Reviewer’s report

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

Version: 3 Date: 05 Jun 2019

Reviewer: Sungho Won

Reviewer's report:

In this manuscript, VDR polymorphisms were genotyped by DNA sequencing and in-house validated ARMS assays in 443 HBV infected patients including chronic hepatitis B, liver cirrhosis and hepatocellular carcinoma and in 238 healthy control individuals (HCs). Logistic regression models were applied in order to determine the association of VDR polymorphisms with manifest HBV infection as well as with progression of related liver diseases in different genetic models. Authors found that among the four VDR polymorphisms, Apal is associated with the clinical outcome and liver disease progression in Vietnamese HBV-infected patients.

Manuscript is generally written well but I have some comments.

1. Authors should provide some evidences about the absence of population stratification. Genetic association is very sensitive to population substructure and thus it should be carefully adjusted. Otherwise sample size is small and results are not reliable.

2. If race variable is available, authors should adjust its effect by adding it as a covariate. It is not clearly stated how controls were selected. At the same time authors should compare the allele frequencies of controls with public reference data.

Please check the minor allele frequencies of 4 SNPs with 1000 Genome project data, etc.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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