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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13835

Title: Decreased liver expression of hepcidin and ferroportin is involved in efficacy of peg-IFN plus RBV for chronic hepatitis C

Reviewer code: 02528284

Science editor: Ya-Juan Ma

Date sent for review: 2014-09-04 16:27

Date reviewed: 2014-09-26 16:55

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"/> Existing	<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	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript deals with the idea that HCV infection affects the expression of iron-metabolism-related genes, leading to iron accumulation in hepatocytes and indicates the importance of hepatocytic iron retention for viral response during peg-IFN + RBV treatment. It is an almost well written manuscript and merits publication after a revision. Major comments: All figure legends need a more detailed description. Minor comments: a. Please add molecular weight markers in Fig.3b b. Please provide a more detailed section material and method about the antibodies used in the study. c. How the authors have measured IRP1 and IRP2?



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13835

Title: Decreased liver expression of hepcidin and ferroportin is involved in efficacy of peg-IFN plus RBV for chronic hepatitis C

Reviewer code: 00008874

Science editor: Ya-Juan Ma

Date sent for review: 2014-09-04 16:27

Date reviewed: 2014-09-16 17:20

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 checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

COMMENTS Authors investigated the iron-metabolism-related gene expression profiles in HCV-infected liver, and the relationship between the profiles and therapeutic efficacy of pegylated interferon and ribavirin treatment. They concluded that HCV infection affects the expression of iron-metabolism-related genes, leading to iron accumulation in hepatocytes. Decreased expression of hepcidin and ferroportin in SVR patients, which can be regulated via the BMP/BMPR pathway, indicates the importance of hepatocytic iron retention for viral response. The results were interesting for readers and have worth to publish. Minor 1. Figure 3A Please explain the Hep-20 and Hep-25.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13835

Title: Decreased liver expression of hepcidin and ferroportin is involved in efficacy of peg-IFN plus RBV for chronic hepatitis C

Reviewer code: 00503590

Science editor: Ya-Juan Ma

Date sent for review: 2014-09-04 16:27

Date reviewed: 2014-10-13 03:25

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"/> Existing	<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"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Review report Decreased liver expression of hepcidin and ferroportin is involved in efficacy of peg-IFN plus RBV for chronic hepatitis C By Motoyuki Kohjima et al The authors present data on gene expression of different genes involved in iron metabolism in relation to treatment for chronic HCV infection. 100 patients and 18 controls are included in the report. The authors present novel data and have presented a good context for the findings. The language is generally acceptable, though a few orthographic curiosities remain. There are, however a few flaws that I recommend to address before publication, please see below for details. Major issues: 1. The choice of housekeeping gene is a bit curious. I could not find an evaluation of the stability of this gene as a housekeeping gene in the present context - if a reference exists please add, or present the evaluation. 2. I recommend analyzing effects of gene regulation on SVR in several subgroups in a multiple regression model (preferably logistic regression) in order to detect independent effects and estimate effect size as well as to avoid type I error by mass significance. This approach also allows correction for common confounders like age, sex, HCV genotype, etc. Alternatively, authors must apply a corrected critical P value (e.g. Bonferroni correction) to avoid type I error by multiple testing. 3. Similarly, I recommend analyzing the regulation of hepcidin gene transcription by multiple linear regression in order to explore independent effects of the proposed regulator genes as well as implementing confounder corrections. Minor comments: 4. Title: please consider to avoid abbreviations in title



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(*pegylated interferon; *ribavirin). 5. Abbreviations: RT-PCR is brief for *Reverse Transcript Polymerase Chain Reaction 6. How did the authors calculate the difference in gene expression? Please add this in "methods" 7. Table 1: please state which type of values are reported (mean? median? +/- SEM? SE? 1.96XSEM?) 8. Table 1: As local variations in population and lab technology may apply, please state the normal range for each analysis. 9. Do the authors have any data on how the patients contracted HCV?