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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15912
Title: The downregulation of microRNA-382 is associated with poor prognosis of esophageal squamous cell carcinoma
Reviewer's code: 03026970
Reviewer's country: China
Science editor: Yuan Qi
Date sent for review: 2014-12-17 15:27
Date reviewed: 2014-12-30 20:40

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

COMMENTS TO AUTHORS

This study first provides the evidence of the divergent expression of microRNA-382 in tumor tissue from esophageal squamous cell carcinoma (ESCC) patients, which indicate that it is associated with prognosis and may develop a novel biomarker for both diagnosis and treatment. However, several questions regarding the manuscript should be addressed. Major comments: 1. Many microRNAs that are related to ESCC have been reported. The authors found a new microRNA, microRNA-382, is also related to ESCC. It would be better if any introduction of microRNA-382 was added in the background. 2. materials and methods : (1)Did the authors detect the expression of microRNA-382 in normal population , or normal tissues adjacent to the tumor tissues, and what's the result? (2) Did the patients receive other treatments after surgeries, such as chemotherapy and radiotherapy? Were there any differences between the two groups, because these treatments would influence the result? (3)As mentioned in this article, the high-throughput real-time quantitative PCR was used to evaluate 754 microRNAs levels from 2 ESCC patients previously. Were there any other microRNA downregulated in the ESCC patient with poor prognosis besides microRNA-382? (4)Real-time

RT-PCR is a benchmark technology for the detection of RNA levels for its simplicity, specificity and sensitivity, did you check the result? (4)Definition of the down regulation is ambiguous. What are the control samples which are mentioned in the gene expression formula (materials and methods). 3. Result: (1)In the study, 46 patients were divided into good and poor prognosis, but what are the specific criterions? A reference should be provided in this part. Did the authors exclude those patients survived more than 1year and less than 5years after surgery? This should be mentioned in the manuscript. (2) When the authors try to create a COX regression model, did they enroll other variables such as age, family history, alcohol consumption and smoking status? (3) It would be better if the authors could provide the RNA sequence of microRNA-382, as readers would be interest in this. 4. Discussion: (1)The authors considered microRNA328 to be a potential biomaker for the prognosis of ESCC patients, it would be better if there was some exploration about the mechanism in the discussion part. (2)The authors mention that microRNA-382 as a tumor suppressor could be a useful biomarker for prognosis and outcome prediction in ESCC. The research is not enough to prove microRNA-382 is a tumor suppressor. More research is needed for the conclusion, such as in vivo and in vitro study. Minor comments: 1. Method: (1)PCR methods description should report whether all samples' Ct value are in a reasonable range. (2)Does the formula in correct form? Is it should be F =2-Δ Δ Ct? 2. Results: (1)There is a discrepancy between the total number of patients in table 1 and the text.Which is correct? (2)The number of patients evaluated in this study was relatively small. (3)Fig 3would be better if the legend of X axis is added.

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ESPS PEER-REVIEW REPORT

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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

I thank the authors for their submission and the opportunity to review the paper. Overall it is an interested topic aiming to advance management for this difficult disease. Through mainly "tightening" the paper in its scientific reporting, and partly by further expressing the clinical implications of their work, I believe the paper is worthy for publication. Below are my specific comments. abstract: methods - the term prognosis needs to be changed to "outcome" or "post-operative longevity" for example last para intro - "but different prognosis" - different wording should be used to make clear it was based on eventual patient outcome (prognosis is a term used before outcome is known)....I would suggest making this consistent throughout paper, including the figures, as outcome is a more accurate term and would make the paper clearer to read.....also state if the 2 patients previously studied was for published work or not methods: first paragraph - make clearer selections that applied. ?consecutive patients? No note is made of post-operative treatments (esp. chemotherapy) which could confound results. This is also not reported in results section. It is implied but not stated that "mid-term" prognosis patients were excluded or not studied, given those

surviving 1-5 years seem not to have been studied - this should be specified if this is the case. There is no description of the standardised follow-up? did all receive the same? Did the clinicians know the miR-382 result when they were following the patients up and therefore could they have monitored those with higher levels more closely? results: - the lymph node metastases percentages do not add up (47.5% plus 67.5% does not equal 100!)....also the stage percentages do not add up despite being 46 patients?? - were there any stage 4 patients operated on and excluded?.....The sentence describing the level of miR-382 in each group does not specify if mean/STD or otherwise. figure 3 - no x-axis label...no specification of what is "higher" level cutoff and why it was chosen as the cutoff - also not specified in the main text. discussion - second sentence is confusing in the way it is written. An assumption throughout is that the metastases relate to death. Was this the case for all patients or did some have local recurrence as their mode of death? Is the inference that miR-382 relates to metastases as opposed to local aggressiveness or is this not determined? conclusion - I recommend a further note being made about what specifically should be the next study point - ?determining the cut-off level of the marker for clinical utility? or prospectively comparing to TNM staging tool? or determining usefulness of the marker for post-op chemotherapy decisions, for example.

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	PubMed Search:	[ ] Accept
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

It's an interesting well written study. Just 2 points for future studies or to add in the present study if possible: - it should be interesting to know if the analysis of the miR-382 is applicable also to forceps biopsies obtained during upper gi endoscopy and if it correlates to that expressed in the surgical specimen. - I would specify better how the stage was established before surgery (EUS, miniprobes, CT,Pet-ct) and how the patients were followed up(which imaging technique). - Figure3: please, specify the caption of the x-axis (weeks? Months?).