



## PEER-REVIEW REPORT

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

**Manuscript NO:** 54976

**Title:** CITED2 and the modulation of the hypoxic response in cancer

**Reviewer's code:** 00506472

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor

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

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

**Manuscript submission date:** 2020-02-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-02-27 21:37

**Reviewer performed review:** 2020-02-28 07:03

**Review time:** 9 Hours

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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>Re-review</b>	<input 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



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

It is a well written paper on CITED2 effect on modulation of the hypoxic response in cancer. No comments



### PEER-REVIEW REPORT

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

**Manuscript NO:** 54976

**Title:** CITED2 and the modulation of the hypoxic response in cancer

**Reviewer's code:** 02687374

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

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

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

**Manuscript submission date:** 2020-02-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-03-02 11:21

**Reviewer performed review:** 2020-03-08 11:27

**Review time:** 6 Days

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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>Re-review</b>	<input 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



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

This manuscript systematically reviewed CITED2 as a negative regulator of HIF with demonstrated roles in various types of cancer. The authors compile the roles reported for CITED2 in health and disease, namely through the modulation of HIF activity, and also discuss the various context-dependent roles for CITED2 in cancer. As a result, the authors concluded that a better understanding of the interplay between CITED2 and HIF-1 $\alpha$  may potentially lead to novel strategies for the development of innovative targeted therapies. From the results and conclusions of this study, the authors have comprehensively and extensively introduced the regulatory role of CITED2 in physiology and disease, especially in cancers, which highlights the important role of CITED2 in cancer-targeted therapy. It will give readers more inspiration. In short, the structure of this article is clear, the introduction is detailed, and references are more suitable. I recommend its publication in your journal.



## PEER-REVIEW REPORT

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

**Manuscript NO:** 54976

**Title:** CITED2 and the modulation of the hypoxic response in cancer

**Reviewer's code:** 02460781

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Attending Doctor, Postdoc, Surgeon

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

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

**Manuscript submission date:** 2020-02-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-03-02 09:15

**Reviewer performed review:** 2020-03-08 12:44

**Review time:** 6 Days and 3 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 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 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**

The article reviewed CITED2 and the modulation of the hypoxic response in cancer. It is informative in the field. This is a good review. It would be better if the authors analyzed the mechanism of the different functions in the context and type of tumors.



## PEER-REVIEW REPORT

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

**Manuscript NO:** 54976

**Title:** CITED2 and the modulation of the hypoxic response in cancer

**Reviewer's code:** 03465354

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** United States

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

**Manuscript submission date:** 2020-02-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-03-04 21:07

**Reviewer performed review:** 2020-03-10 18:40

**Review time:** 5 Days and 21 Hours

<b>Scientific quality</b>	<input checked="" 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 type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 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**

The proposed review manuscript by Fernandes et al. summarizes the role of CITED2 (CBP/p300-interacting transactivator with Glu/Asp-rich C-terminal domain 2) as a hypoxia modulator in cancer. Since CITED2 functions as hypoxia-inducible factor (HIF) competitive function inhibitor and it is known that it plays a role in the maintaining of cancer stemness, researching this topic is of importance in the oncology field. The authors of the manuscript provided a well-organized systematic introduction of CITED2 classification and function and drew the major signaling pathways activated by CITED2 as well as described the major molecular mechanisms by which CITED2 modulates the hypoxic response in normal physiology and pathological conditions. Particular emphasis in the manuscript was placed on the role of CITED2 in cancer, as the authors devoted separate sub-chapters to the different types of cancer. In my opinion as a peer reviewer, the present review is a well-organized summary of the literature. I do not find any issues with the manuscript and I do not have any major comments, except for the minor recommendation listed below. Minor comments: - Figure 1: The authors may consider increasing the font size of O<sub>2</sub>, HIF-1 $\alpha$  and HIF-1 $\beta$  in the figure, since after the figure scales down, these labels will not be readable.