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PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 82568

Title: Molecular Signalling in Cancer stem cells of tongue squamous cell carcinoma: therapeutic implications and challenges

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02929648
Position: Editorial Board
Academic degree: PhD
Professional title: Academic Research, Director
Reviewer's Country/Territory: China
Author's Country/Territory: India

Manuscript submission date: 2022-12-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-03 01:25

Reviewer performed review: 2023-01-03 01:48

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty

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Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Good article.

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Peer-review model: Single blind

Reviewer's code: 03850246
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: India

Manuscript submission date: 2022-12-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-12 08:10

Reviewer performed review: 2023-01-12 08:33

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Authors summarize the current understanding of molecular signalling associated with the maintenance and regulation of CSCs in tongue squamous cell carcinoma in order to emphasize the need to get deeper understanding to unravel novel targets. The paper is focused on a relevant topic. The manuscript is clear and presented in a well structured manner. I kindlt ask to complete the discussion considering the role of PD L1 in this context with the important questions/implications related to the progression from dysplasia to carcinoma and the management of the specimens as well as the assessement by the pathologist, given the important effects on prognosis and therapy. In this regard quote: - Atlas of PD-L1 for Pathologists: Indications, Scores, Diagnostic Platforms and Reporting Systems. J Pers Med. 2022 Jun 29;12(7):1073. doi: 10.3390/jpm12071073. PMID: 35887569 - PD-L1 in oral squamous cell carcinoma: A key biomarker from the laboratory to the bedside. Clin Exp Dent Res. 2022 Jun;8(3):690-698. doi: 10.1002/cre2.590. Epub

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2022 May 20. PMID: 35593124 - PD-L1 evaluation in head and neck squamous cell carcinoma: Insights regarding specimens, heterogeneity and therapy. Pathol Res Pract. 2021 Oct;226:153605. doi: 10.1016/j.prp.2021.153605. Epub 2021 Sep 1. PMID: 34530257 - Prevalence of PD-L1 expression in head and neck squamous precancerous lesions: a systematic review and meta-analysis. Head Neck. 2020 Oct;42(10):3018-3030. doi: 10.1002/hed.26339. Epub 2020 Jun 22. PMID: 32567746

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PEER-REVIEW REPORT

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Manuscript NO: 82568

Title: Molecular Signalling in Cancer stem cells of tongue squamous cell carcinoma: therapeutic implications and challenges

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06486190

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: India

Manuscript submission date: 2022-12-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-16 11:03

Reviewer performed review: 2023-01-25 12:26

Review time: 9 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty

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Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This article focuses on tongue squamous cell carcinoma and summarizes signal transduction pathways and markers related to cancer stem cells. It introduces the findings related to these while citing relatively recent papers and I believe that they are of a certain value. 1. Does CD44v8 exist? (page 4 line 7) Reference No.6 describes CD44v8-10, which is a variant containing three consecutive exons v8, v9, and v10. 2. References should be correctly listed. Papers that should be described with Article ID are not described as such. Examples: References Nos. 27, 28, 32, 33, 34, 38, 41, 43, 52, 55, 76, and 85. Reference No. 7 does not include the name of the journal. The doi of reference No. 9 is incomplete. Reference No. 69 has no page numbers or article ID. 3. The figures are all too general. It should relate to the events observed in tongue squamous cell carcinoma (TSCC), and the diagram should be made so that the role of each signal pathway in TSCC can be understood.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 82568

Title: Molecular Signalling in Cancer stem cells of tongue squamous cell carcinoma: therapeutic implications and challenges

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03850246

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: India

Manuscript submission date: 2022-12-22

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2023-03-14 09:01

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Reviewer performed review: 2023-03-14 09:04

Review time: 1 Hour

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

all the questions/issues raised have been managed by authors in a proper way with the R1

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Stem Cells*

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06486190

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: India

Manuscript submission date: 2022-12-22

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2023-03-14 09:53

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Reviewer performed review: 2023-03-16 00:59

Review time: 1 Day and 15 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The points pointed out in the previous report have been improved, and the manuscript is considered acceptable. There are some typos in the text, which I recommend be corrected. Page 1, line 10 & 15: Adavanced -> Advanced Page 5, line 16: mostspecific -> most specific Page 7, line 14 & 18: HNSSC -> HNSCC Page 8, line 8: Krueppel -> Krüppel Reference 29: The trailing "IDENTIFICATION" should be removed. Regarding the figure, the only thing that concerns me is the illustration of the transmembrane receptors. Frizzled and SMO are thought to be 7-transmembrane type receptors, and Ptch is thought to be a 12-transmembrane type receptor, so I think it would be better if the illustration reflected these facts.