

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15654

Title: Association of HGFR/CDX2 coexpression to mucosal regeneration in active ulcerative colitis

Reviewer's code: 00044509

Reviewer's country: Japan

Science editor: Jing Yu

Date sent for review: 2014-12-03 09:59

Date reviewed: 2014-12-11 19:21

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 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 checked="" 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

1. The authors should discuss whether the results in this study are specific for UC or common of chronic colitis such as Crohn disease. 2. It seems that the story of carcinogenesis by CD133 and HGFR in this study is a logical leap. 3. The introduction in this manuscript is too long. The author should describe briefly the background and aim of this study.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15654

Title: Association of HGFR/CDX2 coexpression to mucosal regeneration in active ulcerative colitis

Reviewer's code: 03000422

Reviewer's country: Japan

Science editor: Jing Yu

Date sent for review: 2014-12-03 09:59

Date reviewed: 2014-12-20 14:02

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"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input checked="" 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

The manuscript entitled "Association of HGFR/CDX2 coexpression to mucosal regeneration in active ulcerative colitis" by Sipos et al. demonstrated that higher number of HGFR, CDX", CD133 and Musashi-1 positive cells were detected, and that HGFR/CDX2 and Musashi-1/CDX2 coexpression were found in blood and lamina propria of UC samples. These results are interesting. However, there are several problems that should be addressed prior to the publication in "World Journal of Gastroenterology". 1. All data were shown by fluorescent immunolabelings confirmed by RT-PCR. These results indicate the presence of HGFR/CDX2 and Musashi-1/CDX2 etc in lamina propria of UC sample. However, additional data on the function of HGFR/CDX2 double positive cells etc are needed to support the hypothesis that mesenchymal-to-epithelial transition might be a crucial event in tissue regeneration. For example, it is necessary to explain the mechanism to recruit HGFR/CDX2 double positive cells from blood to lymphoid aggregates. 2. What are CD133/CDX2 and Musashi-1/CDX2 double positive cells associated with HGFR/CDX2 double positive cells and HGF/HGFR system in the process of mucosal regeneration? The authors should describe this point



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in discussion. 3. Where is the origin of CD133/CDX2 and Musashi-1/CDX2 double positive cells? Are these cells derived from bone marrow? It might be necessary to show the expression of these cells in bone marrow if possible.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15654

Title: Association of HGFR/CDX2 coexpression to mucosal regeneration in active ulcerative colitis

Reviewer's code: 02999941

Reviewer's country: United States

Science editor: Jing Yu

Date sent for review: 2014-12-03 09:59

Date reviewed: 2015-04-06 02:41

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 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 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

In this manuscript, the authors investigate the association of HGFR/CDX2 coexpression in mucosal regeneration in active ulcerative colitis. They evaluate these markers in peripheral samples and colonic biopsies. Significance: Previous studies have established that HGFR+ cells may have a role in mucosal healing in ulcerative colitis. However, as the authors point out, the migration pathway of HGFR+ cells from the blood stream to the lamina propria (LP) has not been elucidated. I anticipate and hope that the authors will collect more longitudinal data in patients in different stages of disease (healed vs inflamed, disease for 2 years vs 10 years, on specific treatments vs not) to further clarify the differences in these groups. Major points: 1. The reader would benefit from further discussion of the choice in controls. The first sentence of the materials/methods discusses the inclusion criteria but this seems to be the description for the cases. Furthermore, the reader could appreciate clarification of whether small bowel Crohn's disease was effectively ruled out in the cases, as this could have an impact (particularly on the evaluation of the peripheral blood). 2. The reader could benefit from quantification of endoscopic/histologic inflammation and correlation

to both tissue and peripheral blood levels. A “dose-response” trend would be helpful in further confirming the authors’ interpretation of the results. Minor points: 1. The reader could benefit from knowing whether colonoscopic prep (with lavage) has any effect on the tissue levels of these markers (as the blood samples were collected pre-colonoscopy but the tissue samples were performed after colonic lavage). 2. The reader could benefit from knowing whether location of tissue biopsy (right/left colon) make a difference in the expression patterns – perhaps the authors can discuss their reasoning for choosing all left-sided biopsies. 3. On page 15, the authors purport that colonic fibrosis is an intermediate stage between inflammation and carcinogenesis. This could be clarified as dysplasia seems to be a predictors and not colonic fibrosis.