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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 38355

Title: Regulatory Polymorphism of CXC 0 rs1439490 with seronegative occult hepatitis C virus infection

Reviewer's code: 03562683

Reviewer's country: Serbia

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-11

Date reviewed: 2018-02-16

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [ ] No

SPECIFIC COMMENTS TO AUTHORS

General opinion: I think this article has a strong connection with previous researches within this population of patients, but as well it has its own contribution and scientific significance, which makes it a candidate to be published. Still, there is lack in methods

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describing, especially genotyping, which I think it is important. Finally, the clinical implication of the work should be more emphasized. Minor revision: 1. Aim should include interleukin-28B polymorphisms. It is important determinant that is used to select patients into groups. Probably authors wanted distinction between their work and work of other authors (ex. Bartolomé J et al), but it is not necessary, it is almost completely different. Also, the aim should be more précised and include measuring serum and liver CXCL10 levels, and HCV RNA levels. 2. Aim should be stated more accurate in the abstract 3. Genotyping methods should be given more detailed not only the one sentence and reference. ''SNP analysis primers were based on published reports (CXCL10 rs1439490 and rs1440802 [18], IL-28B rs12979860 [20]) and synthesized by Sango Biotech (Shanghai, China)'' 4. Abbreviations should be checked again for the explanations. 5. Authors (Introduction part) need to explain the actual basis of CXCL10 gene polymorphisms and why they decide to investigate. '' In addition, lower serum levels of IFN gamma inducible protein-10 (CXCL10) were found in IL-28B C/C OCI patients than in CHC patients [17]. The importance of CXCL10 expression during chronic HBV infection has been recently emphasized. Two single nucleotide polymorphisms (SNPs) of CXCL10 (G-201A and C-1513T) were reported to have high allele frequency in chronic HBV infection in Chinese populations'' It is stated in Discussion, I think it should be also stated in Introduction part. ''G-201A locates within the CXCL10 promoter region and is proximal to the NF-κB1/2 binding sites. G-201A SNP was associated with the expression of CXCL10 in PBMC and chronic HBV disease progression'' 6. This clinical application of this genotyping should be detailed and emphasized. 7. English is correct.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 38355

Title: Regulatory Polymorphism of CXC 0 rs1439490 with seronegative occult hepatitis C virus infection

Reviewer's code: 02941317

Reviewer's country: Turkey

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-18

Date reviewed: 2018-02-19

Review time: 16 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [ ] No

SPECIFIC COMMENTS TO AUTHORS

I congradulate the authors for this well written manuscript with an interesting topic

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 38355

Title: Regulatory Polymorphism of CXC 0 rs1439490 with seronegative occult hepatitis C virus infection

Reviewer's code: 02540709

Reviewer's country: Spain

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-18

Date reviewed: 2018-02-23

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [ ] No

SPECIFIC COMMENTS TO AUTHORS

I have read with deep interest the manuscript by Wang X et al, a very interesting study showing CXCL10 G-201A polymorphism is associated with occult hepatitis C. This is a well done study, although some minor concerns should to be taken into account in

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order to improve the manuscript: 1. A list of abbreviations used might be included 2. Clearly state the aim of the study and the primary outcome in the abstract. "OCI is a pattern of chronic HCV infection with unclear etiology" is the background, not the aim of the study. 3. Methods for IL28B and CXCL10 should be described in the methods section rather than only a reference 4. Please indicate if all patients included belonged to the same ethnic group. Patients from 5 hospitals have been included, and although all of them are located in the northeastern China, authors do not clarify if all patients had the same genetic background. 5. GG genotype of CXCL10 G-201A is associated with OCI. The p value shown in the first paragraph of page 14 and in table 2 is the corresponding p value of the 2x3 contingency table comparing the three genotypes in OCI and CHC? Please indicate. Also, include the p value, OR and 95% CI when comparing the GG and non-GG genotype.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 38355

