



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36612

Title: Hepatitis C virus core protein-induced miR-93-5p inhibits IFN signaling pathway through targeting IFNAR1

Reviewer's code: 01551432

Reviewer's country: Japan

Science editor: Ke Chen

Date sent for review: 2017-10-28

Date reviewed: 2017-11-04

Review time: 8 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 checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear Authors Thank you for submitting the manuscript entitled, "Hepatitis C virus core protein-induced miR-93-5p inhibits IFN signaling pathway through targeting IFNAR1 " for WJG. The manuscript is well written and the topic is interesting and timely, however, I wonder if the experiments were properly performed and the data were properly analyzed. Several criticisms should be addressed as major comments. 1) I think the Western blot method is very difficult, and I have experienced it. The authors described that the exam have performed two or three times on the exams of Figure 3. ABCDE and Figure 4. CD. what are the participants on the experiments? all participants, several, some or only one case? Please represent all the actual quantification data or films of western blot exams to me and editors for confirmation. After our confirmation, the authors should add the short comments, "(data not shown)" in the descriptions. 2)



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Figure legends: No description of methodology, qRT-PCT, Western blot, or other procedures. Please clarify it on all the figures. No description of these in the section of "Result". 3) Please add the schematic figure on the relations among HCV-core protein, miR-93-5p, IFNAR1, STAT1, pcDNA, and so on, referring the manuscript No.8-13. 4) What are the participants and samples in Figure 1,2,3,4,5? All participants, several, some or only one, healthy or illness? Please clarify it and do proper descriptions.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36612

Title: Hepatitis C virus core protein-induced miR-93-5p inhibits IFN signaling pathway through targeting IFNAR1

Reviewer's code: 02997214

Reviewer's country: Turkey

Science editor: Ke Chen

Date sent for review: 2017-11-08

Date reviewed: 2017-11-15

Review time: 7 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
<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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

1.Introduction , lines 16-18; "Several studies indicated that the expression of multiple miRNAs was regulated by IFN in inhibiting HCV replication[9].", please add more references. Also, explaine which "miRNAs"? 2. In Cell culture, "DMEM/HIGH GLUCOSE (Hyclone)" should be written as "DMEM high glucose (Hyclone, USA)". "10% FBS (Gibco)" should be "10% Fetal Bovine Serum (FBS)". 3.In RNA extraction; "TRIzol reagent (Invitrogen)" should be "TRI reagent (Invitrogen, Carlsbad, CA, USA)". 4. In RNA extraction; "C.elegans miR-39 (GenePharma)" should be "GenePharma (Shanghai, China)". Other instruments and substances should be followed by the company name and also the country in paranthesis. I gave some examples, in 2 and 3, please carefully revise your manuscript not to miss any reagent, instruments etc.. 5. In Quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR); "Two



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microliter" should be "Two microliters". 6. In Statistical analysis "Graphpad Software Inc, Caligornia" should be revised as "Graphpad Software Inc, California". 7. In miR-93-5p concentration in serum of patients with HCV-1b infection is involved in pegylated IFN α resistance; "The results showed an AUC value of 0.8846 for serum miR-93-5p in distinguishing HCV-1b-infected patients from healthy subjects, with sensitivity of 76.19% and specificity of 100%, cut-off value of 0.009774 amol/ μ l (Figure 2A), an AUC value of 0.8562 in distinguishing HCV-1b-infected patients with pegylated IFN α sensitivity from healthy subjects, with sensitivity of 70% and specificity of 100%, cut-off value of 0.009774 amol/ μ l (Figure 2B), an AUC value of 0.9265 in distinguishing HCV-1b-infected patients with pegylated IFN α resistance from healthy subjects, with sensitivity of 85.29% and specificity of 100%, cut-off value of 0.01087 amol/ μ l (Figure 2C), an AUC value of 0.8359 in distinguishing HCV-1b-infected patients with pegylated IFN α resistance from those with pegylated IFN α sensitivity, with sensitivity of 76.47% and specificity of 100%, cut-off value of 0.03030 amol/ μ l (Figure 2D)". Please exclude these results from the text and draw a plain table indicating these values, you should also keep the Fig 2. This is an optional suggestion, if you desire, you can keep the same format but it is very difficuklt to understand. 8. In Discussion "miR-93-5p has been shown to target several mRNAs in HCC cells, such as PTEN, CDKN1A, and also to regulate the c-Met/PI3K/Akt pathway[14]," When I evaluated reference 14, I noticed they used miR-93 not miR-93-5p, please explaine or revise it as "miR-93". Please add the following sentence from the reference 14 as "They indicated the mechanisms through which miR-93 inhibits PTEN and CDKN1A, thereby activating proliferation through the c-Met/PI3K/Akt pathway and inhibiting apoptosis in HCC.", this information is needed. 9. In Discussion, use miR-93-5p/IFNAR1 axis promotes gastric cancer metastasis through activating the STAT3 signaling pathway as "Using an mRNA microarray, Ma et al., (reference) found that miR-93-5p significantly downregulated IFNAR1 expression in GC cells by promoting gastric cancer metastasis , which was further identified as a direct target of miR-93-5p.", reference DOI: 10.1016/j.canlet.2017.08.017 Cancer Lett. 2017 Nov 1;408:23-32. doi: 10.1016/j.canlet.2017.08.017. Epub 2017 Aug 24. miR-93-5p/IFNAR1 axis promotes gastric cancer metastasis through activating the STAT3 signaling pathway. The reference indicates other cancer but with the same mechanisms due to the downregulation of IFNAR1 expression. 10. In Discussion, page 2, line 2-3;" by synthesizing five databases five databases" What do you mean, by investigating or evaluating etc.. but "by synthesizing" does not seem an adequate word. 11. In Discussion, line 3, "we found IFNAR1, a receptor of IFN α ". But as I know, the protein encoded by IFNAR1 is a type I membrane protein that forms one of the two chains of a receptor for interferons alpha and beta. Please revise it. 12. In Discussion, line 5, " but we believed" is not scientific, please use " but we suggested". 13. In Discussion, lines



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19-23, “In addition, hepatitis delta virus (HDV) can also impair the phosphorylation level of STAT1 and STAT2 through blocking the IFN- α -stimulated tyrosine phosphorylation of IFN receptor-associated JAK kinase Tyk2, without affecting the expression of type 1 IFN receptor subunits[23]. Although HDV infection also regulates IFN signaling pathway, the molecular mechanism may be different from HCV infection.”. Why did you write down this part. There is no relation with your study. Do you have any case with HDV. This is another possible pathogenesis mechanism related to HDV. I suggest to excludr this part from the text. 14. In Figure 1, miR-93-5p should be written inside the figures, miR-93-5p in the legend is not informative, please write down miR-93-5p inside the Figures.