



**ESPS PEER REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13730

**Title:** MiR-19a promotes epithelial-mesenchymal transition through PI3K/ AKT pathway in Gastric cancer

**Reviewer code:** 00615183

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-08-31 21:38

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

In this manuscript the authors analyzed miR-19a expression in gastric cancer tissues and cell lines, and found that over expression of miR-19a is associated with cancer cell growth, migration, and metastasis. The authors further found that miR-19a over expression in cancer cells promotes EMT by activating the PI3K/AKT pathway, and blocking the PI3K/AKT could prevent EMT by miR-19a. miR-19a upregulation in cancer tissues and its functional link with PTEN/AKT are well known. The most interesting finding of this manuscript would be promotion of EMT by miR-19a through PI3K/AKT. I have some minor suggestions to improve the manuscript. 1. The first paragraph of the Discussion can be moved to the Introduction with some modifications. 2. Page 9, section 3.2: Because the cell lines already express excessive miR-19a, I think the knockdown, rather than the over expression is more meaningful. Thus, it would be better to emphasize the knockdown. 3. Fig 3a: Morphological changes regarding EMT by miR-19a over expression should be shown (general, immunostaining etc.) - this is important. 4. Similarly, Fig 4c needs a photo to show morphological changes.



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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13730

**Title:** MiR-19a promotes epithelial-mesenchymal transition through PI3K/ AKT pathway in Gastric cancer

**Reviewer code:** 02568380

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-08-31 21:38

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

**COMMENTS TO AUTHORS**

The authors investigate the expression level of miR-19a in gastric cancer and the function of miR-19a on gastric cancer progression. The study is well designed and there some minor issues need to be addressed. 1. The authors missed many references and should examine the article carefully. 2. There are missing words or grammar mistakes need to be corrected. 3. In part 2.4, the authors claimed that they used MTT assay to measure cell proliferation, however the kit provided in the article (cell counting kit-8) does not contain MTT at all. 4. Please clarify how they define "normal" tissue. The normal tissue used to compare miR-19a level should be normal gastric mucosa, not other layers of stomach. 5. Please explain why they used lentiviral infection for cell proliferation and transient transfection for other experiments. 6. The picture quality is very poor. The authors also need to provide pictures for EMT phenotype.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13730

**Title:** MiR-19a promotes epithelial-mesenchymal transition through PI3K/ AKT pathway in Gastric cancer

**Reviewer code:** 02935012

**Science editor:** Su-Xin Gou

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
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<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Comments to “MiR-19a promotes epithelial-mesenchymal transition through PI3K/AKT pathway in Gastric cancer” in World Journal of Gastroenterology ----- In recent years, the role of miRNAs, in particular, miR-19a was increasingly described in cancers, previous studies include breast cancer, non-small cell lung cancer, colorectal cancer, bladder cancer, etc., of note, the majority of these studies indicated that miR-19a was positively correlated with the poor prognosis of the patients. For gastric cancer, Qin et al reported that miR-19a promotes cell growth and tumorigenesis (Qin et al. Asian Pac J Cancer Prev. 2013.). In current study, Lu et al also demonstrated that miR-19a was a poor prognostic factor for GC patients, in addition, high expression of miR-19a was associated with the metastasis of GC and have a series of functions in GC cell lines. Further, they uncovered its underlying mechanism would be attributed to the regulation of PI3K/AKT pathway. This paper further elucidated the role of miR-19a in different solid tumors and addressed its potential regulation mechanism. Although most of descriptions within the paper are interesting, the paper includes required features. 1. The paper should be further edited and all the abbreviation (such as AKT, Akt), upper and lower case as well as the citations should be in uniform. 2. In the section of Introduction, the authors mentioned: “Recent reports have highlighted the importance of microRNA as a powerful regulator of EMT in cancer cells”, these references are very important to cite, the authors should list these studies in the end of the paper. 3. In section 2.1, the authors mentioned: “Non-tumor samples



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from the macroscopic tumor margin were isolated at the same time...". I wonder how the authors define these "Non-tumor samples". I recommend the following reference: Liu et al. Decreased expression of IGFBP7 was a poor prognosis predictor for gastric cancer patients. *Tumor Biol.* 2014 Jun 4. [Epub ahead of print]. 4. The authors described that they used the cell lines SGC-7901 and NUGC-3, however, in section 2.4, MKN28 was used. 5. In section 2.5, again, the authors said: "Migration and invasion assays were performed as described previous", but no references were cited. 6. As one of the important results addressed in the Abstract, miR-19a could promote cell proliferation; the authors should display the data of MTT assay. 7. Figure 2, the figure legends was not corresponding to the figure. 8. In the paper, the cell line NUGC-3 often miswritten into SUGC-3. 9. In the section of Discussion, the authors should highlight the main results in the first paragraph. 10. The quality of the figures was extremely poor, which makes it very hard to understand the results. In section 3.2, the hint of the figure is wrong. 11. For figure 4, the authors should mark the concentration of the Ly294002, not only state -, +. 12. The marker for EMT is very important in this paper, although the authors performed the western blotting to check these markers, but more directly results should come from the IHC study, I recommend the authors display some representative figures for EMT.