Reviewer's report

Title: Estrogen Receptor alpha Gene Polymorphisms and Risk of HBV-Related Acute Liver Failure in the Chinese Population

Version: 1 Date: 4 March 2012

Reviewer: Ming-Whei Yu

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Acute liver failure (ALF) is an end-stage liver disease. There is a remarkable difference in the severity of liver disease between the sexes among HBV carriers, and advanced liver disease tends to be more frequent in men than in women. This case-control study was conducted to evaluate the relationships between two functional SNPs in the estrogen receptor alpha (ESR1) gene and HBV-related ALF. Genotyping was performed using peripheral leukocyte DNA from a total of 359 ALF cases and 857 asymptomatic HBV carriers.

The research group has carried out a series of case-control studies on the relationships between the two ESR1 SNPs and HBV infection-related sequelae, including persistent HBV infection and hepatocellular carcinoma, as well as recently the HBV-related liver cirrhosis (Yan Z, et al. Human Mutat 2011;32:1128-36.). The present study further suggests that the two ESR1 SNPs are associated with ALF overall and in stratified analyses according to age and sex.

Comments

1. In studies of western populations, it has been demonstrated that acetaminophen overdose and idiosyncratic drug reactions have replaced viral hepatitis as the most frequent apparent causes of ALF. Thus, the authors should clarify how well they excluded drug-induced ALF cases from the analysis and how well they diagnosed HBV-related ALF in this study.

2. Two haplotype-tagging SNPs were chosen for analysis. Are there other tagging SNPs that the authors did not select? If so, the authors should discuss the limitation about capturing incomplete genetic information in the genomic region of interest.

2. In addition to the two ESR1 SNPs tested, it may be better to add a brief introduction on the studies of other genetic polymorphisms and HBV-related ALF.

3. It is reasonable to speculate that the effects of the two ESR1 SNPs on the occurrence of ALF may be different between postmenopausal and premenopausal women. Thus, distribution of selected characteristics in Table 1 should be presented according to sex and disease status. Furthermore, in women the SNP-ALF association should be re-analyzed by menopausal status.

4. Table 2. Odds ratios and their 95% CIs should be added for the genotype effect.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.