ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9912

Title: MicroRNAs: promising biomarkers for chemoresistance in gastric cancer with diagnostic and therapeutic potential

Reviewer code: 02505493

Science editor: Gou, Su-Xin

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D (Fair)		BPG Search:	
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This review manuscript contains information regarding the applicability of miRNAs as biomarkers in prediction of sensitivity towards different chemotherapeutics, as well as modulators of sensitivity and resistance towards chemotherapy in gastric cancer. The current information, although limited as the authors also mention, is of high interest and well presented in the manuscript, so it can be accepted for publication after the following corrections: Page 2, Abstract: The terms "microRNA" and "miRNA" must be used in lines 8 and 9. Page 3, line 17: … water soluble ….. Page 4, line 5: …. messenger RNA ….. Page 4, line 10: miRNA Page 4, line 23: "from a" is written twice Page 6, line 13: use "are" instead of "is" Page 6, line 21: add the right parenthesis after the number of ref. 58 Page 8, line 1 (title): miRNA Page 8, line 15: …. (table 1). Page 11, conclusion: the sentence "Based on the fact that miRNAs are on the one hand accessible and detectable in different tissue types including blood samples with great stability, and play on the other hand an important role in the development and regulation of multidrug resistance, these molecules seem to have great potential as new biomarkers for diagnostic and therapeutic approaches." should be reorganised to "Based on the fact that miRNAs play an important role in the development and regulation of multidrug resistance, and in addition are accessible and detectable in different tissue types including blood samples with great stability, these molecules seem to have great potential as new biomarkers for diagnostic and therapeutic approaches." Pages 24 and 27, legend of Fig. 1: Add a reference for DianaPath Page 27, Figure 1: miRNAs up- or down-regulation in gastric cancer should be indicated in the figure

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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COMMENTS TO AUTHORS

This manuscript concerns a concise review on the use of miRNAs as biomarker and/or therapeutic tool in gastric cancer. Despite being an interesting topic I would have liked to see a more critical approach of the current literature and a section on hurdles that need to be taken before wide-spread application of miRNA biomarkers / therapeutics in the clinic. Major comments 1. Please include a section on future prospects listing the hurdles that need to be taken before miRNAs can be safely employed in the clinic. For example larger prospective clinical studies are necessary that systematically analyze miRNA expression both in serum and tumor tissue in relation to the response to defined chemotherapy regimens. Alternatively one may want to perform studies on animal models of gastric cancer before going to the clinic. The use of miRNA therapeutics comes with its own set of difficulties, what is the current state-of-affairs and what are the specific difficulties? The distinction between diagnostic and therapeutic miRNAs is somewhat artificial. Please define exactly when a miRNA is of diagnostic use and when it does have therapeutic value. Are there any specific characteristics that need to be taken into account when dealing with gastric cancers? 2. Figure 1 – It is unclear to me how this figure was generated and how it should be read. For example in the circle labelled "Jak-STAT signaling pathway" I notice cyclin D1, a cell cycle protein as well as two proteins involved in apoptosis Bcl-2 and Bcl-XL what is the link to the Jak-STAT pathway? Similarly, the circle MAPK signaling pathway is unclear. Please carefully check the figure and clearly describe how the figure was made. 3. Page 6, line 24, page 7 line 1 – "In addition, several anti-cancer-drugs……resistance via miRNAs" Please note in this respect that the regulation of known cancer related genes by miRNAs is much more frequently reported simply because these

genes are well studied. In addition not all miRNAs show similar sensitivity phenotypes in different cancer types.   Minor comments 1. Page 3, line 9 – Please give appropriate references to MAGIC and ACCORD trials. 2. Page 3, line 13 – What exactly do the authors mean by "somewhat" resistant. Omit somewhat. 3. Page 3, line 22-23 – Use correct gene nomenclature for P-gp, ABCB1 and for breast cancer resistance protein, ABCG2. 4. Page 4, line 7 – So far, more over 2500 human ….. should be: "So far, over 2500 human….." Throughout the manuscript there are more small typographical /grammatical errors, please proofread   carefully for these mistakes. 5. Page 4, line 9 – As for most miRNAs it is not shown that they are truly able to target hundreds of mRNA, I recommend to rephrase this sentence clearly stating that "… each single miRNA can potentially target up to hundreds of mRNAs".   6. Page 5, heading – omit the word "promising" from the heading. 7. Page 5, line 11 – What do the authors mean with "present a certain stability…." One wants biomarkers to be stably present , refractory to degradation, in the clinical samples in order to obtain reliable data. Please rephrase the text. 8. Page 8 – please indicate that Adriamycin is in fact doxorubicin 9. Page 9, line 6-18 – When describing studies involving patients / clinical samples it is important to mention the number of patients/ biopsies studied. In fact these are the more interesting studies as they entail direct measurements on patient samples and may be more "predictive" than studies involving cell lines. 10. Page 10, line 3 and line 5 – Please refer to Yang et al and Zhao et al by a reference number at the end of the sentence. 11. Page 16 – Reference 35, "Cucc Opin Pharmacol" should be "Curr Opin Pharmacol" 12. Page 19 – Reference 60, Zhao JP et al is not correct. This paper deals with miRNA expression in a tree namely Populus trichocarpa. Please correct! 13. Page 20 – page numbers and journal abbreviation in reference 63, Akao, Y et al

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COMMENTS TO AUTHORS
Reviewer's comment on MicroRNAs

This article entitled "MircroRMAs: promising biomarkers for chemoresistance in gastric cancer with diagnostic and therapeutic potential" by Borchardt et al shows an extensive and thorough review on Mi-RNAs so far reported up to present time. It is highly educational paper and the authors are commended.
Comments:
While describing more than 20 miRNAs, authors can make a more succinct summary by putting informations in two groups than describing every individual miRNA; an example, on pages 8 through 10, when miRNAs are described as diagnostic and therapeutic potential. There are two groups of miRNAs, one group that downregulated and the other upregulated. While the authors summarized in tables 1 and 2, it is important to describe these MiRNAs in the text but in a simplified way.   By this way, it would be far easier for the readers to follow the story.

Minor comments
For references in serial numbers, only the first and the last
Number of references may be listed.
In tables, if abbreviations (Target) are written out below the table, it would
    be easier for the readers.