

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 32914

**Title:** Biliary Tract Cancer Stem Cells – Translational Options and Challenges

**Reviewer's code:** 02566177

**Reviewer's country:** Australia

**Science editor:** Yuan Qi

**Date sent for review:** 2017-02-01 07:52

**Date reviewed:** 2017-02-06 11:49

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"/> 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 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 review focuses on new concepts and recent discoveries on cancer stem cells related to the biliary tract. These concepts are relatively new and very important to understand tumor biology and natural history of these cancers that still have a dismal prognosis overall. The review is reasonably well written (a review by an English first language expert is warranted). My only point: I would probably underscore in more detail the role of inflammation and particularly chronic inflammation and its relations to cancer stem cells establishment and natural history of the disease.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 32914

**Title:** Biliary Tract Cancer Stem Cells – Translational Options and Challenges

**Reviewer's code:** 03471529

**Reviewer's country:** Japan

**Science editor:** Yuan Qi

**Date sent for review:** 2017-02-01 07:52

**Date reviewed:** 2017-02-06 12:52

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"/> 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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 think that the manuscript is very well written, intensively reviewing biliary tract cancer stem cells, and insighting the pathophysiology of biliary tract cancers. However, it is conceivable that the authors should comment as follows in the section of Cancer Stem Cell Markers in Biliary Tract Cancer – an Overview. ESC-genes such as POU5F1, SOX2 and NANOG are essential for their self-renewal ability and pluripotency. Therefore, CSCs should express these genes at a level equivalent to those of ESCs for such function. From a functional point of view, POU5F1, SOX2 and NANOG were not always the marker genes for CSCs and drug resistance. In addition, lower level of the expression was not always functional for the self-renewal ability and pluripotency.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 32914

**Title:** Biliary Tract Cancer Stem Cells – Translational Options and Challenges

**Reviewer's code:** 03478635

**Reviewer's country:** Japan

**Science editor:** Yuan Qi

**Date sent for review:** 2017-02-01 07:52

**Date reviewed:** 2017-02-01 13:28

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" 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 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"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[ Y ] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[ Y ] No	

## COMMENTS TO AUTHORS

This review article contains new visions in which biliary tract cancer has cancer stem cells. Please clarify more in detail and discuss how interleukin (IL)-6 / JAK / STAT cascade is involved in CSC signaling in terms of cross-talk with NOTCH, Wnt or Hh signaling in Relevance of stemness pathways in biliary tract cancer stem cell section. Please check references and abbreviations carefully again.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 32914

**Title:** Biliary Tract Cancer Stem Cells – Translational Options and Challenges

**Reviewer's code:** 03370303

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**Science editor:** Yuan Qi

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**Date reviewed:** 2017-02-02 16:43

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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"/> 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
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		BPG Search:	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This review is very well written, intensively illustrating the characteristics and impact of biliary tract cancer stem cells from both scientific and clinical point of view. It will make a great contribution to an advanced understanding of the pathophysiology of biliary tract cancers. Although the quality of English is satisfactorily high throughout the main text, there are several points to be modified in Abstract and Core tip. Before publication in World Journal of Gastroenterology, they should appropriately be addressed. Grammatical/terminological concerns: 1. In the 6th line in Abstract, the phrase "...due to their suspected contributions..." sounds rather peculiar since the word "suspected" is generally used with a negative (bad) connotation. It would be better to rewrite the phrase as "...due to their potential contributions...", for example. 2. In the 1st line in Core tip, the phrase "researchers could demonstrate ..." should be written in the past tense without using the word "could", because this auxiliary verb even implies "possibility" or "conjecture". It would be better to rewrite the phrase as "researchers successfully demonstrated...", for example. 3. In the 6th line in Core tip, it would be better to rewrite the phrase "Following these results..." as "Based on these results...". 4. In the 6th line in Core tip, it would be better to rewrite the phrase "the existence of



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cancer stem cells in biliary tract is likely..." as "the existence of cancer stem cells in biliary tract is well founded" or "the existence of cancer stem cells in biliary tract is valid". The word "likely" rather lacks scientific tone. 5. In the last sentence in Introduction, the word "BTC" should be written together with its non-abbreviated form since this is the first appearance of this term in the manuscript. 6. In line 8 in page 5, the phrase "very few cells are seeded..." should be rewritten with concreteness. For example, it should be written as "very few cells (e.g. 100 cells /25 cm<sup>2</sup>) are seeded...." .