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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 30486

**Title:** Hsa-mir-183 is frequently methylated and related to poor survival in human hepatocellular carcinoma

**Reviewer's code:** 02997239

**Reviewer's country:** Egypt

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-10-08 19:15

**Date reviewed:** 2016-10-16 18:21

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"/> 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 checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input 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 issue that is searched for in this paper is very interesting. however, there are some comments: 1- the pathological criteria of the studied specimens should be presented. 2- impact of deregulated studied microRNAs and DNA methylation on pathological criteria of studied specimens. 3- the discussion is in need to focus on hepatocellular carcinoma and the studied microRNAs. 4- minor language changes should be done



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

**ESPS manuscript NO:** 30486

**Title:** Hsa-mir-183 is frequently methylated and related to poor survival in human hepatocellular carcinoma

**Reviewer's code:** 00006931

**Reviewer's country:** United States

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-10-08 19:15

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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 type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

In this manuscript, Anwar et al., described the status of miR-183 and related to poor survival in human hepatocellular carcinoma. In general, this is an interesting manuscript, explaining epigenetic regulation of miR-183 in HCC and its potential role as a novel surrogate and prognostic marker. However, the authors need to address the following concerns for improving the manuscript.

Specific Comments

1. In methods section and in table 2, authors mentioned 10 samples with HCAs but in results section on page 7 about DNA methylation analysis in benign liver tumors and healthy liver tissues authors mentioned 15 cases of HCAs. Please revisit this discrepancy and also include the information about the healthy liver tissues (n=5) (their source, characteristics and how they obtained) in the Table 1.
2. Authors did three sequential transfections in HLE cells to knock down DNMT. How was the cell viability after knocking down DNMTs?
3. Authors described mRNA quantification on page 6 but its not clear which mRNA expression was determined in the manuscript.
4. Please correct the sentence on page 9 in the discussion section 'since microRNAs modulate several microRNAs and transcription factors' to since microRNAs modulate several mRNAs and



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transcription factors. 5. In Figure 1, miRNA expression is shown after knocking down DNMT in cell line. Please show the methylation level of miR-183 promoter in the same figure as a different panel to conclude methylation-mediated regulation of this miRNA. 6. The authors need to discuss their findings to reveal the mechanistic details about miR-183 methylation and the associated impact on cell proliferation and HCC development. Similarly miRNA targets should be validated in tumor tissues. There should be a correlation between miRNA silencing by methylation, higher expression of target mRNA and increased HCC progression before concluding with poor survival in HCC. 7. In supplementary figure 2, methylation level of hsa-miR-23 is shown in clinical samples (panel A) and hsa-miR-25 level in cell lines (panel B). Why the hsa-miR-25 methylation is not determined in clinical samples as in panel A? The authors please discuss.