

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 79346

Title: Prevention of malignant digestive system tumors should focus on the chronic inflammation

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00504362

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Chile

Author's Country/Territory: China

Manuscript submission date: 2022-10-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-10 11:55

Reviewer performed review: 2022-11-10 13:02

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting manuscript, however, this reviewer has some concerns: The section on MECHANISM OF CHRONIC INFLAMMATION IN THE OCCURRENCE OF DIGESTIVE SYSTEM MALIGNANT TUMOR lacks a more extensive and detailed overview of the mechanistic insights on how chronic inflammation triggers relevant phenotypical changes toward the malignant transformation. It is not enough to mention a couple of enzymes and transcription factors, chronic inflammation is much more complex than what is stated in this section. This reviewer missed a section about the contributions of gut microbiota. Compelling evidence are supporting that alteration of gut microbiota, particularly the dysbiosis condition might produce enrichment in pro-inflammatory opportunistic pathogens and a decrease in butyrate-producing bacteria, which may lead to an imbalance in intestinal homeostasis that could ultimately lead to tumor formation. Nothing is mentioned about the contribution of *Salmonella typhi*, which is now considered an oncogenic bacteria that alter the human immune system and thus contributes to gallbladder cancer. *Helicobacter pylori* must be written in italics. appears as *H. pylori* and sometimes as *helicobacter pylori*. Please abbreviations must be defined in the first use.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503405

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Senior Lecturer, Senior Scientist

Reviewer's Country/Territory: Hungary

Author's Country/Territory: China

Manuscript submission date: 2022-10-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-11 06:26

Reviewer performed review: 2022-11-11 10:48

Review time: 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

Based on the title of the article, the authors undertook to summarize a very exciting and hot topic. At the same time, the description contains many misleading and incorrect statements, poorly worded sentences, and errors in the interpretation of the relationship between inflammation and tumorigenesis. In the introductory part, it should have been discussed which mechanisms can be influenced by inflammation in the GI tract to cause cancerous changes. The authors do not even mention the protumor and antitumor effects of the innate immune system, autophagy, inflammasome activation, and the plexin-semaphorin system in relation to inflammation-carcinogenesis. Mentioning these would form the basis of how it is possible to not therapeutically influence chronic inflammation with a pro-tumor effect. These sentences are false: „In acute inflammation, immunosuppression occurs after tissue repair or ends inflammation by eliminating pathogens and necrotic cells. However, in chronic inflammation, due to the lack of normal negative feedback mechanisms, immunosuppression permanently persists." Immunosuppression is not equal to anti-inflammatory immune processes. „Chronic inflammation usually triggers colon cancer through three main mechanisms, namely chromosome instability [14], microsatellite instability, and CpG island methylation." The tumorigenesis of sporadic and colitis-associated CRCs is different. This sentence is not correct. „Upon the time point when inflammation affects DSMT pathogenesis, three types can be distinguished: chronic inflammation before tumorigenesis, inflammation caused by tumor and inflammation induced by treatment." These sentences are not professionally written. Instead of these classifications, one can distinguish between inflammation-associated tumorigenesis and tumor-associated inflammation. Treatment-

induced inflammation is not the correct phrase. Though the topic is very interesting, the manuscript is not acceptable for publication in its current form.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04062289

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Research, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

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Reviewer chosen by: Dong-Mei Wang

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Reviewer performed review: 2022-12-20 07:07

Review time: 5 Days and 7 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input checked="" type="radio"/>] Yes [<input type="radio"/>] No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

This paper is a well-written review article summarizing oncological role of chronic inflammation in carcinogenesis and tumor progression of gastrointestinal malignant tumor. The treatment strategy for cancers with a chronic inflammatory background is very important because prevention is possible by treating the cause of the chronic inflammation. Those involved in the treatment of gastrointestinal cancers need to be knowledgeable about cancers with a chronic inflammatory background, and this review article is useful from that perspective. As noted in Figure 2 of this paper, the strongest and most significant message seems to be that medical intervention early in life for chronic inflammation can reduce the risk of subsequent carcinogenesis. This paper clearly summarizes the impact of chronic inflammation in colorectal, hepatocellular, and gastric cancer and its preventive measures, and no special additions or corrections seem necessary.