



ESPS PEER-REVIEW REPORT

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ESPS manuscript NO: 16587

Title: Linked polymorphisms of PNPLA3 confer susceptibility to non-alcoholic steatohepatitis and decreased viral load in chronic hepatitis B patients

Reviewer's code: 00052926

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Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various quality grades and misconduct types like Google Search, Duplicate publication, and Plagiarism.

COMMENTS TO AUTHORS

The article of Qin Pan et al is an interesting work on the effect of PNPLA3 polymorphisms and their association with NAFLD/NASH and HBV viral load in patients with chronic hepatitis B. The work is well designed, performed and analysed and the findings are clear and well presented in the Results section and Figures. However in the Discussion section, the interpretation of the data needs correction and restatement in multiple sites. 1. 1st phrase of the Discussion ..."underlying" instead of "basic" diseases. 2. 1st paragraph"There are similar findings" instead of "Similar evidences have been shown" for multiple PNPLA3 SNPs, 3. 1st paragraphmodifier for the development of a full spectrum of NAFLD: which includes simple steatosis, steatohepatitis, and liver fibrosis. 4. Please restate in a more comprehensible way "Despite the discrepancy in mechanisms, the effect of PNPLA3 polymorphism on NAFLD may, but not necessary, be attributed to the abnormalities in plasma ALT and AST levels, fasting triglyceride level and IR, etc" 5. Please correct "When evaluated by the NAS score (≥ 3), CHB patients with rs738409 G allele, rs3747206 T allele, rs4823173 A allele, and rs2072906 G allele had much higher susceptibility to have suspected NASH or NAFLDNASH



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than those with rs738409 C allele, rs3747206 C allele, rs4823173 G allele, and rs2072906 A allele. These findings are similar to those found provide us with the fact that the role of PNPLA3 polymorphisms in CHB patients was well consistent with that in normal populations. Thus, in contrast to the HCV-induced hepatocyte steatosis in CHC patients, host metabolism rather than viral infection is responsible for the development of fatty liver disease, especially NASH, in Chinese CHB patients.” 6. Please restate in a more comprehensible way “Another noticeable result lies in the effect of PNPLA3 polymorphisms on liver fibrosis” 7. Please correct “These data suggested that PNPLA3 polymorphism is a critical part...” 8. Please correct “It seems thereforeIn result that, PNPLA3 polymorphisms seem to serve as the negative regulator of HBV replication. Nowadays, NAFLD and CHB have been uncovered demonstrated to share....”. 9. Please restate in a more comprehensible way. “Contrastively, activation of TLR4, which is recognized to be the ligand of LPS, by high fat diet (HFD)-induced NAFLD stimulates the innate immune response in both hepatocytes and kupffer cells” 10. Please correct “In agree with our deduction, tThe NAFLD-based down-regulation of viral replication was previously is confirmed shown in a clinical trial of chronic hepatitis C (CHC) patients [20] and in animal model of HBV transgenic mice”