

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 30625

Title: miR-145 exerts tumor-suppressive and chemo-resistance lowering effects by targeting CD44 in gastric cancer

Reviewer's code: 03310535

Reviewer's country: Australia

Science editor: Jing Yu

Date sent for review: 2016-10-12 10:40

Date reviewed: 2016-11-02 14:13

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 checked="" 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 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 is an interesting study describing a novel mechanism by which miR-145 modulates gastric cancer cell growth and chemo-resistance through direct inhibition of CD44 expression. The aim is clearly stated, the findings are well described and the data are convincing. The paper is generally well written, but there are some minor typographical and grammatical errors throughout (in addition to those noted below). Specific comments: ? The method used to measure the level of CD44 mRNA should be stated in the abstract. ? There is unnecessary repetition of 'improved' and 'gastric cancer' in the first sentence of the introduction. ? According to GLOBOCAN 2012 data (and the cited paper), gastric cancer is the 5th most common cancer worldwide and the 3rd leading cause of cancer-related death. ? The reason for the specific reference to China in the third sentence of the introduction is not clear. There is a higher incidence of gastric cancer in China, but the low survival rate is applicable worldwide ? A reference is required to support the statement that CD44 expression is upregulated in advanced gastric lesions. ? Each subfigure should be referenced in the text body when the relevant data is discussed. ? A brief description of ABCG2 would be helpful. ? In graphs showing mRNA



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expression levels, 'calculated' and 'calibrated' should be replaced by 'normalised' in the y axis label. ? The X axis labels are missing in Figures 1D, 2D & 2E ? The X axis legend for Figures 2B & 2C appears to be incorrect. I assume that the solid bar represents the miR-145 mimics on the left & the miR-145 inhibitor on the right in both graphs. ? While CD44 is associated with cancer progression and treatment resistance, it is not in itself an 'oncogene'. ? A weakness of the study is that only in vitro data using one cell line are presented. It remains unknown whether the mechanism identified is more widely applicable or is relevant in vivo. This should be acknowledged in the discussion. A specific comment on the potential clinical relevance of the findings would also add to the discussion. ? Abbreviations, including miRNA, MRE, WT, MT, RLU, 5-FU and MTT should be written in full on first use. ? 'Tumorspere' should read 'tumorsphere'; 'Turkey' should read 'Tukey'; 'westerin' should read 'western'.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 30625

Title: miR-145 exerts tumor-suppressive and chemo-resistance lowering effects by targeting CD44 in gastric cancer

Reviewer's code: 03440494

Reviewer's country: Tunisia

Science editor: Jing Yu

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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 checked="" type="checkbox"/> Grade C: Good	<input checked="" 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 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

-The manuscript is interesting, the design and methodology appear adequate but not overall well written (correct English mistakes), especially in the discussion part. -The results are not extensively discussed. -There is much detail in the discussion part:"The latter sported by the following observations. (a) miR-145 was down-regulated, whereas CD44 was up-regulated in gastric tumor spheres, highly enriched in GCSCs; (b) forced expression of miR-145 through transfection of miR-145 mimics in MGC-803 cells decreased the expression of CD44; (c) knock-down of miR-145 by miR-145 inhibitor in MGC-803 cells increased the expression of CD44; (d) forced expression of miR-145 through transfection of miR-145 mimics in MGC-803 cells decreased the activity of CD44-3'UTR; (e) knock-down of miR-145 by miR-145 inhibitor in MGC-803 cells increased the activity of CD44-3'UTR; (f) mutation of the MRE for miR-145 on CD44 3'UTR abrogated the regulatory effects by the miR-145 mimics or miR-145 inhibitor. These results indicate that miR-145 negatively regulates the expression of CD44 in gastric cancer cells". Please reduce and present clearly your findings. -The authors say "Our result demonstrated that enforced expression

stimulates ABCG2 mRNA expression". In fact the expression of what? -Please read and add this references in the discussion part : ? "ABCG2 regulates self-renewal and stem cell marker expression but not tumorigenicity or radiation resistance of glioma cells BoyoungWee*, Alexander Pietras*, TatsuyaOzawa, Elena Bazzoli, Ondrej Podlaha, ChristopheAntczak,? , BengtWestermarck, Sven Nelander, Lene Uhrbom, Karin Forsberg-Nilsson, Hakim Djaballah, Franziska Michor & EricC. Holland. Scientific Reports | 6:25956 | DOI: 10.1038/srep25956 ? "New trends for overcoming ABCG2/BCRP-mediated resistance to cancer therapies. David Westover and Fengzhi Li ?. J Exp Clin Cancer Res. 2015; 34: 159. ? Andre R. Jordan,1,? Ronny R. Racine,2,? Martin J. P. Hennig,2,3 and Vinata B. Lokeshwar2,4,5,* The Role of CD44 in Disease Pathophysiology and Targeted Treatment. Front Immunol. 2015; 6: 182. -There are many human gastric carcinoma cell lines "GES-1, BGC-823, SGC-7901, HEK293T cells...). Why you chose to work with MGC-803 cell? -The authors investigate several gastric cancers stem cell marker expression in the tumor spheres and monolayer cells. Why they chose "Sox2, OCT-4 and Nanog mRNA expression" and what they play in the gastric tumor environment? They increase malignancy or affect tumorigenicity or what? Please clarify and discuss you findings in correlations with your results. -Please indicate the abbreviation of MREs (a Putative miRNA regulatory element) . -Why the Luciferase activity was measured at 36 h after transfection? -What do you authors mean by this sentence: " We used the TargetScan database (<http://www.targetscan.org>) to identify miR-145 predicted to target CD44". Please clarify?