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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 35718
Title: Down-regulation of miR-30a-3p/5p promotes ESCC cells proliferation by activating WNT signaling pathway
Reviewer's code: 03001816
Reviewer's country: USA
Science editor: Ke Chen
Date sent for review: 2017-08-18
Date reviewed: 2017-08-18

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

COMMENTS TO AUTHORS

This is an acceptable paper, which makes a solid contribution to the field. However, some minor revisions are required. First, with respect to the RNA isolation and subsequent quantitative real time RT-PCR, were any controls performed to test for genomic DNA contamination? For example, were any samples processed without the RT step, which should yield no PCR product in the absence of DNA contamination? The methods section also needs a description of the WNT luciferase reporter assay from Figure 5B. What reporter was used? Was a mutant control also evaluated to ascertain whether effects are specific to Wnt activity? For example, if TOPFlash was used as the WNT reporter, then that activity needs to be normalized to the FOPFlash control. While I understand that Wnt target genes exhibited altered expression as shown in Fig. 5C, one could argue that that the effects are not necessarily specific to WNT signaling. Therefore, using the mutant control promoter in Fig. 5B would strengthen the

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conclusions for both 5B and 5C. In the Discussion, the sentence that begins "Colorectal tumorigenesis is activated…" suggests that colorectal cancer is initiaated by WNT ligand-Frizzled receptor binding (which is actually what normal WNT signaling is). In actuality, most colorectal cancer is initiated by mutations in the WNT signaling pathway (e.g., APC or beta-catenin) that constitituvely activate the pathway even in the absnce of ligand-receptor buindinf. Of course, such neoplastic cells can also have additional WNT signaling through ligand-receptor activity, and that can promote progression, however, the main activity of WNT signaling in colorectal cancer is typically the result of mutations that drive WNT signaling even in the absence of ligand-receptor binding. That should be modified as well. A minor issue: there are some grammar errors, please edit. For example, should be "ESCC cell proliferation" not "ESCC cells proliferation. Also, should be either "activating the WNT signaling pathway" or "activating WNT signaling" not "activating WNT signaling pathway.

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[ ] No	

COMMENTS TO AUTHORS

In this study, authors identified the potential role of miR-30a-3p/5p in esophageal squamous cell carcinoma progression. This is a well-defined study and the MS is written and organized well. Authors showed that down-regulating miR-30a-3p/5p promotes ESCC cells proliferation by activating WNT signaling pathway. However, the connection between miR-30a-3p/5p and WNT signaling is weekly shown in the MS. Concerns: 1. KEGG pathway enrichment analyses of miR-30a-3p and miR-30a-5p target genes (figure. 5) shows that multiple pathways are enriched (Ras, MAPK, FoXo, Hippo and WNT). How authors selected WNT signaling among the other signaling events? Ras, MAPK are highly enriched. Authors should explain this. 2. In figure 6 C. did authors check the inhibitory effects of miR-30a-3p and miR-30a-5p on different Wnt ligands?