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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15916
Title: miR-122 negatively correlates with liver fibrosis as detected by histology and transient elastography
Reviewer's code: 03020620
Reviewer's country: China
Science editor: Yuan Qi
Date sent for review: 2014-12-17 13:51
Date reviewed: 2015-01-02 23:25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	PubMed Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In general, this is an interesting study assaying the expression of several fibrosis- and hepatocarcinogenesis-related miRNAs in fibrotic liver biopsy samples of various etiology and investigating their correlation with fibrosis stage and LS values. The approach taken by these authors is potentially appropriate. My major concern is the conclusion of this manuscript was based on analyses from a small sample size of the studied cohort with a mixed etiology in the case of lacking a validation cohort. It is necessary to increase numbers of samples (patients) in major etiology groups in this study cohort. It would be more convincing if a validation cohort can been applied. Based on this major concern, this manuscript should be reviewed after its revision.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15916
Title: miR-122 negatively correlates with liver fibrosis as detected by histology and transient elastography
Reviewer's code: 00007519
Reviewer's country: Italy
Science editor: Yuan Qi
Date sent for review: 2014-12-17 13:51
Date reviewed: 2014-12-22 20:57

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	PubMed Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this pilot study the authors evaluated the correlation between altered expression of HCC-related miRNA and fibrosis grade, as measured by histological staging with METAVIR scoring system or by liver stiffness measure by elastographic method (Transient Elastography). Comments: 1) The novelty of the study is the correlation of two non-invasive approaches (TE and measurement of miRNA expression levels) in determining the stage of fibrosis severity in samples obtained from chronic liver disease of different aetiologies. The study examined a limited sample size for each subgroup of fibrosis-related liver diseases, however the results presented are in agreement with recent reports from other researchers that support a strong correlation between decrease of miR-122 levels and severity of fibrosis/ increase in liver stiffness. The relevant point is that miR-122 levels are altered independently of the aetiological cause of liver damage. The evidences presented in this study are in support of the usefulness of miR-122 as an indicator of fibrosis progression. However, in order to become an easily-available staging tool, the proposed method should be able to discriminate between intermediate stages of fibrosis (F2 or F3 vs F0-F1). Please discuss this point. 2) The

values of ALT serum levels show great variability in individuals belonging to the same aetiology subgroup (Table 1), perhaps indicating different grade of intrahepatic inflammation. Coco B. et al reported that major changes of serum transaminases activity should be taken into account in elastographic measurements (Coco B, Oliveri F, Maina AM, et al. Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. J Viral Hepat 2007; 14: 360-369 and Bonino F. et al. Antiviral Therapy 2010 Suppl 3:69-78 and references therein). A necroinflamatory activity index (AT) should be provided especially for the autoimmune subgroup to evaluate the inflammatory background. Lannerstedt H, et al. recently proposed FIB-4 index (see Lannerstedt H , et al. Combining transient elastography with FIB4 enhances sensitivity in detecting advanced fibrosis of the liver. Scand J Gastroenterol. 2013 Jan;48(1):93-100. 3) To overcome the lack of statistical significance when examining individual oncomiRNAs expression levels in relation to METAVIR, especially in samples with intermediate fibrosis stages from different subgroups, miR-214, miR-222 and miR-224, miR-21 tissue distribution should be visualized by in situ hybridization in representative samples of different subgroups (i.e. HCV,Autoimmune with low/high ALT). For example, see Yamada et al. Respiratory Research 2013, 14:95 who reported that staining for miR-21 was observed in cells surrounding fibrotic foci, but not in cells within fibrotic foci. 4) In mouse and rat animal models of low graded liver fibrosis, the low expression pattern of 3 miRNAs miR-140, 27a, and 27b has been reported. MiR-140 suppresses NFkB activity trough inhibition of its coactivators NRP1 and NcoA1. To rule out the possibility that mild variations of miR140 occur qPCR data analysis should be performed using an alternative internal control. In many publications RNU6B was found to be the most stable internal reference RNA with an M value of 0.7. 5) The manuscript requires minor language polishing