

Name of Journal: World Journal of Stem Cells

Manuscript NO: 55007

Dear Prof. Ma, Editors-in-Chief, and members of the Editorial Board,

RE: Reviewer commentary

Primarily, I would like to thank the editor and the reviewers for their positive feedback and the valuable comments. Please find enclosed the original copy of the revised manuscript.

The comments provided were found to be fair and incredibly useful. As recommended, the manuscript has been revised accordingly and believe that we were able to satisfy the reviewers' proposed questions and suggestions. Furthermore, the manuscript has been grammatically amended.

We hope that you would find our revised manuscript acceptable for publication in the World Journal of Stem Cells.

Yours sincerely,

Ramin Radpour, MSc, PhD
Tumor Immunology,
Department for BioMedical Research (DBMR),
University of Bern, Murtenstrasse 35,
3008 Bern, Switzerland.
Email: ramin.radpour@dbmr.unibe.ch
Telephone: +41-31-6320956
Fax: +41-31-6323297

Reviewer's comments:

Reviewer 1

This The manuscript described the divergent role of autophagy in cancer stem cells and cancer cells, and attempts to elucidate the molecular mechanisms involved in autophagy. This paper is benefit to understand the complex interactions of autophagy and cancer stem cells, and analyze the relationship between cancer therapy and the clinical outcome for these patients based on autophagy. Thus, this manuscript is interesting.

Several suggestions should be addressed. Apoptosis and autopahgy are two different event and have different pathways. The authors should reduce the description of apoptosis.

Authors: As per your recommendation, the description of apoptosis has now been reduced.

The grammar and spelling mistakes often occur in this manuscript, fox example may to my. The authors should correct and modify them seriously.

Authors: The revised manuscript has addressed these errors and has made amendments accordingly.

In the part " TARGETING CANCER CELLS AND CSCS USING AUTOPHAGY MODULATORS", some studies demonstrated that oncolytic virus also inhibits cancer stem cell via autophagy (Biochem Biophys Res Commun. 2017 Sep 16;491(2):469-477).

Authors: Oncolytic virotherapy is an emerging therapeutic strategy for eliciting antitumoral effects. The utilization of oncolytic viruses and its modulation via autophagy has now been included in the present manuscript in the following section: INTERACTION BETWEEN AUTOPHAGY AND IMMUNOTHERAPY.

In addition, the authors should disscuss the relationship of between autophagy and cancer immunotherapy expecially immune checkpoint inhibitors such as PD1, PDL1, CTLA4.

Authors: We thank the reviewer for suggesting to discuss the relationship between autophagy and immunotherapy checkpoint inhibitors (as named above). In the literature it is apparent autophagy mediates multiple immune responses. This has now been included and discussed in the manuscript in the following section: IMMUNE CHECKPOINT INHIBITORS IN MODULATION OF AUTOPHAGY.

Reviewer 2

I have read with great enthusiasm the manuscript of Mandhair HK et al. entitled "Molecular modulation of autophagy: new venture to target resistant cancer stem cells". Comments: -Title: reflects the main subject of the MS -the Abstract reflects the work described in MS -Background informations are adequately reported -Methods and results : N/A -Discussion is accurate and reports a comprehensive review on the current knowledge in autophagy and his role in cancer and cancer stem cells -Figures are of good quality -Biostatistic: N/A -References: the authors cite the latest references on the subject - Quality of the MS: it is concise and well organized -Research methods: N/A -Ethics statement: N/A Minor revisions : the authors should amend a few grammar typos: Pag 4: "Signally" replaced with "signalling" Pag 4: mTOR (M is not "mechanistic" but "mammalian") Pag 6: "Blabbing" should be replaced with "blebbing" Pag 13: and in any other part of the MS: "Vinmentin" should be replaced with "Vimentin"

Authors: We would like to thank the reviewer for positive comments. The errors have now been resolved within the manuscript.