

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 54891

Title: Energy metabolism in cancer stem cells

Reviewer's code: 00004010

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-02-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-02-25 15:12

Reviewer performed review: 2020-03-06 15:43

Review time: 10 Days

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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 Grade E: Do not publish |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 type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input 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 |



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SPECIFIC COMMENTS TO AUTHORS

Energy metabolism in cancer stem cells Authors: Zhu X et al; W J Stem Cells The current review article by Zhu et al summarizes the metabolic characteristics of cancer cells and cancer stem cells (CSCs) and the mechanisms of the metabolic interplay between the TME (tumor micro environment) and CSCs, and discusses clinical implications of targeting CSC metabolism. It has been reported that CSCs exhibit a unique metabolic phenotype compared to non-CSCs. It has been demonstrated that non-CSCs metabolize glucose to produce lactate through glycolysis even in the presence of sufficient oxygen. However, unlike non-CSCs, CSCs are thought to be highly glycolytic or oxidative phosphorylation (OXPHOS)-dependent depending on the niches where the CSCs are located. Thus, targeting the metabolism of CSCs could be a new strategy for CSC treatment. Although the focus of the current review article is somewhat narrow, it is nonetheless an important area of investigation, one that has not been reviewed extensively and is likely to have a large and broad audience. In general, the review article is informative and would be useful to investigators pursuing studies on cancer. However, I have a few concerns which the authors may like to address, which will strengthen the manuscript. Although the authors have briefly discussed the therapeutic strategies for CSCs, it is not clear how inhibition of glycolysis or glucose deprivation lead to the death of non-CSCs. The authors need to expand on this issue. Although the current review article provides considerable information about energy metabolism by CSCs and non-CSCs, the authors failed to interpret the data. Lastly, the authors need to add a section on "Future Direction".