

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 89067

Title: Inflammatory response in gastrointestinal cancers: Overview of six transmembrane epithelial antigens of the prostate in pathophysiology and clinical implications

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05769914

Position: Peer Reviewer

Academic degree: PhD, MD

Professional title: Professor, Researcher, Doctor

Reviewer's Country/Territory: Mexico

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-27 16:51

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <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 checked="" 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

The manuscript by Fang et al. entitled “The inflammatory response in gastrointestinal cancers: an overview of STEAPs as novel biomarkers in pathophysiology and clinical implications”, describes the relationship between inflammation and the implications of STEAPS in gastrointestinal cancers. The paper is interesting; however, it needs major corrections.

- The writing of the manuscript needs to be reviewed by a native English speaker because it has grammatical errors (some verbs and words are written incorrectly; e.g., was exposed for...).
- The abstract section should be focused on inflammation and STEAPs implications in gastrointestinal cancers. For instance, the main effects of the inflammatory process and STEAPs (processes that inhibit or activate to promote the development of gastrointestinal cancers).
- In vivo is written in different ways, please write only “in vivo”.
- In the keywords section, the word treatment should be eliminated because the manuscript does not contain this information.
- In the core tip

section, systematic review is used incorrectly due to this manuscript is only a review.

-In the introduction section, the authors should define which types of gastrointestinal cancers are included in the paper. -The following information should be reviewed to confirm the prevalence of the cancers. In addition, the authors should include that this data is from the United States. "Among them, colorectal cancers (CRCs) are not only the fourth rank as the third and sixth causes of cancer-related deaths worldwide, respectively [1]." -In the introduction section, the molecular mechanisms or pathological processes caused by inflammation that promotes the different types of gastrointestinal cancers should be addressed. -The next information is already considered in the abstract section, in fact it is exactly the same " The gastrointestinal tract was exposed to diverse food and/or drugs daily, which may be related to various degrees of inflammatory response and kinds of diseases." -In the following paragraph, please add another reference related to cancer because the reference 6 is about skin disorders: " Recently, the six-transmembrane epithelial a..... has been associated with the overexpression of a range of proinflammatory cytokines [6]," -In the introduction section, please add more information about STEAPs related to different types of gastrointestinal cancers, such as how they promote or inhibit cancer progression.

-There is no information on the molecular weight of STEAP1 in the references 11 and 14, please add another reference: "STEAP1 is the first reported STEAP family member with a molecular weight of 39.9kDa and an intramembrane heme binding site [11, 14]." -The Rosman folding motif is not mentioned in the references 18 and 19, please add another reference: "he N-terminus of STEAP2-4 (except for STEAP1) have the Rosman folding motif, which is thought to be vital for binding nucleotides such as flavin adenine dinucleotide (FAD) [18, 19]." -The acronym DMT1 is not defined correctly, please review their definition, thus the word iron should be eliminated: "divalent metal-iron transporter 1 (DMT1)". -The reference 25 is not appropriate for the next paragraph:

“STEAP3 co-localizes with Tf, TfR1, and divalent metal-iron transporter 1 (DMT1) to participate in iron-uptake mediated by transferrin endosome in erythroid cells [25]”. -In the heading “THE STRUCTURAL CHARACTERISTICS OF STEAP FAMILY MEMBERS”, please only add information related to the structural characteristics of the STEAPs; for example, the following information is not related to the structural characteristics of the STEAPs: “Latest studies reported that STEAP3 is up-regulated in non-alcoholic fatty liver disease (NAFLD) and that its overexpression.....regulating liver ischemia-reperfusion injury, hepatocellular carcinoma, myocardial hypertrophy and other diseases [26].” -In figure 2, what do the colored regions and the acronym TM mean?, please add this information in the figure legend. -In the heading “INFLAMMATORY RESPONSE OF STEAPS IN PHYSIOLOGICAL AND PATHOLOGICAL PROCESSES”, please focus this section with the inflammatory response of STEAPs. -Please add the name of proinflammatory cytokines as examples in the following phrase: “.....revealing a positive association between STEAP1 and STEAP4 with in vivo proinflammatory cytokines in several neutrophil-driven diseases in humans.” -The authors should check reference 57 because it does not relate to the information in the next paragraph: “The latency of Hp leads to a variety of changes in the gastric mucosa, such as gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and eventually cancer [57, 58].” -The references 63 and 64 are not related to gastric cancers: “In the acute lung injury model caused by sepsis,and restoring mitochondrial morphology [63], while in obesity, anti-STEAP4 antibodies can..... insulin-induced glucose uptake [64].” -With respect to the following information: “CRC is the second most common cause of cancer death in the United States and other developed countries, with more than 1 million cases worldwide annually [69].” The reference 69 is from 2009, please update the reference and data. -Please review again if STEAPs are involved in energy metabolism, how do

