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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36574

Title: circRNA_0046366 inhibits hepatic steatosis by normalization of PPAR signaling

Reviewer's code: 02860897

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-10-09

Date reviewed: 2017-10-13

Review time: 3 Days

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input checked="" type="checkbox"/> No | <input type="checkbox"/> Major revision |
| | | BPG Search: | |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

Recent discovery of a special class of RNAs has stimulated many investigators and has produced hundreds of new experimental studies. Circular RNAs are produced in the process of the transcription, and both ends of these are covalently closed. Most of these circular RNAs are expressed in cytoplasm. This report may have an interesting aspect of the regulation of PPAR α . Major 1. In the section of material method is insufficient, it hampers to confirm this result by other investigators. You should add detail condition of your experiment, especially administration of circ RNA. In the section of phenotypic evaluation, there is no definition of each subgroup. 2. Circ RNAs tend to be expressed weakly in usual. On the contrary, we can detect huge amount of miRNA-34 in the liver. Did you quantify the amount of the circ RNA in HepG2 cell? If one to one binding between the miRNA and the circ RNA has regulatory effect of downstream signals, circ RNA should be huge amount. 3. Why dose FAA reduce the expression of circ RNA



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0046366? Show the reduction mechanism of circ RNA by FAA. 4. Is the circ RNA is stable in cytoplasm of HepG2 cell? Add the stability data of the circ RNA.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36574

Title: circRNA_0046366 inhibits hepatic steatosis by normalization of PPAR signaling

Reviewer's code: 00006071

Reviewer's country: Spain

Science editor: Ze-Mao Gong

Date sent for review: 2017-10-09

Date reviewed: 2017-10-20

Review time: 11 Days

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
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| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> No | <input type="checkbox"/> Major revision |
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COMMENTS TO AUTHORS

Xing-Ya et al report the effect of circRNA_0046366 on neutral lipid-loading in a cellular model of liver steatosis. Although the results are interesting, and the methods and experimental design appropriate, the manuscript should suffer fundamental changes before further consideration: . Steatosis is a descriptive word used to name the accumulation of lipids, mainly neutral lipids, in an organ of a living organism. The most frequent form of steatosis is liver or hepatic steatosis, often referred as fatty liver. In the present work, an in vitro experimental model is used to verify the lipid loading of hepatoma cells after incubating them with fatty acids. In this experimental setting, it is not correct to use terms such as liver steatosis, hepatic steatosis, hepatocyte steatosis, etc. to refer to hepatoma cells (not normal hepatocytes) loaded with triglycerides after a short term of incubation. Although this model allows to study molecular mechanism involved in the accumulation of lipids inside liver cells, it is not a true "hepatic steatosis"



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situation. . It is very difficult to understand the meaning of the abstract, starting with the fact that nowhere in the text appears the experimental model used, culture HepG2 cells. Please, rewrite the abstract in a more concise, informative and understandable style. A similar situation happens with the Core tip section. . Although the English writing is generally correct, some sentences or words are difficult to understand. For example: . What means cerebral apoplexy (first paragraph in the introduction section). Are you talking about cerebrovascular diseases, such as occlusive ictus? . miR-34a discriminates patients with hepatic steatosis from healthy controls with an area under the receiver operating characteristic curve of 0.781. This sentence is very confusing. . circRNA_010567 in diabetic mice inactivate miR-26b-5p and miR-141, respectively, by the complementation between MREs and miRNAs. Are you referring to the fact that the physical interaction between the MRE domain of the circular RNA and the corresponding response element in the sequence of the miRNA inhibits its physiological activity? . Please, you do not administer anything to cultured cells, you administer to living organisms. . The methods section should give more information. Which are the exact incubation protocol for loading hepatoma cells? Where is the description of the bioinformatic analysis? . PPARalpha controls a wide array of target genes in liver (apo AI, HMGCS, LPL, VLDL-R, Apo CIII, etc.). It will be interesting to know if at least several of these genes behave similarly to CPT-Ialpha.