Reply to Liao et al

To the Editor—We recently published a study demonstrating the association of human leukocyte antigen (HLA)-DP and interleukin 28B (IL-28B) polymorphisms with hepatitis B surface antigen (HBsAg) seroclearance in chronic hepatitis B virus (HBV) infection, illustrating the influence of the host genome on disease outcomes in chronic hepatitis B [1]. In response, Liao and colleagues wrote about the current conflicting evidence concerning the association between IL-28B and HBV clearance [2].

The studies quoted by Liao and colleagues were mainly cross-sectional in nature, in which HBsAg-positive individuals were compared with persons who “recovered” from HBV, defined by as HBsAg negative, antibody to the hepatitis B core antigen positive at a single time point. Our recent study compared HBsAg-positive patients with chronic hepatitis B patients who achieved HBsAg seroclearance. Both of our patient cohorts were longitudinally followed up for many years, with serial serologic measurements from the latter group of patients demonstrating at least 3 years of HBsAg positivity followed by subsequent HBsAg seroclearance lasting for >6 months [3]. In addition, this group of patients had attained a favorable serologic milestone with HBsAg seroclearance but had not completely recovered from HBV, and hence our study results cannot be directly compared with the studies quoted by Liao and colleagues.

Chronic hepatitis B patients achieving HBsAg seroclearance are not cleared of the HBV infection. Although the majority of such patients have undetectable serum HBV DNA, intrahepatic total and covalently closed circular HBV DNA are still detectable in a majority of these subjects [4], indicating the persistence of HBV at a low replicative and transcriptional level after HBsAg seroclearance. Although HBsAg seroclearance in chronic hepatitis B is usually associated with favorable clinical outcomes, development of hepatocellular carcinoma is still possible if HBsAg seroclearance is achieved at ≥50 years of age [5].

As correctly pointed out by Liao and colleagues, IL-28B variants are associated with favorable outcomes during treatment in chronic hepatitis B [6, 7]; our study further substantiated that IL-28B variants could also influence disease outcomes in treatment-naive patients.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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