STEAPs regulate energy metabolism?: “As members of metalloreductases, STEAPs are involved in energy metabolism and iron/copper homeostasis [79].” -In the following paragraph, the reference 89 is from 2001, please update it. I recommend the next good reference (PMID: 36612019) for this interesting paper. -Please state the units for the value 1.18 (mGy/MBq?): “Another research group constructed and the highest mean absorbed doses to the normal organ was in the liver as 1.18 [95].” -The authors should check reference 98 because it does not relate to the information in the next paragraph: “Interestingly, after HCV infection, STEAP3 was found to be, as a potential monitoring biomarker for the development of HCC [98].” -In table 1, please use assigned numbers as references instead of PMID numbers, because it is easier to identify them in the references section. The title should be restructured as “The function/mechanism of STEAPs involved in GICs”, because there is little information on the inflammatory response. In addition, all acronyms used in this table should be defined in the table legend. -In the next heading: “THE CLINICAL IMPLICATION OF STEAPS IN GIC”, this section does not have enough information with this approach. -In the next paragraph the reference 113 does not belong to Cherl: “ Scherl et al. identified transferable IgA-coated *Odoribacter splanchnicus*and production of SCFAs, resulting in limitation of colitis [113].” -Is there a relationship between supplementation of Vitamin A and STEAPs expression?: “The supplementation of Vitamin A also ameliorates ulcerative colitis in a gut microbiota-dependent manner, which restores the intestinal barrier and inhibits inflammation [114].”

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Reviewer's code: 03261315

Position: Editorial Board

Academic degree: FACE, PhD

Professional title: Academic Research, Chief Doctor, Doctor, Full Professor, Postdoc, Professor, Senior Researcher

Reviewer's Country/Territory: Romania

Author's Country/Territory: China

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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
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Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <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

The abstract did not summarize the study and it is too long. The introduction does not highlight the issue. There are a lot of inadvertence. Here are few examples: Do you mean that CRC and GC are both the 3rd cause of cancer-related death in the world? "Among them, colorectal cancers (CRCs) are not only the fourth most common malignancy but also the third main cause of cancer-related death in the world. Meanwhile, gastric cancers (GCs) and esophageal cancers (ECs) rank as the third and sixth causes of cancer-related deaths worldwide, respectively [1]. "Although effective colonoscopy and upper endoscopy screening can detect polyps and precancerous lesions in the gastrointestinal tract, many patients are still at an advanced stage for their first diagnosis, and the prognosis is poor with existing treatment methods [2]. I disagree, there is a huge differentiation between CRC and GC in terms of screening and diagnosis. The authors extracted false conclusions from different studies, some



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of them are not in concordance with the issue or subject. For example: "In the acute lung injury model caused by sepsis, inhibition of STEAP1 reduced the inflammatory response and ROS production, improving cell viability and restoring mitochondrial morphology [63], while in obesity, anti-STEAP4 antibodies can cause increased ROS level and decreased cellular ATP production, resulting in reduced insulin-induced glucose uptake [64]. These investigations indicate the potential role of STEAPs in inflammatory response for Hp-related GC. " ?????? I do not understand, the authors rely on which studies??? Are the acute lung injury, obesity, Hp and GC related? The paper is too long, is not clearly written, there are some misunderstandings. From my point of view the paper is not suitable for the journal .

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" 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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



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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
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SPECIFIC COMMENTS TO AUTHORS

-inflammatory process, change proces to processes -disassociation, change disasociation
to dissociation