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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4661

Title: Bile acid increases histamine producing enzyme, histidine decarboxylase, expression in gastric cells

Reviewer code: 00068443

Science editor: Gou, Su-Xin

Date sent for review: 2013-07-14 18:46

Date reviewed: 2013-07-17 22:06

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 checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In their present manuscript, Cheong and colleagues show that Histidine decarboxylase production is associated with bile acid exposure and its related transcriptional regulation network of FXR, SHP and CDX1. Overall, the experiments are performed and presented in a clear and appropriate manner and the conclusions are supported by the presented data. Major comments: Specimens taken from gastric cancer patients are important for this study. Minor comments: line 106: The full name of "IM" line 245: "Increased expression has also been observed in the adult during growth or 245 regeneration, including the rat liver after a partial hepatectomy [22]," what expression



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4661

Title: Bile acid increases histamine producing enzyme, histidine decarboxylase, expression in gastric cells

Reviewer code: 00051227

Science editor: Gou, Su-Xin

Date sent for review: 2013-07-14 18:46

Date reviewed: 2013-07-22 19:02

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 checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input 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

This paper describes the effect of bile acid on histidine decarboxylase (HDC) gene expression (and other important genes involved in bile acid action) in biopsy specimens taken from antrum and corpus of normal stomach and gastric precancerous state as well as in gastric cell lines. The main thrust of the paper is that the authors claim to have demonstrated the positive association between HDC gene expression in the stomach and bile acid exposure. This paper well written and reports a potentially interesting and an important study, however there are a couple of issue that need attention. Specific comments: 1.The numbers of examined patients is relatively small to confirm last sentence of the Discussion. Please comments this as limitation of this study. Moreover, the authors have not measured histamine production. 2. The methods are very strong, however I have not found description of RNA isolation from biopsy specimens. There are only description of RNA isolation from cell lines. Moreover, it would be better to use real-time polymerase chain reaction (qPCR) to quantitatively measure genes expression, especially HDC gene expression (mRNA) in biopsy specimens. Since there is evidence that some housekeeping genes can also be influenced by some conditions, at least one further housekeeping gene should be used to confirm the observed changes in mRNA levels. 3. To confirm the conclusion the authors should measure not only mRNA but also HDC protein level by Western-Blot or HDC-activity. 4. The title should be slightly modified as follow : Bile acid increases histidine decarboxylase gene expression in gastric cells. It seems to me that the proposed title more accurately reflects contents of the study. ?

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4661

Title: Bile acid increases histamine producing enzyme, histidine decarboxylase, expression in gastric cells

Reviewer code: 00053385

Science editor: Gou, Su-Xin

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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)		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

Ku et al. have submitted a manuscript titled “Bile acid increases histamine producing enzyme, histidine 1 decarboxylase, expression in gastric cells” I have numerous concerns with this study. 1. This appears to be a series of experiments with little or no rationale for how these experiments are related to each other. 2. Page 4, line 78:” higher levels of bile acid occur in patients with atrophic chronic gastritis and intestinal metaplasia in gastric carcinoma.” I don’t understand what authors mean by it. Are they talking about luminal bile acid levels, serum bile acid levels or biliary bile acid levels? No reference is provided either. 3. Page 5, line 106: abbreviation IM is not defined. 4. Why did they do RT-PCR and not qPCR? 5. Results page 7, line155-157: The patients were defined by their possession of an aberrant high level of bile acid in the bottom of the stomach. Did they measure bile acid levels? How did the authors rule out presence of H. pylori? This method of patient selection is subjective, erroneous and susceptible to bias. Obviously this experiment lacks an adequate control group as well. Since the PCR was performed in archived tissue, It is not clear how the tissue was stored and how the RNA was isolated. 6. I don’t understand what is the rationale for evaluating the PPAR expression as shown in Fig. 1C with no further follow-up. 7. Fig. 1D, did the authors evaluate the effect of DMSO on bile acid mediated effect on HDC? I did not understand it. 8. I did not understand the importance of experiments outlined in Figure 2. While it obvious that addition of exogenous FXR enhances HDC expression. It is not clear that bile acid induced HDC expression in FXR dependent manner. And adequate experiment would be evaluating for bile acid-mediated translocation of FXRRXR complex into the nucleus and assessing for HDC transcription; this would require using controls where nuclear translocation of FXRRXR is prevented. Moreover effect of



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guggulsterone can be non-specific and siRNA for FXR should have been used. 9. In some experiments CDCA was used. In others DCA was used. Some experiments were done with both. Is there a rationale for it? 10. If you look at Fig. 2B it appears that FXR expression increases the expression of HDC with and without addition of CDCA. Authors assessed the effect of DCA on HDC expression. Did they look at the effect of CDCA on HDC expression? Moreover, these results may suggest that HDC expression is independent of CDCA. 11. If you look at Fig. 2D it appears that guggulsterone decrease the HDC expression with and without addition of CDCA or DCA. These results may suggest that HDC expression is independent of stimulation with bile acid. 12. Other experiments outlined in Figs 3 and 4 suffer from similar flaws.