Lack of Association Between Interleukin 28B Polymorphisms and Spontaneous Viral Clearance in Hepatitis B Virus Patients

TO THE EDITOR—We read the article by Seto et al [1] with interest. The authors investigated the correlation of HLA-DP and interleukin 28B (IL-28B) polymorphisms with hepatitis B surface antigen (HBsAg) seroclearance in hepatitis B virus (HBV) patients, and found that IL-28B haplotype CG (rs12979860/rs8099917) was associated with HBsAg clearance. The role of IL-28B polymorphisms in HBV has been increasingly explored, but till now only conflicting results have been achieved.

Recently we reviewed current studies delving into IL-28B and spontaneous HBV clearance and searched databases including PubMed, Embase, Web of Science, and Chinese National Knowledge Infrastructure using the terms interleukin 28B and hepatitis B through 1 March 2013. In total, 145 articles were searched. After preliminary screening, 9 articles in English and 1 in Chinese investigating the association between IL-28B and HBV seroclearance were encompassed. Among them, 1 article obscured the genotype distributions and was omitted from our analysis [2], and 1 with virus clearance after interferon treatment was excluded [3] as well. Therefore, 8 studies in which genotype distributions of IL-28B were shown or could be figured out were included ultimately (7 studies involving rs12979860, 3 involving rs8099917, and 2 involving rs12980275, most of which were conducted in Asians; see Supplementary Table 1). We analyzed the correlation between IL-28B polymorphisms and HBV seroclearance through meta-analysis in a recessive model and allele model.

For rs12979860, 1380 patients with persistent hepatitis B and 1305 controls with spontaneous HBV seroclearance were...
included. Meta-analysis results showed that rs12979860 did not correlate with virus clearance in HBV patients, with no heterogeneity existing among the studies (recessive model CC:CT + TT, odds ratio [OR] = 0.921, 95% confidence interval [CI] = 0.788–1.063, P = .847; allele C > T: OR = 0.990, 95% CI, 0.819–1.179, P = .921).

For rs8099917, only 3 studies presented the genotype distributions and thus were finally selected, including 487 patients and 389 controls. No significant relationship between IL-28B and virus clearance was observed (recessive model: OR = 1.084, 95% CI, 0.722–1.629, P = .442; allele T > G: OR = 1.092, 95% CI, 0.753–1.585, P = .643). Additionally, we analyzed rs12980275 as well, but only to find insignificant results (recessive model: OR = 0.949, 95% CI, 0.556–1.618, P = .847; allele A > G: OR = 0.956, 95% CI, 0.584–1.654, P = .857) (Table 1).

Therefore, confirmative evidence to support that IL-28B polymorphisms correlate with virus clearance in HBV patients is lacking, although the correlation has been exemplified in HCV patients. Seto et al [1] found that IL-28B haplotype CG correlated with HBsAg seroclearance and considered IL-28B to be pertinent to virus eradication, but the frequencies of haplotype CG in both case and control groups were <0.03 (0.025 and 0.002, respectively). Such a low frequency would spark concern on its clinical influence on the seroclearance of HBsAg as few people have such genetic background. Additionally, Lampertico et al [3] and Sonneveld et al [4] corroborated the association with seroclearance after interferon treatment, whereas Martin et al [5] found no correlation with spontaneous clearance in white individuals. Besides, most of the studies included in the meta-analysis were conducted in Asians and no remarkable correlation was observed. Therefore, IL-28B polymorphisms did not correlate with spontaneous seroclearance of HBV, irrespective of race, but might associate with treatment response after administering interferon.

**Supplementary Data**

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

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

**References**


Dear Editor,

I am writing to correct an error in our manuscript titled “IL28B Polymorphisms and Virus Seroclearance” that was published in Clinical Infectious Diseases (CID) 2013; 57(15 August): 621. The error occurred in Table 1, which presents the meta-analysis results for the correlation between interleukin 28B polymorphisms and virus seroclearance. The corrected Table 1 is provided below:

<table>
<thead>
<tr>
<th>SNPs (recessive model)</th>
<th>Included Articles</th>
<th>Case/Control</th>
<th>OR</th>
<th>95% CI</th>
<th>P OR</th>
<th>I²%</th>
<th>P Hetero</th>
<th>Effect Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs12979860 (CC:CT + TT)</td>
<td>7</td>
<td>1380/1305</td>
<td>0.921</td>
<td>0.748–1.135</td>
<td>.442</td>
<td>0</td>
<td>.487</td>
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<tr>
<td>rs8099917 (TT:GG + GG)</td>
<td>3</td>
<td>487/389</td>
<td>1.084</td>
<td>0.722–1.629</td>
<td>.696</td>
<td>0</td>
<td>.705</td>
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<tr>
<td>rs12980275 (AA:AG + GG)</td>
<td>2</td>
<td>288/246</td>
<td>0.949</td>
<td>0.556–1.618</td>
<td>.847</td>
<td>0</td>
<td>.769</td>
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</tr>
</tbody>
</table>

SNPs (allele)

<table>
<thead>
<tr>
<th>SNPs</th>
<th>Included Articles</th>
<th>Case/Control</th>
<th>OR</th>
<th>95% CI</th>
<th>P OR</th>
<th>I²%</th>
<th>P Hetero</th>
<th>Effect Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs12979860 (C:T)</td>
<td>5</td>
<td>2120/1706</td>
<td>0.990</td>
<td>0.819–1.197</td>
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<td>0</td>
<td>.594</td>
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<tr>
<td>rs8099917 (T&gt;G)</td>
<td>3</td>
<td>974/778</td>
<td>1.092</td>
<td>0.753–1.585</td>
<td>.643</td>
<td>0</td>
<td>.625</td>
<td>F</td>
</tr>
<tr>
<td>rs12980275 (A&gt;G)</td>
<td>2</td>
<td>576/492</td>
<td>0.956</td>
<td>0.584–1.654</td>
<td>.857</td>
<td>0</td>
<td>.788</td>
<td>F</td>
</tr>
</tbody>
</table>

Cases were patients with persistent hepatitis; control subjects were individuals with spontaneous virus seroclearance.

Abbreviations: CI, confidence interval; OR, odds ratio; P OR, value for the odds ratio; SNP, single-nucleotide polymorphism.

* Values of the heterogeneity.

* The P value of the heterogeneity test, no heterogeneity was deemed to exist when P > .1.

* Fixed-effects model.

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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