Hepatitis Monthly
Volume 23 · Issue 1 · e133758

OPEN PEER REVIEW

# Vitamin D Improves the Lipotoxicity of Liver Cells by Adjusting Epigenetic Characteristics of Genes

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| SUBMITTED | REVISED | ACCEPTED | DOI |
| --- | --- | --- | --- |
| 26 Nov 2022 | 7 Jun 2023 | 28 Jun 2023 | 10.5812/hepatmon-133758 |

## 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.

More about open peer review: brieflands.com/knowledgebase/opr

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## 1 Original submission

3 comments · 26 Apr 2023 – 26 Apr 2023

### Ramtin Mohammadi Reviewer

MAJOR REVISION 26 Apr 2023

This is really an up-to-date in-silico study on an important topic that could be crucial for NAFLD management in the near future. But I suggest that you provide an article with experimental results to prove your findings.
1. Your manuscript is well written; however, it needs improvements in some places.
keywords:
2. Sort keywords alphabetically.
methods:
3. Although you used GEO2R, which is completely appropriate, please explain why you did not use Rstudio for the analysis.
4. In section 3.2. you have mentioned that GEO2R is a part of the GEO database, but please cite GEO2R.
discussion:
5. Use more recent studies (<5 years) to prove your results.
6. In line 207, I couldn't understand whether "Chavez Tapia et al." is an unformatted reference or the beginning of the next sentence; this needs correction.
figures:
7. Figure legends need improvements and details; in particular, please provide the sources.
8. For figures 3.4.5. please cite the pathview.
9. The use of more databases and resources is advised to improve the quality of the results.
10. KEGG pathways must be clarified further to depict a logical concept of the roles of vit D.
11. An illustration showing the different steps of the method is suggested to improve the flow of the study methodology.

### Associate Editor

MAJOR REVISION 26 Apr 2023

Major Revision

### Editor-in-Chief

MAJOR REVISION 26 Apr 2023

Dear Authors,

Please follow the peer-review comments and submit a revision.

Regards,
EIC

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# 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.

**05/31/2023**

**Dear Editor:**

Thank you for your letter and the reviewers' comments concerning our manuscript entitled " **Vitamin D improves lipotoxicity of liver cells by adjusting epigenetic characteristics of genes**". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer's comments are as following:

**Responds to the reviewer's comments:**

**Reviewer: 1**

**Comment 1**

Sort keywords alphabetically.

**Response:** ***Thanks for the reviewer's professional comments. According to the modification opinions, we have sorted the keywords alphabetically.***

**Comment 2**

Although you used GEO2R and it is completely right; describe your reason why didn't analyze by the aid of Rstudio?

**Response:** ***Thanks for the reviewer's professional comments. GEO2R provides a simple interface that allows users to perform complex r-based analysis of GEO data to help identify and visualize differential gene expression. More than 90% of GEO studies can be analyzed in this way. The statistical results table contains various categories of statistical data, including P values, t statistics and fold change, and gene annotation. As an editor for the R language, Rstudio makes it easy and efficient to use R. Even though both Rstudio and GEO2R are based on the R language, compared to Rstudio, GEO2R makes the analysis of***

***GEO data faster, more practical, more accurate, and more reliable.***

**Comment 3**

In section 3.2. you have mentioned that GEO2R is a part of GEO database but please cite GEO2R.

**Response:** ***According to the modification suggestions, GEO2R has been cited in section 3.2.***

**Comment 4**

Use more and recently (<5 years) studies to prove your results.

**Response:** ***According to the modification suggestions, more and recent (<5 years) research has been used to prove our results.***

**Comment 5**

In line 207, i couldn't understand "Chavez Tapia et al." is an unformatted reference or the initiation of next sentence, which needs correction.

**Response:** ***Thanks for the reviewer's professional comments. In line 207, 'Chavez Tapia et al.' is an unformatted reference. Therefore, while revising the paper, we also made revisions to the citation format of the literature.***

**Comment 6**

Figures legends need improvements and details, especially provide the sources.

**Response:** ***According to the modification suggestions, the details of the legend have been improved and the source has been marked.***

**Comment 7**

In case of figures 3.4.5. please cite the pathview.

**Response:** ***According to the modification suggestions, the pathview has been citeed in Figure 3.4.5.***

**Comment 8**

More data bases and resources are advised to be recruited for promotion of the results quality.

**Response:** ***Thanks for the reviewer's professional comments. We found that there is only one study on the cellular protective function of vitamin D in human liver cell lipotoxicity in the GEO database. Although we are striving to recruit more databases and resources, we have not found any database resources related to similar research. Although the results of this study still need to be verified, while providing a new perspective on the epigenetic regulation mechanism of genes, it also provides important clues for further exploration of the pathogenesis of NAFLD.***

**Comment 9**

KEGG pathways must be more clarified to depict a logical concept of vit D roles.

**Response:*****According to the modification suggestions, the logical concept of the vitamin D action pathway has been described in the results section.***

**Comment 10**

An illustration showing the different steps of method is suggested to improve the flow of study methodology.

**Response:** ***According to the modification suggestions, the illustrations have been used to display different steps of the method.***

**Reviewer: 2**

**Comment 1**

Background is very brief. It would be better to add several similar studies that may agree or disagree with the results of this study.

**Response:** ***Thanks for the reviewer's professional comments. According to the revision suggestions, we***

***have added similar research in the background section.***

**Comment 2**

And in objective, only indicate the novelty and aim of this study.

**Response:** ***According to the modification suggestions, we have objectively demonstrated the novelty and purpose of this study.***

**Comment 3**

This sentence needs revision to be clear and correct “The genes with log FC>1 or log FC<-1 were up-regulated differentially expressed genes, and the genes with log FC<-1 were down-regulated differentially expressed genes”

**Response:** ***According to the revision suggestions, this sentence in the article has been revised.***

**Comment 4**

Add the statistical data such as p value in text and clarified their related signs in figure captions.

**Response:** ***According to the modification suggestions, statistical data such as p-values have been added to the text and their relevant symbols have been clarified in the graphic title.***

**Comment 5**

It would be better to classified the discussion in to discrete paragraphs according to the different pathways studied here, cell cycle, apoptosis, complement and coagulation cascades pathway, in order to the results would be more clear for the audience.

**Response:** ***Thanks for the reviewer’s professional comments. According to the modification suggestions, different approaches to the study have been discussed in segments.***

## 2 Revision 1

2 comments · 26 Jun 2023 – 28 Jun 2023

### Associate Editor

ACCEPT 26 Jun 2023

Dear EIC,
The great effort in improving the manuscript is highly appreciated.
The authors have addressed all the comments. Now, it is acceptable.

### Editor-in-Chief

ACCEPT 28 Jun 2023

Dear Author,
Thank you for correcting the pitfalls and answering all questions.