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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31642

Title: Validation of a panel serum microRNA as biomarkers for early diagnosis of hepatocellular carcinoma post hepatitis C infection in Egyptian patients

Reviewer's code: 00069015

Reviewer's country: China

Science editor: Jing Yu

Date sent for review: 2016-12-01 09:51

Date reviewed: 2016-12-07 23:04

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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript aimed to look for a non-invasive method for early diagnosis of HCV-related HCC. The authors demonstrated that a panel of four serum miRNA (miR-214-5p, miR-375, miR-1269, and miR-125b) that had a significant correlation with HCC and that serum miR-145 monitoring might be a possible diagnosis tool for progression of fibrosis to HCC. The finding is very interesting and valuable. However, there are several questions which should be concerned by authors. 1. The abstract and introduction parts are a little bit long, the authors should make it briefer. 2. In the table 1, there might be a mistake about the number of Non-malignant chronic HCV. 3. In the table 1, the meaning of P value is not clear enough, the authors should explain it more specifically. 4. There are several grammar mistakes in this manuscript.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31642

Title: Validation of a panel serum microRNA as biomarkers for early diagnosis of hepatocellular carcinoma post hepatitis C infection in Egyptian patients

Reviewer's code: 03536815

Reviewer's country: Italy

Science editor: Jing Yu

Date sent for review: 2016-12-01 09:51

Date reviewed: 2016-12-08 02:04

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

I read with great interest the manuscript titled "Validation of a panel serum microRNA as biomarkers for early diagnosis of hepatocellular carcinoma post hepatitis C infection in Egyptian Patients. By MN Elemeery et al. It deals with the advancement of more dependable markers for diagnosis of HCC at early stage and better methodologies for HCC screening and early detection. A collection of little non-coding circulating RNAs associated with HCC in HCV patients have been studied. Authors investigated microRNAs, as prospective biomarkers for HCC in patients with HCV related hepatitis, and found miR-214-5p and miR-1269 as a biomarker for liver fibrosis progression to HCC. I think the manuscript need extensive major revisions before to considerate it for publication. -In the introduction please specify the acronyms FLD and CLD. -Authors stated: The urinary miRNAs marks found in this study might be of incredible value and applied for diagnosis of HCC early, before the onset of progression in patients infected with HCV. The manuscript does not involve urinary biomarker. Please specify that it is a citation. -I suggest to add a brief mention on urinary biomarkers of HCC. This concise review could be helpful. Trovato FM, Tognarelli JM, Crossey MM,



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Catalano D, Taylor-Robinson SD, TrovatoGM. Challenges of liver cancer: Future emerging tools in imaging and urinary biomarkers. *World J Hepatol.* 2015 Nov 18;7(26):2664-75. -Please mention in the Patients and methods section the 84 controls. -The miRNA selection section is inconsistent, please improve it. -In the statistical analysis do you use Mean or Median? -In Clinical and pathological Aspects for HCC patients -Please check the number and reformulate this sentence, it is not clear: Concerning CT imaging, 112 patient showed one focal lesions in liver, 128 patients of them showed focal size more than 5 cm, with 48 patients with portal vein thrombosis as shown in table (2). -In the section Serum miRNA profile in HCC patients please specify this sentence, it is not clear: In comparison to HCV patients, miR-1269, miR-214-5p, miR-375 and miR-145 significantly increased in expression fold, whereas miR-125b, miR-138-5p, and miR-494 significantly decreased in HCV groups -In the Regression analysis for studied miRNA section: -Please specify the word "circularibg" used in the AUROC figure 4. -In table 4 please highlight in bold the statistically significant results. -The Discussion is confusing. I suggest to mention that miR-1269 and miR-494 are related also to other types of cancer: for example: Bu P, Wang L, Chen KY, Rakhilin N, Sun J, Closa A, Tung KL, King S, Kristine Varanko A, Xu Y, Huan Chen J, Zessin AS, Shealy J, Cummings B, Hsu D, Lipkin SM, Moreno V, Gümü? ZH, Shen X. miR-1269 promotes metastasis and forms a positive feedback loop with TGF- β . *Nat Commun.* 2015 Apr 15;6:6879. -In the Discussion please specify the acronyms PV. I think that this manuscript needs extensive improvements. The reading is difficult. Grammatical corrections and punctuation are needed in the entire manuscript, in order to make the discussion fluent and understandable. There are also some distraction mistakes. I suggest to require the help of an English native speaker.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31642

Title: Validation of a panel serum microRNA as biomarkers for early diagnosis of hepatocellular carcinoma post hepatitis C infection in Egyptian patients

Reviewer's code: 03664164

Reviewer's country: China

Science editor: Jing Yu

Date sent for review: 2016-12-01 09:51

Date reviewed: 2016-12-18 22:48

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
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this manuscript, the authors investigated 7 miRNAs to verify if they could be used as prospective biomarkers for HCC related HCV. Sensitivity and Specificity of each miRNA was been demonstrated. This work is of potential interests and significance. The following issues need to be addressed: 1. Why did the author choose 7 miRNAs mentioned in the paper, please give your explanation. 2. I wonder if the level of serum miRNA will be discordance in different stage of HCC, could the author state the serum miRNA in different stages of HCC? 3. I would suggest giving the reader a standard table, such as omitting redundant vertical moulding... 4. In Fig 2, the separately graphs can be combined as one picture. There had the same phenomena in Fig 3. 5. Please the author checked the manuscript carefully; eg, "Non-malignant chronic HCV (n = 125)" in Table 1?? "circularing miRNA panel (HCC against early fibrosis)" appeared twice in Fig.4.