



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14444

Title: Role of the Wnt/ β -catenin pathway in gastric cancer

Reviewer’s code: 00255764

Reviewer’s country: United Kingdom

Science editor: Xue-Mei Gong

Date sent for review: 2014-10-05 11:07

Date reviewed: 2014-10-24 20:44

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		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

The author focuses on the covering the role of Wnt signalling in gastric cancers with a particular focus on the role of H.pylori infection. While interesting I do feel that the manuscript needs a significant number of changes before it is suitable for publication. Major comments: 1. The readability of the manuscript suffers from a number of grammatical errors, awkward sentences and some clumsy turns of phrase. The abstract needs particular attentions as this probably the most important piece of text to grab a reader’s attention. Try to make it clearer and more concise. 2. Early on in the manuscript a brief overview (and potentially a figure) of the histological/pathological development associated with gastric cancer initiation/development/progression would help put the cellular and molecular work discussed into context. 3. A brief introduction to H.pylori and it major virulence factors would again help provide some context. Is H.pylori infection important for initiation, development or maintenance of gastric cancers? What is CagA and how it might function (transcriptional regulator, kinase etc? Minor comments or suggestions: 1. There are too many intriguing, but poorly developed points that leave the reader “hanging”. For example: “This action of TC1 is achieved relieving the antagonistic function of Cby on β -catenin-mediated transcription[76].”



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What is Cby and how does it antagonise B-catenin-mediated transcription? Should Cby's mechanism be explained in the "pathway antagonist" section? "Consequently, this induces aberrant expression of the intestinal-differentiation marker goblet-cell mucin gene MUC2 [82]." What is MUC2 and how does it influence tumour progression or Wnt signalling. Does it act in the same way as MUC1? "... E3 ubiquitin-protein ligase RNF138, which negatively modulates Wnt/?-catenin signaling pathway, was downregulated by H. pylori[86,87]." How does RNF138 inhibit Wnt signalling? These and the other examples need to be explained/developed further. 2. The general introduction to Wnt signalling would benefit from a section on the regulatory mechanisms governing B-catenin import / cytoplasmic sequestration. 3. I would suggest distilling down the "genomic alterations" section and incorporating it into new subheadings concerning "Gain of Wnt activator function in gastric cancer" or "Loss of Wnt repressor function in gastric cancer" sections. 4. The existing text in the "Wnt ligands" and "Wnt antagonist" sections can also be incorporated into the "Gain" and "Loss" sections. Within each section the author can have "Genetic, epigenetic and post-translational" subheadings. Together this structure should make the review more coherent. 5. Removal of the passive voice ("that have been shown... etc") 6. I would explicitly point out some of the apparent paradoxes in Wnt signalling, as well as potential explanations. For example: Wnt negative feedback mechanisms normally prevent rampant, unrestrained Wnt signalling, but selective repression of certain Wnt target genes may uncouple the negative feedback. 7. What is the actual mutation frequency of CTNNB1 in gastric cancer? It is not clear from the following sentence. Is it 30% of all gastric cancers or 30% of those gastric cancers identified with mutant CTNNB1? "Some mutations in CTNNB1, the gene that encodes β -catenin protein, have been frequently detected in intestinal- and diffuse-type gastric cancer with 30% of tumors showing nuclear accumulation of β -catenin[7,95,99-103]."



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14444

Title: Role of the Wnt/ β -catenin pathway in gastric cancer

Reviewer's code: 00646379

Reviewer's country: United States

Science editor: Xue-Mei Gong

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Date reviewed: 2014-10-28 04:49

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		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

This is well organized manuscript. Need to perform some editing and following references should be included for clarity of the field. Dig Dis Sci. 2013 Mar;58(3):724-33. Int J Oncol. 2011 May;38(5):1375-83. Int J Mol Med. 2014 Jul;34(1):197-204 Eur J Cancer. 2013 Nov;49(17):3718-28 Cancer Lett. 2013 Oct 28;340(1):72-81. Oncol Rep. 2013 Sep;30(3):1137-42. Mol Med Rep. 2013 Jun;7(6):1751-6. Tong et al. Oncotarget. 2014 Sep 25. [Epub ahead of print] Zhang et al. Proton pump inhibitor pantoprazole abrogates adriamycin-resistant gastric cancer cell invasiveness via suppression of Akt/GSK- β / β -catenin signaling and epithelial-mesenchymal transition. Cancer letters, DOI: 10.1016/j.canlet.2014.10.016



