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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9079

Title: HIF-1alpha induces expression of VE-cadherin and modulates vasculogenic mimicry in esophageal squamous cell carcinoma cells

Reviewer code: 00061678

Science editor: Ya-Juan Ma

Date sent for review: 2014-01-20 13:44

Date reviewed: 2014-01-21 01:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> 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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Dear Editor, Authors Thank you for sending the manuscript"HIF-1alpha induces expression of VE-cadherin and modulates vasculogenic mimicry in esophageal squamous cell carcinoma cells" to be revised. The paper is well organized and well written, has a unique idea. minor comment is that title need to be modified as it is too long. Thanks



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9079

Title: HIF-1alpha induces expression of VE-cadherin and modulates vasculogenic mimicry in esophageal squamous cell carcinoma cells

Reviewer code: 02563046

Science editor: Ya-Juan Ma

Date sent for review: 2014-01-20 13:44

Date reviewed: 2014-02-16 16:35

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"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is an interesting and novel piece of work that certainly deserves merit. The authors provide evidence that vasculogenic mimicry exists in ESCC and that HIF1-alpha is intimately involved in this process. However, although the data presented are convincing, there are some minor concerns that should be resolved before publication:

1. The introduction and discussion section appear not yet complete and both are to some extent rather short: As the authors address with their data aspects of tumor microenvironment, hypoxia, and metastasis, which strongly relates to intra-tumor heterogeneity and clonal cancer development, they should discuss their data along recent progress in the field as reviewed in Grunewald TG et al. (J. Transl. Med. 2011) and Merlo LM et al. (Nat. Rev. Cancer 2006).
2. Also, the authors should expand their discussion on the stability of HIF1-alpha referring to recent articles in the field such as that of Chen K and Chen S et al. (Biology of the Cell, 2013), as well as to recent progress in terms of methodology to assess endothelial structures detailed in Prigozhina NL et al. (Biol Cell, 2011).
3. Another aspect that should be discussed by the authors is that vasculogenic mimicry might be part of the EMT program of cancer cells, which is induced by epigenetic alterations such as aberrant miRNA expression and changes in barrier functions by altering expression of VE-cadherin and other important proteins as reviewed in Bullock MD et al. (Biol Cell 2012) and Guelte AL (Biol Cell 2011).
4. Although the overall level of English is acceptable, the manuscript could benefit in certain passages (especially in the results section) of proofreading by a native English speaker to enhance grammar and readability.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9079

Title: HIF-1alpha induces expression of VE-cadherin and modulates vasculogenic mimicry in esophageal squamous cell carcinoma cells

Reviewer code: 00555673

Science editor: Ya-Juan Ma

Date sent for review: 2014-01-20 13:44

Date reviewed: 2014-02-24 22:47

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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The present manuscript by Tang et al reports the relevance of both VE-cadherin and HIF-1alpha for the phenotypic properties of two esophageal squamous cell carcinoma (ESCC) lines, specifically in the context of the vasculogenic mimicry phenomenon. The authors provide various cellular and xenograft approaches to get their conclusions. Importantly they analyzed a series of molecules known to be implicated in these kinds of processes. Although the results are clear the authors do not provide the right information to really discriminate a what level the absence of HIF-1alpha or VE-cadherin is affecting cell functionality in general. The knocking down of both genes is clearly affecting cell proliferation, migration, and even apoptosis. According to these results, it is not clear if the deficiency of forming capillary-like structures in Matrigel is just a result of defects on basic cellular machinery as proliferation and migration; maybe the alteration of vasculogenic mimicry is just the consequence of the proliferative and migratory defects. It would be important to find that VM is affected but in an independent manner of proliferative and migratory pathways. In any case the only conclusions I get from this manuscript are: (i) the lack of HIF-1alpha affects basic cellular processes, probably because many genes are also down-regulated; and (ii) the lack of VE-cadherin is also affecting basic cellular mechanisms. Some other points: - Immunohistochemistry in Figure 3B is not clear and it is difficult to do any interpretation. - In Figure 3C, while the down-regulation of the protein is clear, the PCR data do not show any changes. Quantitative PCR would be more valuable. - According to the nature of VE-cadherin protein, the immunoanalysis of this protein will help to interpret their results.