

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 55783

Title: 6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy

Reviewer's code: 03590448

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Canada

Author's Country/Territory: China

Manuscript submission date: 2020-04-03

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-05-09 02:01

Reviewer performed review: 2020-05-09 02:06

Review time: 1 Hour

Scientific quality	<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 Grade E: Do not publish
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" 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

SPECIFIC COMMENTS TO AUTHORS

The authors evaluation of autophagy is very weak. The autophagy evaluation should be confirmed using TEM, ICC for LC3 puncta, and measuring autophagy flux. The localization of Bcl2 family should be provided.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 55783

Title: 6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy

Reviewer's code: 03478635

Position: Peer Reviewer

Academic degree: PhD

Professional title: Senior Research Fellow

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2020-04-03

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-16 09:50

Reviewer performed review: 2020-07-17 01:15

Review time: 15 Hours

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 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
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 checked="" 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

This study evaluated the effect of 6-GIN on ROS-induced apoptosis in NPMSC. The molecular mechanisms in which 6-GIN increases Bcl-2 expression may be discussed more in detail.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 55783

Title: 6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy

Reviewer's code: 04055018

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-04-03

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-17 11:03

Reviewer performed review: 2020-07-24 10:28

Review time: 6 Days and 23 Hours

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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

The manuscript by Nan et al, "6-Gingerol protects nucleus pulposus derived mesenchymal stem cells from oxidative injury by activating autophagy" reports a protective effect exerted by 6-Gingerol against hydrogen peroxide-induced injury on nucleus pulposus derived mesenchymal stem cells (NPMSC) showed. The experiments are well designed and described. The results are satisfactorily exposed and discussed. The literature is properly cited. Minor suggestions: Line 14: "Expressions of extracellular matrix (ECM)", "Expression" should be deleted; Line 98: "complete medium for MSCs", please specify; Line 108,265: "HLA-DR" should be explained and mentioned in the results (line 238) Line 130: bafilomycin A1 (BAF) should be explained at its first appearance; Line 138: "(5 × 10⁵ cells/well)", please check; Line 150: "2',7'-dichlorofluorescein diacetate", please add "(DCFH-DA)" Line 196: "Capasee" should be "Caspase" Line 258: bar calibrations are poorly visible; please check "800μm" in Fig. 2D: Line 274, 303: "cell viability induced by hydrogen peroxide", in this form the expression might be misleading, please rewrite. Line 351, 407, 447: please check magnification "100X" and "200X"; Line 405: "(D-F)" should be "(D-G)"; Line 448: "(G)" should be "(G-I)"; Line 472: Panels A and B should be mentioned in the legend; I believe that a further language revision is suitable. Namely, some expressions should be checked: Line 99: "Next, resuspended the cells in complete medium for MSCs and cultured at 37°C with 5% CO₂. Refreshed the culture medium every 3 days. Each primary culture were digested..."; Line 128: "To further with 10 mM 3-MA (3-Methyladenine, MedChem, China, catalog no. HY-19312) prior to exposure to hydrogen peroxide for 2 h"; Line 146: "The analyzed the ratio of green to red fluorescence by flow cytometry"; Line 320: "In additionally, the....";

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 55783

Title: 6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy

Reviewer's code: 03808474

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Iran

Author's Country/Territory: China

Manuscript submission date: 2020-04-03

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-16 14:28

Reviewer performed review: 2020-07-28 02:45

Review time: 11 Days and 12 Hours

Scientific quality	<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
Language quality	<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
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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

The results presented in the manuscript entitled “6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy” are in a logical sequence with appropriate analysis with figures and table to that contain data to inform the readers. The manuscript builds upon previous important research that is appropriately referenced. The data from this manuscript does move the canon of knowledge forward and may be considered by the Top 10 % of the research field. The manuscript is sufficiently novel and interesting to warrant publication in “World Journal of Stem Cells” after revision. 1) Why is the “Abstract section” so long? Please re-write it briefly. 2) Which passage of cells were used? Please specify in the text of manuscript. 3) The identification and characterization method of isolated mesenchymal stem cells must be discussed in detail. Also, it could better to add the flow cytometry diagrams in the “figure 2”. You can use and refer the following paper which explained elaborately and completely the “flow cytometric analysis and multi-lineage differentiation method for characterization of mesenchymal stem cells” in “Identification of Immunophenotype” and “Multilineage differentiation” sections:

Immunophenotypic characterization, multi-lineage differentiation and aging of zebrafish heart and liver tissue-derived mesenchymal stem cells as a novel approach in stem cell-based therapy. *Tissue and Cell*. 2019 Apr 1;57: 15-21. 4) Also, the Annexin/V assessment method must be explained in detail. You can use and refer the following paper which explained and analyzed elaborately the “Annexin-V/PI”. Cytokines secreted from bone marrow derived mesenchymal stem cells promote apoptosis and change cell cycle distribution of K562 cell line as clinical agent in cell transplantation. *PloS one*. 2019;14(4). 5) It could be better to calculate the Bax/Bcl2 ratio in the figure 4. This calculation was previously reported by Fathi et al. (2019) as appears bellow:

Cytokines secreted from bone marrow derived mesenchymal stem cells promote apoptosis and change cell cycle distribution of K562 cell line as clinical agent in cell transplantation. PloS one. 2019;14(4). 6) Which software was used for primer designing? Please involved in the text of the manuscript. 7) The number of ethical code must be added in the section of “methods section”.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 55783

Title: 6-Gingerol protects nucleus pulposus-derived mesenchymal stem cells from oxidative injury by activating autophagy

Reviewer's code: 05029935

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2020-04-03

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-17 00:03

Reviewer performed review: 2020-07-30 14:12

Review time: 13 Days and 14 Hours

Scientific quality	<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
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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

This manuscript is presenting that the protective effect of 6-GIN on oxidative stress-induced injury of NPMSC by controlling the autophagy signaling regulation for the first time. In Figure 6, the protein expressional changes of Beclin-1 did not seem to be appropriately changed with 6-GIN treatment. Additionally, the beta-actin expression also presented with significant changes. Furthermore, the phosphorylated AKT expression also showed no significant changes with 6-GIN treatment in Figure 7. Authors need to make these protein expressional changes concrete as well as make clear which residue of AKT was phosphorylated. Although it seems that it is well-organized manuscript, still it needs to be further taken the English editing including typos and errors. Besides aforementioned issue, authors need to correct and add more explanation in detail list below, which were also marked in yellow highlight with comments in attached file.