

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 30246

**Title:** Association between *TLR7* copy number variations and hepatitis B virus infection outcome in Chinese

**Reviewer's code:** 03664146

**Reviewer's country:** Switzerland

**Science editor:** Jing Yu

**Date sent for review:** 2016-09-22 17:46

**Date reviewed:** 2016-11-28 19:55

| CLASSIFICATION                                    | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | 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"/> The same title        | <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"/> Duplicate publication | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D: Fair            | <input type="checkbox"/> Grade D: Rejected                           | <input type="checkbox"/> Plagiarism            | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E: Poor            |  | <input checked="" type="checkbox"/> No         | <input type="checkbox"/> Major revision                |
|   |  | BPG Search:                                    |  |
|   |  | <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 is well written and new findings are presented. Specific comments to manuscript sections are the following: Introduction: - The study design would be clearer if the introduction included 1-2 sentences why it is important to analyze male and female groups separately (as described in the discussion) and why it is interesting in the framework of the study to compare patient groups based on hepatitis B e-antigen titer. Material and Methods: - It is stated that 923 individuals were enrolled in the study. Were individuals with chronic HBV somehow selected or were just all individuals enrolled who presented with predefined diagnostic criteria and gave consent for this study? Results: - In the sample demographics section it would be clearer to first state that there was no significant difference in age distribution between AHB and CHB (since cases and controls were matched, as described in the material and methods section), but that there was a difference if the CHB group was divided into CHB, LC and HCC. - In the current manuscript, the authors present copy number data as <1, >1 (males) or <2, >2 (females). It would be interesting to see the copy number distribution (1, 2, 3... and number of individuals) e.g. as supplementary info, if



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possible? - Since the Figure legends for Figure 1 and 2 as well as for Figure 3 and 4 are the same (except for gender), I would suggest to combine Figure 1 and 2 as well as Figure 3 and 4. Figure 1A: male patients, Figure 1B: female patients, Figure 2A: male patients, Figure 2B: female patients according to e-antigen titer. Discussion: - Please discuss shortly findings for patient groups with different e-antigen titers.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 30246

**Title:** Association between *TLR7* copy number variations and hepatitis B virus infection outcome in Chinese

**Reviewer's code:** 02540709

**Reviewer's country:** Spain

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| CLASSIFICATION   | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | 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"/> 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

The manuscript entitled "Association between *TLR7* copy number variation and HBV infection outcome in Chinese" presents an interesting hypothesis about the possible influence of *TLR7* CNVs in HBV infection. The results from this study suggest that low CN could be a risk factor for chronic HBV infection. Patients with chronic HBV infection have been classified as CHB, LC and HCC, and results from this study suggest that *TLR7* CNVs are not associated with disease progression. Natural history of chronic HBV progress from no fibrosis to cirrhosis, and some of them culminate with the development of HCC. One common and possible limitation when including patients with progressive chronic diseases such as chronic hepatitis B, is classification of patients outcome because patients with cirrhosis may develop HCC sometime later. This limitation must be discussed in the manuscript. Some other concerns should be addressed in order to improve the manuscript: - Institutional review board statement has to be included in the methods section. - "AHB controls were age and sex matched with CHB cases" statement has been included in materials and Methods section. However, CHB group includes 495/600 males (82.5%) while AHB group includes 165/300

males (55%) as indicated in the text and in table 2, and they are not sex-matched. - table 2: please indicate the p value comparing age and gender among groups. Males are less represented in the AHB than in all other groups, and patients with CHB are younger than patients with LC or HCC. - how many males had 1 TLR7 copy, and how many females carried 2 copies? Authors only indicate <1 and >1 copy for males and <2 or >2 in females. In which group are included carriers of 1 copy (males) and 2 copies (females)? - table 3 and figures 1 and 2 are redundant. Include only table 3 or figures 1-2. - Please revise references have been correctly placed. For example, references 2-5, in page 5, lines 1-5, do not correspond to studies supporting the idea that host genetic susceptibility plays an important role in outcome of HBV infection. Also, update reference 1.