by these revisions and hope that it is suitable for publication in WJCC. Point-by-point responses to comments are illustrated as following.

With best regards

Ebrahim Eftekhari

Reviewer No ID 02841708

Comment 1: Author should delete some introduction before publication.

Author's Response: In introduction section some sentences were omitted or changed.

This sentence was omitted in the introduction: "Different tissues in the human body including colon and rectum are involved in cancer, where any abnormality can cause colorectal cancer"

Some other highlighted sentences were condensed or changed.

Reviewer No ID 02505493

Comment 1: The text contains the terms UFA and UFAs, as well as PUFA and PUFAs, with the same meaning. The authors must carefully correct accordingly.

Author's Response: The text was read carefully. The word UFA was omitted and PUFA was correctly used.

Comment 2: The authors must carefully examine the references cited, i.e., ref 53 does not correspond to page 6, line 2.

Author's Response: The refe. 53 was checked again and it was not true. It was mistaken by another reference. So the new reference was inserted. The new reference 53 was highlighted in reference section.

Comment 3: Page 12, lines 20-22: There is misleading information, or the authors have confused the data presented in ref 104.

Author's Response: The refe. 104 was not correct. It was mistaken by another reference. The presented information was true. The correct reference 104 was inserted. The new reference 104 was highlighted in reference section.

Comment 4: The presentation of “Epigenetic modification by PUFA” and especially of “PUFA and possible DNA methylation mechanisms in CRC” contain a lot of information inserted in text like a list without any continuity and criticism by the authors. Moreover, this information is rather incomplete. For example, at page 13, lines 20-22, a sentence that informs for first time on hydroxymethylation of DNA by ω -3 PUFAs was inserted without any reference (although seven lines before, the study presenting the hydroxymethylation of DNA was cited). The use of one or two Tables replacing that text would be helpful.

Author’s Response: in “Epigenetic modification by PUFA” section, the effect of PUFA on methylation status of genes in different cell lines (human cord blood leukocytes, U937 leukemic cells, neuroblastoma cell) and mice were reported and discussed. The appropriate reference for DNA hydroxymethylation and ω -3 PUFAs was added (page 14, line 9). Additionally the new reference was added to this section (refe. 104).

In “PUFA and possible DNA methylation mechanisms in CRC” section, at first the anticancer property of PUFA against colorectal cancer was discussed. The number of studies in this regard was limited. The conclusion of this part was added (Page 14, lines 17-19). In other part of this section, the effects of PUFA on DNA methylation processes of colorectal cancer was presented. Six possible mechanisms for the effects of PUFA on DNA methylation processes of colorectal cancer were extracted from different articles and discussed in details. We prefer to use text instead of table, because for every mechanism we have to explain the mechanism at first and then providing the supporting related works.

Comment 5: Minor points 1. Page 3, line 28: It is better to write ‘maintenance of methyltransferase activity, which plays...’. 2. Page 4, line 2: It is better to write “tissues, such as breast and hepatocellular carcinomas, as well as cell lines, have elevated”. 3. Page 4, line 3: Replace “Different” with “Various” or “A plethora of”. 4. Page 4, line 20: Replace “is” with “are”. 5. Page 11, line 23 and Page 14, line 26: Do not start new paragraph.

Author’s response: all of these comments were included in text and highlighted.