Peer Review File

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Reviewer A

In this manuscript, the authors investigated the expression of REXO4 in HCC tissues and analyzed its prognostic value as a novel biomarker. This is a first report to correlate the function of REXO4 in HCC tumorigenesis. They found that the expression of REXO4 is upregulated in HCC tissues and diagnostic value of REXO4 is high. Further, they insisted that the overexpression of REXO4 is correlated with poor survival of HCC patients, and the function of REXO4 is associated with immune infiltration and activation. However, I do not recommend this manuscript for further consideration for publication in JGO due to following defects. First, this manuscript should be further edited by a professional English Edition Service. Overall, the current manuscript is not readable. Second, they even mistyped their target disease in the Abstract. Third, although they tried to analyze the importance of REXO4 expression by various bioinformatics approaches, evidences from in vitro or in vivo functional analysis were not provided at all. Wet laboratory data should be supplemented to support their conclusion. For example, they need to observe if inhibition of REXO4 expression could suppress proliferation and/or induce apoptosis in HCC cells and that what was the underlying molecular mechanism to mediate the phenotypic changes.

Reply 1: LEXIS (Scientific Editing Experts, United States. LEXIS Academic Service, LLC) helps us polish our manuscript before submission,we revised the mistakes in the abstract,and the revised version of this article will be retouched. In vivo and in vitro experiments can further confirm the function of this molecule in liver cancer, but three weeks for these function experiments is certainly not enough.We first provides evidence regarding the potential of REXO4 as a biomarker in HCC, however, wet laboratory data is not available in the short term, this is the deficiency of this paper.

Changes in the text: We modified the mistakes, and revised the full text at the same time.

Reviewer B

The manuscript of Chen et al. evaluated the prognostic value of REXO4 in HCC. The Authors found that REXO4 was up regulated in HCC patients and was associated to a worse clinical outcome and to immune infiltration. The analysis was based on databases screening. No validation of the results was performed, besides mRNA and protein quantification in tissues and cell lines; therefore the results remain mainly on the hypothesis level.
The Authors offer no clear background of their study; in particular, they might explain more in detail why they focused on REXO4. In addition, they could propose more concrete clinical applications when targeting this protein.
The entire study has been performed on database analysis. Although this study is explorative,

to support the finding it would be relevant to include also key validation experiments to show that REXO4 is not only overexpressed in HCC but also that it plays a role in cancer development.
The description of the different analysis is very short and in most of the cases not sufficient. Authors should describe more in detail the type of liver cancer analyzed, which etiologies were included and so on.
Minor points:
1) In some part of the abstract, the study is referred to lung cancer
2) Were really the cells grown in 100g/mL (rather than 100μg/mL) Streptomycin?
3) Why the protein validation experiments were performed only on cell lines and not on proteins extracted from the patients' tissues?
4) Having the tissue available, why an IHC validation was not performed?
5) Typos were found along the whole text.

Reply 2: Thank you for your comments. In this paper, the expression of REXO4 in hepatocellular carcinoma and its possible role were comprehensively described.Our conclusion is that REXO4 is highly expressed in HCC and affects the prognosis of patients.REXO4 is a protein that we found during data mining. It is highly expressed in liver cancer and affects the prognosis of patients, so we are interested in it.Finally,we supplement some conclusions in this paper.
Minor points:
1) In some part of the abstract, the study is referred to lung cancer
This is a mistake,and we revised the mistake in the abstract.
Changes in the text:Page2, line 38

2) Were really the cells grown in 100g/mL (rather than 100μg/mL) Streptomycin?
We used 100μg/mL Streptomycin in experiments,and we revised this mistake in the methods.
Changes in the text:Page9, line 182

3) Why the protein validation experiments were performed only on cell lines and not on proteins extracted from the patients' tissues?
Due to the improper preservation of the specimens, only the extracted RNA from the patients stored in the refrigerator can be used.In the short term, we can not to obtain patients' tissues.

4) Having the tissue available, why an IHC validation was not performed?
The previously preserved tissue has been damaged, at present, we can't get tissues which can be used,so we used immunohistochemistry from the database.

5) Typos were found along the whole text.
We revised the article and retouched it.