

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Oncology*

**Manuscript NO:** 85687

**Title:** Immune responses of six-transmembrane epithelial antigen of the prostate 4 functions as a novel biomarker in gastric cancer

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03270609

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-05-10

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-05-10 08:29

**Reviewer performed review:** 2023-05-18 19:28

**Review time:** 8 Days and 10 Hours

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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input 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 checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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

Manuscript NO: 85687 Title: The immune responses of STEAP4 functions as a novel biomarker in gastric cancer Gastric cancer remains a serious medical problem. Despite the decrease in the incidence of gastric cancer, mortality from this pathology remains high. This is primarily due to late diagnosis and low efficiency of systemic treatments. In this regard, the search for new prognostic and predictive markers remains relevant. The authors propose to use the assessment of STEAP4 expression in tumor tissue as such a promising marker. The association of the marker with immune and stromal responses suggests that STEAP4 may play an important role in the regulation of the tumor immune microenvironment. Thus, STEAP4 can be used as a prognostic biomarker in gastric cancer and a potential target for the treatment of this pathology. The manuscript is written in good English. Tables and figures complement the text and contribute to its better perception. Despite the relevance of the study to the authors, there are several inaccuracies in the manuscript, mostly of a technical nature, that should be corrected.

Abstract. Incorrect sentence: "The expression level of STEAP4 in 96 GC patients and adjacent non-cancerous samples was characterized by immunohistochemistry." Perhaps

the authors meant that "The expression level of STEAP4 was characterized by immunohistochemistry in tumor and adjacent non-cancerous samples in 96 GC patients" Materials and methods Considering that the analysis is based on the stratification of cases with high and low expression of STEAP4, the methodology for assessing the expression of the marker should be given in its entirety. In this case, it is not entirely correct to provide a link to an earlier work (Fang ZX, 2022). It is also necessary to indicate what sum of points was used to divide the samples into cases with high and low expression of the marker. It would be optimal if the authors illustrated all variants of the STEAP4 expression level (no, light yellow, brown yellow, and dark brown). In addition, it is not entirely clear if the authors observed dark brown staining (was scored as 3) in the samples, why the image with light brown yellow coloration was chosen as a representative image of high expression. Table 2. "Lymph node invasion", the string "Yes" - the amount of interest must be equal to 100.

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**Peer-review model:** Single blind

**Reviewer's code:** 05751232

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

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**Reviewer chosen by:** AI Technique

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**Review time:** 1 Hour

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

<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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

该研究整体设计一般，STEAP4 并非胃癌的特异性标志物，可能在其他的肿瘤中也有高表达，对于胃癌特异性不强，由此研究团队得出结论过于片面，不推荐优先发表。

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**Peer-review model:** Single blind

**Reviewer's code:** 03259131

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Surgeon, Surgical Oncologist

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

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**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-05-26 17:37

**Reviewer performed review:** 2023-06-01 05:41

**Review time:** 5 Days and 12 Hours

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
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
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Review comments WJG-85687\_reviewer. It is my great honour and pleasure to review such an interesting manuscript. The authors tried to prove that six-transmembrane epithelial antigen of the prostate 4 (STEAP4) serves as a potential therapeutic target for gastric cancer(GC) to improve immune infiltration, as well as a prognostic biomarker for judging the prognosis and immune infiltration status of gastric cancer. This study is retrospectively analyzed by using the immunohistochemistry and the clinical data. There are some limitations in this study as below; 1. This data is only retrospectively assessed by a single institute analysis. 2. Statistically, this study is performed by a univariate, not multivariate analysis. 3. There is no data concerning the chemotherapeutic regimens and their effects. 4. A total of 96 individuals are enrolled in this study, →I respect the authors' efforts of collecting the samples. However, the sample size is not enough. Cut off level of STEAP4, The authors should disclose how the cut off level was determined. Please show the ROC, etc. Table2, In order to evaluate the clinicopathological parameters in gastric cancer (GC) patients, at least, serum CEA, serum CA19-9 and Ki67 labeling index, etc. are needed in this table. STEAP4



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should be evaluated comparing with the conventional useful biomarkers. The prognostic value of STEAP4 in GC Survival analysis, The authors should disclose the number, the methods, the immunoreactivity, chemotherapy regimens, backgrounds, etc. It is difficult to read. Above all, this manuscript is interesting. However, the present manuscript needs some revisions for the publication of "World Journal of Gastroenterology".