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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6518

Title: HEPCIDIN EXPRESSION IN COLON DURING TNBS-INDUCED COLITIS IN RATS

Reviewer code: 00503587

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-22 18:59

Date reviewed: 2013-11-08 15:14

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 manuscript focuses on hepcidin in an animal model of gut inflammation. The management of iron, and the mechanisms leading to iron deficiency in IBD are important issues. This work adds further to this area. Specific comments 1. There are a number of errors of English construction or grammar that need correction. 2. It was surprising that there was no histological inflammatory score included. Available slides should be used to derive a score for each group and added to the results. 3. There are a number of reports of hepcidin in IBD in the last 3 years or so: these should be added to the manuscript with relevant discussion. This will provide further relevance of this work to the human situation



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6518

Title: HEPCIDIN EXPRESSION IN COLON DURING TNBS-INDUCED COLITIS IN RATS

Reviewer code: 00012328

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-22 18:59

Date reviewed: 2013-11-15 05:31

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 manuscript reports the intestinal expression of hepcidin in a rat model of TNBS-induced colitis. This response correlates with activation of the IL-6/Stat3 signaling pathway and accumulation of iron deposits in intestinal cells. Treatment of human colon adenocarcinoma HT-9 cells with IL-6 and LPS recapitulates hepcidin induction in vitro. The data are sound the conclusions are novel and meaningful. The work may contribute to understanding intestinal iron metabolism and the role of hepcidin under inflammatory conditions. The study is well designed and the experiments are of high technical quality. A few issues require attention: 1) The authors should address the functional implications of intestinal hepcidin induction in their model. Does it affect the expression of ferroportin? Is ferroportin detectable by immunohistochemistry in intestinal sections? Do the cells which accumulate iron deposits (Fig. 3B) express ferroportin and if yes, is ferroportin expression modulated by hepcidin induction? 2) Table 3 shows serum levels of hepcidin, iron and transferrin. Measurement of serum transferrin is not very informative, because this does not fluctuate significantly in response to hepcidin. The authors should provide values for transferrin saturation. 3) The age of experimental animals should be specified in the materials and Methods. 4) In the legends to Figures 1B and 2C, please specify how many animals were analyzed in the 4 experiments used for quantification. 5) In Fig. 2, it is better to combine the two panels of the Western blot into Fig. 2A; in this case, the quantification would be Fig. 2B. 6) In the Discussion (lane 8), the sentence starting with "Hepcidin transcription seems to be primarily..." is inaccurate. Please, modify to: "The innate immune response leading to hepcidin transcription seems to be primarily..."



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6518

Title: HEPCIDIN EXPRESSION IN COLON DURING TNBS-INDUCED COLITIS IN RATS

Reviewer code: 02746983

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-22 18:59

Date reviewed: 2013-11-29 17:12

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 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 checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Comments on the manuscript (No.ID: 02746983) This study describes hepcidin expression in colons of rats with colitis induced by local administration of trinitrobenzene sulfonic acid (TNBS). It is a new finding that hepcidin is induced in colon by local inflammation, but the study purpose is not consistent with the used methods. In addition, there are quite a few minor problems. Major points: It seems that the purpose of this study is to investigate hepcidin expression in colons with inflammatory bowel diseases (IBD), which include Crohn's disease and ulcerative colitis. In order to do it, the authors administered TNBS in colons of rats just locally to mimic IBD. However, IBD is not caused by exogenous, local inflammatory substances, but by endogenous, systematic abnormal body status, probably stress, malfunction of immune system, etc. Actually, the rats in this study showed no systematic alterations and only local changes in the colons that contacted TNBS directly. Therefore, there is obvious discrepancy between the purpose of this study and the methods. Minor points: P.5, line 3: Ages in week of rats are necessary here, since they are basic information. P.5, line 7: Explanation about TNBS and related references are necessary here. Especially, the reason why the authors used TNBS to induce colitis that resembled IBD is required. P.5, line 10: Explanation about HT-29 cells and related references are necessary here. P.6, line 11: The numbers of rats used in each group are described as 5-7, but those are 5 in each table. Consistency is necessary. It is recommended that the numbers of rats be shown in each table. P.6, line 19: Why did the authors pick up this experimental procedure, that is, administration of this dose of TNBS for 3 times with about 2 week intervals and scarification 1 week after the last administration? Did the authors consider this procedure would be optimal to mimic IBD? Did the authors do any preliminary experiments to confirm it? The explanation is necessary. P.6, line 21: The control rats received saline, but 50%



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ethanol should have been used, which was vehicle for TNBS. P6, line 27: The method used for measurement of hematological parameters should be described here concretely. P7, line 16: It would be better to write the amount of colon samples obtained here. P7, line 20: Explanation on what MPO indicates and related references are necessary here. P7, line 26: It would be better to write the amount of colon samples collected here. P8, line 3: References about the Biuret method are necessary here. P8, line 7: References are necessary after "as described before". P9, line 4: Why the authors incubated HT-29 cells with these substances in these, different conditions (doses and periods) is necessary to explain. Were they optimal conditions to induce hepcidin? Did the authors do any preliminary experiments to confirm it? P9, line 20: Data are expressed as the means \pm S.E.M, but the means \pm SD are appropriate. P10, line 12: It would be better to put the sentences "Hepcidin levels in colon extracts were increased in colitic animals compared with controls" and "Hepcidin was found to be expressed predominantly in the surface epithelium during colitis" in the opposite order. P10, lines 15-22: It is recommended that these data be shown with those of after-35 days in the same table, which would be easier to understand for readers. P10, lines 25: Serum iron and transferrin levels are not enough to see the status of iron accumulation in the whole body. Serum ferritin levels and hepatic iron concentrations are more precise indicators for it, which should have been measured. P11, lines 3: The iron deposition in the liver should have been observed for the reason mentioned above. P11, lines 6: The word "immune cells" is vague, and there is no evidence to identify them. Specific immuno-staining for them, such as macrophages, is necessary to do it. In addition