Title: Regulatory Polymorphism of CXC 0 rs1439490 with seronegative occult hepatitis C virus infection

Reviewer's code: 03440494

Reviewer's country: Tunisia

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-11

Date reviewed: 2018-02-26

Review time: 15 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [ ] No

SPECIFIC COMMENTS TO AUTHORS

- In the introduction section, the authors should highlight the role of the selected SNPs "CXCL10 rs1439490, rs1440802, and IL-28B rs12979860" in others viral infection or similar diseases. - The references should be updated and more recent references should

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be added. - The authors should more develop the discussion part. - Table 1 should be reorganized and detailed: • Clinical, Virological, Biochemical and Histologic Characteristics of Patients must be developed and reorganised. • Abbreviation in table 1 of "ALT (IU/L), HOMA-IR "must be added and indicated • What did you mean in table 1 by: "Genotype 1 and non Genotype 1" or "Non-C/C genotype"? Please clarify and indicate the genotype with exact genetic notation (name of the appropriate nucleotide bases). • This part in table 1 : IL-28B SNP rs12979860 C/C genotype Non-C/C genotype 97 (94.2%) 6 (5.8%) 128 (82.6%) 27 (17.4%) 0.007 Should be added in table 2 - Table 2 should be written and divided in different part, according to genetic co- dominant and dominant model related to the distribution of different genotype of CXCL10 rs1439490, rs1440802, and IL-28B rs12979860. P value and IC (OR95%) should be added and the reference group should indicate. - Multivariate analysis and adjusted model for different confounding factors should be added to the results in Table 2. - What is the statistical criteria to include Factors in the multivariate model? - The choice of patients' number and the statistical power of this study must be indicated and added in the material and methods section. - Then, the combination and interaction between CXCL10 rs1439490, rs1440802, and IL-28B rs12979860 should be indicated in a separate table. - The interpretation of results should be modified and scientifically introduced based on modified and added results. - The title and the legend of each figure should be detailed. - The legend of each figure should be detailed. - In case of liver lesions study, Lesions were graded (necroinflammation) and staged (fibrosis score) according to the Metavir scoring system. The authors should detail the METAVIR scoring in the manuscript. - Does the liver biopsies are read by an experienced pathologist? Authors should specify. - What are the significances to make a Logistic regression analysis of factors associated with seronegative occult occurrence of HCV as indicated in table 5. Table 5 should be revised. - In case of the measurement of Serum

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CXCL10 Levels, What is the sensitivity of the assay? - What is the nature of the association between fibrosis progression and necroinflammatory activity scores on liver biopsy? - The necroinflammatory process is it implicated in the fibrogenesis process or not and Why?

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 38355

Title: Regulatory Polymorphism of CXC 0 rs1439490 with seronegative occult hepatitis C virus infection

Reviewer's code: 00503345

Reviewer's country: Canada

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-18

Date reviewed: 2018-02-28

Review time: 10 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [ ] No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript the authors report that CXCL10 rs1439490 G/G genotype was more prevalent in patients with seronegative occult hepatitis C virus (OCI) compared to those with seropositive chronic hepatitis C virus (CHC). OCI patient show lower

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levels of serum IL-10 compared to CHC. Among the OCI patients, those with the CXCL10 rs1439490 G/G and IL-28B rs12979860 C/C phenotypes had lower levels of serum and liver CXCL10. The data also suggest that OCI patients with CXCL10 rs1439490 G/G genotype are more susceptible to antiviral therapy. Comment: Overall the data are sound. The study is well presented and the paper is well written. The discussion is fine. However, this study does not represent a substantial contribution to the field but rather confirms previously published evidence from other groups. An interesting observation is that IL-28B rs12979860 C/C patients with CXCL10 rs1439490 G/G genotype show lower serum and liver CXCL10 levels. Is it a cause or a consequence of low viral replication? Monitoring serum and liver levels of IL-28 would greatly improve the impact of this study.

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