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OPEN PEER REVIEW

Exercise Training and Nanocurcumin Induce Down-regulation of EGFR/MAPK/STAT5/FN14 Pathway Genes in Tumor Tissue of Glioblastoma Multiform Model Rats

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

3 comments · 21 Jan 2023 – 24 Jan 2023

Simin Riahy Reviewer

MAJOR REVISION 21 Jan 2023

Thanks for your valuable work.
It is recommended that the text be rewritten to improve the English.
In the discussion section, more relevant information must be given about the effect of exercise on these variables.
Use newer articles.
The abstract section must be rewritten according to standard article-writing conventions.

Associate Editor

MAJOR REVISION 24 Jan 2023

Add the ethics code.

Editor-in-Chief

MAJOR REVISION 24 Jan 2023

major revision

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Dr **Iraj Mirzaii-Dizgah:**
After careful consideration of reviewers' comments, we have completed a revision of the manuscript. In accordance with reviewer suggestions we have changed a point-by-point- response to each reviewer's concerns is addressed below.

Reviewer 1:
Q1: ***It is recommended to rewrite the text again from the point of view of how to write the English language.***
R1: We appreciate the reviewer's comment. With regard of your comment we have made some modifications
Q2: ***In*** **the discussion section, more relevant information must be given about the effect of exercise on these variable.**
R2: Regarding this question, some information regarding the relationship between exercise and the target signaling pathway has been added to the discussion section (highlighted parts; page 7& 8), and less relevant information was removed:

Q3: ***Use newer articles.***
R3: The following references, which are mostly related to 2018 and after, were used:
Liu, F., et al., *Targeting ERK, an Achilles' Heel of the MAPK pathway, in cancer therapy.* Acta Pharmaceutica Sinica B, 2018. **8**(4): p. 552-562.
Meneses-Echávez, J.F., et al., *The insulin-like growth factor system is modulated by exercise in breast cancer survivors: a systematic review and meta-analysis.* BMC cancer, 2016. **16**(1): p. 1-10.
Gannon, N.P., et al., *Effects of the exercise-inducible myokine irisin on malignant and non-malignant breast epithelial cell behavior in vitro.* International journal of cancer, 2015. **136**(4): p. E197-E202.
Guo, N., et al., *MicroRNA-133a downregulated EGFR expression in human non-small cell lung cancer cells via AKT/ERK signaling.* Oncology letters, 2018. **16**(5): p. 6045-6050.
Domańska-Senderowska, D., et al., *MicroRNA profile and adaptive response to exercise training: a review.* International journal of sports medicine, 2019. **40**(04): p. 227-235.
Dufresne, S., et al., *A review of physical activity and circulating miRNA expression: implications in cancer risk and progression.* Cancer Epidemiology, Biomarkers & Prevention, 2018. **27**(1): p. 11-24.
Isanejad, A., et al., *MicroRNA-206, let-7a and microRNA-21 pathways involved in the anti-angiogenesis effects of the interval exercise training and hormone therapy in breast cancer.* Life sciences, 2016. **151**: p. 30-40.

Q4: ***abstract section must be rewrite according to the common way of writing an article.***
R4: We appreciate the reviewer's comment. With regard of your comments we changed abstract.

Reviewer 2:
Q1: ***The introduction includes: "what we know" and "objectives", but does not clearly address the issue of "what we do not know".***
R1: In the end of introduction and in objectives section, we highlighted "what we do not know" and what we are trying to find out. And also in the present study for the first time we evaluated the effect of combined aerobic-resistance training and

nanocurcumin consumption on the EGFR/MAPK/STAT5/FN14 pathway genes in the tumor tissue of glioblastoma multiform model rats.

Q2: ***The researcher did not provide how to calculate or justify the sample size.***

R2: Based on similar articles and standard sample sizes, the animals were randomly divided into 5 groups of 8 rats.

Q3: Inclusion/Exclusion Criteria not explained

R3: The entry criteria of the animals, which were maleness and exact weight range, have been clearly explained, and because the animal samples were kept in laboratory conditions and the exercise and nutrition interventions were completely controlled, there is no reason for the animal's withdrawal from the research process.

2 Revision 1

1 comment · 30 Jan 2023

Editor-in-Chief

ACCEPT 30 Jan 2023

accept