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14444

Title: Role of the Wnt/ β -catenin pathway in gastric cancer

Reviewer’s code: 00066723

Reviewer’s country: Netherlands

Science editor: Xue-Mei Gong

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		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

The manuscript is a comprehensive review of the involvement of the Wnt/ β -catenin pathway in gastric cancer. The author briefly describes the canonical Wnt signaling pathway to subsequently deal with various aspects of this pathway its regulation, involvement in metastasis, pathway antagonists and its dysregulation in gastric cancer to name a few. The reader gets a nice overview of the literature on this topic. Some parts/sentences are not clear, please have the manuscript proofread. Major comments 1. Please check English grammar throughout the manuscript paying particular attention to the abstract. 2. Page 3, line 25 - “proliferation / stem cell” can hardly be considered an oncogenic pathway. Please correct. 3. Figure 3 - from CK1 α and GSK3 β inhibitory lines run to β -catenin (in off-state panel) and to LRP5/6 (in on-state panel). This is confusing as CK1 α and GSK3 β phosphorylate (not inhibit) β -catenin and LRP5/6. Please check and change. Minor comments 1. Page 4, line 22 - “ciliogenes” what exactly is meant ciliogenesis? Please check. 2. Page 5, line 2 - Which “interaction” is meant here? Please rephrase sentence to make this more clear. 3. Page 5, line 24 - Use proper gene abbreviation throughout the text e.g. CCND1 instead of cyclin D1. 4. Please include appropriate reference in Table 1 5. Page 7, line 2 - For the casual reader it is difficult to



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understand what exactly the author tries to convey by "...wnt-6 is a critical mediator of the resisance of gastric cancer cells to anthracycline drugs promoting by caveolin-1" Please rephrase sentence and explain in more detail. 6. Page 9, line 29-30 - "Meanwhile, HMGA2 causes EMT by suppressing the expression of AXIN1 and increased TWIST1 expression through the binding to their promoters." Sentence does not read well, please rephrase. Also the next sentence is somewhat ambivalent, please change. 7. Page 10, line 12 and following - "CagA-independent manner" please explain what CagA is, for the reader not familiar with H. pylori this is unclear and hard to understand. 8. Page 16, line 2 - "consecuense" should this be "consequence"?



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14444

Title: Role of the Wnt/ β -catenin pathway in gastric cancer

Reviewer's code: 02441737

Reviewer's country: Mexico

Science editor: Xue-Mei Gong

Date sent for review: 2014-10-05 11:07

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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
<input 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

It is a very interesting manuscript; although it is recommended that the authors note in the title that this is a review of the literature focuses on findings on Wnt/ β -catenin pathway as it relates to gastric cancer.

Comments

The manuscript is properly presented and discussed in detail the signaling pathways by which Wnt / β -catenin pathway as it relates to gastric cancer. It is encouraged to author if possible, dividing the manuscript in subtitles; i.e. separating sections in which one by one the steps of the signaling via Wnt / β -catenin pathway proposed as the origin of gastric cancer.

It is also recommended, that the author present in the introduction, details in percentage terms of the magnitude (prevalence of gastric cancer and its consequences) locally (Italy), in Europe and around the world.

If possible comment on the document the role of the physical and psychological stress in the activation of the Wnt / β -catenin pathway in gastric cancer.



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Table 1, it is not clear or at least for my document is not, it is advisable to present it more clearly.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14444

Title: Role of the Wnt/ β -catenin pathway in gastric cancer

Reviewer's code: 00531670

Reviewer's country: Turkey

Science editor: Xue-Mei Gong

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" 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"/> 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

This is a nice review on the role of the Wnt pathway in gastric cancer. In my view the manuscript would be suitable for publication following some minor revision. 1. Association of the Wnt pathway with gastric stem cells needs to be addressed thoroughly 2. The section on the involvement of the miRNAs in the control of the Wnt pathway in gastric cancer cells is very short and should be extended.