

## PEER-REVIEW REPORT

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

**Manuscript NO:** 78685

**Title:** Comprehensive analysis of the potential role and prognostic value of sine oculis homeobox homolog family in colorectal cancer

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

**Peer-review model:** Single blind

**Reviewer's code:** 06257301

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

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

**Manuscript submission date:** 2022-07-09

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-07-11 12:31

**Reviewer performed review:** 2022-07-11 12:41

**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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

The author has done a reasonably good work. My only suggestion: Please include number of Ethical approval.

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

**Peer-review model:** Single blind

**Reviewer's code:** 06254455

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

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

**Manuscript submission date:** 2022-07-09

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-07-10 08:32

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**Review time:** 4 Days and 3 Hours

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
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<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
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## SPECIFIC COMMENTS TO AUTHORS

This manuscript aimed to explore the expression pattern of 6 SIXs in colorectal cancers and their relationship with the clinicopathological parameters of CRC patients. This study suggested that SIX4 may be a potential therapeutic target for treatment of CRC patients. It is an interesting article; however, the manuscript needs some revisions that should be considered. There are grammatical errors, please carefully revise the English language throughout the text and correct all the trivial imperfections.

**Introduction:** In my opinion, the authors have addressed the gaps in the current literature to justify the current review very well and made a strong statement on how their study adds to the literature, however, I suggest trying to condense the third paragraph or reduce the amount discussed. It would be better to be more focused on the prognostic value of SIXs in CRC and explain the previous studies results about this topic.

**Method:** How did the authors calculate the sample size? Are 87 and 93 samples statistically enough? The authors did not provide references on how they evaluated the ranks of RNA and protein expression.

**Discussion:** -The discussion is at a very superficial level. It is short and didn't compare the results with the findings from the other studies properly. In fact, "discussion" doesn't add any useful information to the manuscript. The first paragraph of the discussion should address the aim and important results of the study. The results of the study should be discussed one by one, and it is suggested to use the other studies to support your biochemistry claims and hypothesis and extend the objectives of your discussion. Why and under which mechanisms SIX4 can act as a tumor-promoting factor in the intestinal tract? and please discuss the expression pattern of the other SIXs clearly (the author can use more references for the raised claims and hypothesis). Moreover, the

strengths and limitations of the present study should be mentioned and discussed. Also, it would be more interesting to read some sentences suggesting what factors should future studies consider?

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

**Peer-review model:** Single blind

**Reviewer's code:** 03478911

**Position:** Associate Editor

**Academic degree:** PhD

**Professional title:** Chief Technician, Executive Vice President, Research Assistant Professor

**Reviewer's Country/Territory:** South Korea

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

**Manuscript submission date:** 2022-07-09

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-07-09 22:29

**Reviewer performed review:** 2022-07-18 01:27

**Review time:** 8 Days and 2 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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

<b>Re-review</b>	[ <input checked="" type="checkbox"/> ] Yes [ <input 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

It seems that a retrospective study was conducted on the potential role of the Sine Oculis Homeobox Homolog (SIX) Family in colorectal cancer. The study is interesting, but the following issues need to be addressed. 1. The etiological and demographic information of the analyzed patient should be provided in a separate table. The expression pattern of SIX4 according to the stage may vary, and it will be useful to present it as a potential marker for an advanced stage of colorectal cancer. 2. The colorectal cancer-associated mechanism of SIX1 is well established rather to other types of SIXs. In this study, the rationale for selecting SIX4 as a major target for CRC prognosis is unclear. There was also no evidence suggesting that the expression of SIX4 was higher than that of other types of SIXs in the analyzed colorectal cancer tissues. In Figure 3, further, the difference in OS by SIX1 is larger than in other types of SIXs. 4. The potential role of SIX4 in colorectal cancer as a potential biomarker has already been reported (PeerJ. 2017 May 30;5:e3394.). This is pointing out that it cannot be freed from the issue of novelty.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Peer-review model:** Single blind

**Reviewer's code:** 06254455

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

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

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**Reviewer chosen by:** Jing-Jie Wang

**Reviewer accepted review:** 2022-08-31 10:20

**Reviewer performed review:** 2022-08-31 10:30

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous





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statements

Conflicts-of-Interest: [ ] Yes [Y] No

## SPECIFIC COMMENTS TO AUTHORS

I have no comments.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** South Korea

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

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<b>Scientific quality</b>	<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
<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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



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#### **SPECIFIC COMMENTS TO AUTHORS**

All concerns have been well addressed. There is no comment to raise.