

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 64960

**Title:** Epigenetic regulation of autophagy: A key modification in cancer cells and cancer stem cells

**Reviewer's code:** 05315572

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chief Doctor, Professor

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

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

**Manuscript submission date:** 2021-02-25

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-03-17 07:10

**Reviewer performed review:** 2021-03-18 09:47

**Review time:** 1 Day and 2 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 Grade E: Do not publish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 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>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



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

We appreciate the manuscript and agree to accept its publication

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 64960

**Title:** Epigenetic regulation of autophagy: A key modification in cancer cells and cancer stem cells

**Reviewer's code:** 05848970

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Assistant Professor

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

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

**Manuscript submission date:** 2021-02-25

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-02-26 21:41

**Reviewer performed review:** 2021-03-21 01:01

**Review time:** 22 Days and 3 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 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 checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

The authors have reviewed the critical role of epigenetic modification in cancer stem cells (CSCs) and cancer cells through various mechanisms including regulation of tumor suppressor genes and modulation of key signaling pathways. They specifically pointed the role of autophagy in cancer development and how epigenetic modulation mechanism could be used to circumvent the effect of autophagy thereby providing novel cancer therapeutics. The authors pinpointed specific epigenetic mechanisms including DNA methylation, histone modifications and non-coding RNAs, how they mediate genomic instabilities and cause cancer development. However, they also provided a hope through epigenetic therapeutics targeting of autophagy and reactivation of tumor suppressor genes. They highlighted several epigenetic elements including lncRNAs and miRNAs from various studies that are associated with different tumor types. The authors proposed 3 models which is promising and educative, providing a new direction for targeted cancer therapy/treatment. This review is adequate for its objective and is thoroughly written with several current/up-to-date references. Main concerns: My question is that the authors should confirm if figures 1-3 belong to them or not. These figures were not referenced, and I am assuming their proposed model/pathway. It will be nice if your readers know this. Please tell the readers. It is also not a crime if you got it from somewhere else but must reference them.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 64960

**Title:** Epigenetic regulation of autophagy: A key modification in cancer cells and cancer stem cells

**Reviewer's code:** 05928611

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

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

**Manuscript submission date:** 2021-02-25

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-03-19 07:38

**Reviewer performed review:** 2021-03-22 14:48

**Review time:** 3 Days and 7 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 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**

The manuscript 'Epigenetic regulation of autophagy: a key modification in cancer cells and cancer stem cells' discusses the role of epigenetic alterations as a major player within the autophagy of cancer stem cells and also in cancer cells. In detail, the authors provide comprehensive presentations and backgrounds of different epigenetic modifications like DNA methylation, histone modification or non-coding RNAs and outlined respective correlations to the autophagic signaling of cancer cells and cancer stem cells. Moreover, the link from the existing knowledge of cancer (stem) cell-based epigenetic regulation of autophagy to a clinical context with possible therapeutic approaches is well described. However, some minor issues should be addressed: 1. The authors should partially extent their manuscript part of 'DNA methylation' (page 9), concerning the shift from describing the generalized process, to highlighting some selected examples for DNA methylation in context with cancer and cancer (stem) cells. This brief extension will gives a prior information on this type of epigenetic modification, as it is outlined for the directly following chapter of 'Histone remodeling and modifications'. 2. By explaining the 'Histone methylation' and by describing 'Short non-coding RNA and microRNA' as epigenetic mechanisms, the authors briefly mentioned two connections from autophagic signaling to NF- $\kappa$ B transcription factor activation (page 16 and 19). It would be very interesting to shortly recapitulate the common relation from autophagy to NF- $\kappa$ B in cancer (stem) cells, as the NF- $\kappa$ B transcription factor is one of the major regulators of cell survival. 3. The following typos were found in the text and should be revised: "Table 1 DMA methylation or histone modification", "ER: endothelial reticulum" and the change from "CS" to "CC" as an explanation for 'cancer cell' within figure 1, are to be corrected.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 64960

**Title:** Epigenetic regulation of autophagy: A key modification in cancer cells and cancer stem cells

**Reviewer's code:** 03766000

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Research Assistant Professor

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

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

**Manuscript submission date:** 2021-02-25

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-03-17 02:15

**Reviewer performed review:** 2021-03-25 02:53

**Review time:** 8 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 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>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



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

This manuscript by Harpreet K Mandhair et al summarized the recent progress in the roles and mechanisms of autophagy in cancer stem cells, differentiated cancer cells, especially focusing on the epigenetic regulation of cancer stem cells and cancer cells, including DNA methylation, histone remodeling and modifications, non-coding RNAs. This will help people in the related area.