Author’s response to reviews

Title: Vitamin D receptor ApaI polymorphism associated with progression of liver disease in Vietnamese patients chronically infected with Hepatitis B virus

Authors:

Nghiem Xuan Hoan (nghiemxuanhoan@gmail.com)
Nguyen Khuyen (nguyenkhuyenbvdg@gmail.com)
Dao Giang (daophuonggiang@gmail.com)
Mai Binh (Maibinhtieuhoa108@gmail.com)
Nguyen Toan (toannl@vmmu.edu.vn)
Do Anh (Drtuananh103@gmail.com)
Ngo Trung (tatrunngngo@gmail.com)
Mai Bang (bangmh@benhvien108.vn)
Christian Meyer (christian.g.meyer@gmail.com)
Thirumalaisamy Velavan (velavan@medizin.uni-tuebingen.de)
Le Song (lehuusong@108-icid.com)

Version: 3 Date: 13 May 2019

Author’s response to reviews:

Dear Editor,

We would like to submit the revised version of our manuscript MGTC-D-19-00085R2 " Vitamin D receptor ApaI polymorphism associated with progression of liver disease in Vietnamese patients chronically infected with Hepatitis B virus " to be considered for publication in BMC Medical Genetics journal. We thank the editor for providing valuable comments and suggestions. We have carefully considered the comments and have changed some critical points especially the statistical procedures in the manuscript. We believe that the manuscript has been improved.

Thank you very much for your time and consideration.

With best regards
Dr. Nghiem Xuan Hoan
Institute of Clinical Infectious Diseases
Vietnamese-German Center for Medical Research (VG-CARE)
108 Military Central Hospital
Dear Dr. Hoan,

Thank you for submitting your manuscript, "Vitamin D receptor ApaI polymorphism associated with progression of liver disease in Vietnamese patients chronically infected with Hepatitis B virus" (MGTC-D-19-00085R2), to BMC Medical Genetics.

Before it can be sent out for review, please carry out the corrections, below.

Please submit your revised manuscript by accessing the following site:

https://www.editorialmanager.com/mgtc/

If you have forgotten your password, please use the 'Send Login Details' link on the login page at https://www.editorialmanager.com/mgtc/. For security reasons, your password will be reset.

Please note, if your manuscript is accepted you will not be able to make any changes to the authors, or order of authors, of your manuscript once the editor has accepted your manuscript for publication. If you wish to make any changes to authorship before you resubmit your revisions, please reply to this email and ask for a 'Request for change in authorship' form which should be completed by all authors (including those to be removed) and returned to this email address. Please ensure that any changes in authorship fulfil the criteria for authorship as outlined in BioMed Central's editorial policies (http://www.biomedcentral.com/about/editorialpolicies#authorship).

Once you have completed and returned the form, your request will be considered and you will be advised whether the requested changes will be allowed.

By resubmitting your manuscript you confirm that all author details on the revised version are correct, that all authors have agreed to authorship and order of authorship for this manuscript and that all authors have the appropriate permissions and rights to the reported data.

Please be aware that we may investigate, or ask your institute to investigate, any unauthorised attempts to change authorship or discrepancies in authorship between the submitted and revised versions of your manuscript.
We look forward to receiving your revised manuscript before 28 May 2019.

Best wishes,

Ping An, M.D., MPH
BMC Medical Genetics
https://bmcmedgenet.biomedcentral.com/

Editor's comments:

1. Please double check FDR-adjusted P values in table 4; especially 0.01, 0.05. describe FDR procedures in details. provide q values, provide Bonferroni corrected p for comparison, number tests done.

2. Check HWE, genotyping of APaI; genetic mode is unusual, which needs to be explained.

3. HCC vc non-HCC is not significant so it is not a risk factor to HCC.

Responses to editor’s comments

Comment 1: Thank you for the comment. We have reconsidered the statistical points and decided to remove the FDR adjusted method. In the table 4, we have used the logistic regression model adjusted for age and gender to generate the P values. We believe that statistical method used was reliable for interpreting the results.

Comment 2: We have checked the HWE for all SNPs (stated in the result section as “The genotype frequencies of the SNPs among HBV patients and HCs were in Hardy-Weinberg equilibrium (P>0.05).” Genetic models used to interpret the results in the manuscript are usual and appear in many published papers (for example, PMID: 23748017)

Comment 3: When we compared two groups HCC vs. CHB, the results showed the significant association (P=0.0022, table 3). The significant association was still found when we compared HCC vs. CHB + LC (non-HCC) (P=0.013, table 3) and in the conclusion section, we did not mention the risk factor but the association.