

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37113

Title: Behind the curtain of non-coding RNAs; long non-coding RNAs regulating hepatocarcinogenesis

Reviewer's code: 00503516

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2017-11-13

Date reviewed: 2017-11-20

Review time: 6 Days

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 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 checked="" 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 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

Aya. El Khodiry et al describe the biological role of long non-coding RNAs in HCC genesis, spreading and prognosis; in addition the authors discuss the possibility to regulate and target these lncRNAs to find novel future therapeutic tools for HCC. The work contain a lot of information about lncRNAs and HCC; however, some logical connections among different sections are missing. Major points It is not well explained the relation between epigenetic regulation and lncRNAs, i.e. how epigenetic regulates lncRNAs and if this is a relevant mechanism in HCC. The authors properly divide HCC lncRNAs into "Tumor suppressor lncRNA" (pag 6) and "Oncogenic lncRNA" (pag 8); however following these two sections they start to deeply describe other specific lncRNAs (pag 12-22) without any explanation. I think the authors should clarify why some lncRNAs are described in such detail; are they more relevant for HCC than others?



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Are they more studied than others? Are they more strictly related to HCC prognosis? It is not clear whether the lncRNAs described are uniquely dysregulated in HCC or also in the cirrhotic tissue; this information is relevant in term of the possibility to propose the use of some of the lncRNAs as novel specific HCC markers. It is indeed well known that HCC mostly develops in the context of cirrhosis. It would be helpful divide the data according to the fact that the studies have been conducted in vitro, in animal models or in humans and prepare a corresponding table. It would be nice to further subdivide the lncRNAs based on their mechanism of action, i.e. those reported on page 5 lines 5-13 from bottom. Minor points On page 3 second paragraph, it is not clear whether DNMT1 belongs to both maintenance methyltransferase and de novo methyltransferase or just to the maintenance methyltransferase. On page 4 section "Non-coding RNAs", add some reference related to non coding RNAs different from lncRNAs. In addition, explain that the review will be focused on lncRNAs

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Title: Behind the curtain of non-coding RNAs; long non-coding RNAs regulating hepatocarcinogenesis

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Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-11-30

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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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Khodiry et al reviewed the role of long non-coding RNAs (lncRNAs) in development, metastasis and prognosis of HCC to find an efficient treatment for HCC by focusing on lncRNAs. The authors found that lncRNAs such as HULC, HOTAIR, MALAT1 and MEG3 showed extensive roles related to HCC tumorigenesis. They also reported that the serum and tissue levels of lncRNAs could serve as an accurate diagnostic marker for patients with HCC that could overcome AFP's accuracy. They concluded that lncRNA act as an important regulator in various biological processes in HCC and lncRNAs exerts the beneficial effects in diagnosis, treatment and prognosis of HCC. I have only minor comments. 1) On page8 line 9, 'USC7 act as tumor suppressor' must be 'USC7s act as tumor suppressor'. 2) On page 28 line 14, 'These pathways are a good candidate' should be 'These pathways are good candidates' 3) SPRY4-IT1 is also strongly related to cell

proliferation and EMT progression. They should refer the recent paper by Yu G et al (2017) in the literature review.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37113

Title: Behind the curtain of non-coding RNAs; long non-coding RNAs regulating hepatocarcinogenesis

Reviewer's code: 03473431

Reviewer's country: Italy

Science editor: Ze-Mao Gong

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

I congratulate the authors for their work. The paper is a full description of the role of long non-coding RNAs regulation on hepatocarcinogenesis describing all possible mechanisms involved in HCC formation and possible future targeted therapies. The manuscript can be published in the Journal.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37113

Title: Behind the curtain of non-coding RNAs; long non-coding RNAs regulating hepatocarcinogenesis

Reviewer's code: 02941955

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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
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a well written manuscript. This reviewer learn that an enormous effort has been spent to accomplish this work. However, the description was too redundant and might be tough to read through to the end for somebody who are not professional. More concise and comprehensive manner of description may help readers to figure out this theme more clearly.