To the editor:

**Fcγ receptor IIB gene polymorphism in adult Japanese patients with primary immune thrombocytopenia**

Several studies have indicated that platelet recovery occurs in a subgroup of immune thrombocytopenia (ITP) patients after successful *Helicobacter pylori* (*H. pylori*) eradication.1,2 Interestingly, a higher response rate to *H pylori* eradication therapy has been reported in Japan and Italy than in the United States and European countries other than Italy,2 suggesting that the efficacy of *H pylori* eradication is influenced by ethnicity, probably through genetic and environmental factors. In addition, Asahi et al observed that monocytes from *H pylori*–infected ITP patients demonstrated low levels of inhibitory FcγRIIB and enhanced platelet phagocytosis, both of which were reversed after successful *H pylori* eradication.3

The FcγRIIB 232I/T (Ile/Thr) polymorphism (rs1050501) has been identified as a genetic factor associated with susceptibility to various autoimmune diseases.4,5 The FcγRIIB 232T cannot inhibit activating receptors because it is not present in lipid rafts, resulting in decreased FcγRIIB–mediated inhibition of macrophage and B-cell responses.6,7

We analyzed the FcγRIIB 232I/T polymorphisms by restriction-fragment-length polymorphism polymerase chain reaction in 206 adult Japanese patients with primary ITP and in 193 healthy controls (supplemental Methods, available on the Blood website). The FcγRIIB 232T carriers were more frequently detected in ITP patients than in healthy controls (P = .003; odds ratio [OR] = 1.87; 95% confidence interval [CI], 1.24-2.82) (Table 1). Our results differed from those described by Breunis et al using 44 adult Dutch patients with ITP and Xu et al using 178 adult Chinese patients with ITP.8,9 This discrepancy might be explained by study design factors including sample size and ethnic differences. Interestingly, the distribution of the FcγRIIB 232T carriers is more common in Asians than in Caucasians.5 This distribution is similar to the regional differences observed for the effect of *H pylori* eradication therapy in ITP patients.2

We compared the distribution of FcγRIIB 232I/T polymorphisms between *H pylori*–infected ITP patients and healthy controls or *H pylori*–uninfected ITP patients and healthy controls (Table 1). The frequency of the FcγRIIB 232T carriers was significantly higher in *H pylori*–infected ITP patients than in healthy controls (49.0% vs 30.6%; P = .002; OR = 2.18, 95% CI, 1.33-3.59). *H pylori* infection plays a role in ITP pathogenesis by altering the FcγR balance of monocytes in favor of activating FcγR, through downregulation of inhibitory FcγRIIB.3 Furthermore, our data suggest that the functionally impaired FcγRIIB 232T carriers may contribute to disease pathogenesis in a subgroup of *H pylori*–infected ITP patients.

We further evaluated associations between FcγRIIB 232I/T polymorphisms and therapeutic response rates to *H pylori* eradication in

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**Table 1. Genotype distributions of the FcγRIIB 232I/T polymorphism**

<table>
<thead>
<tr>
<th>FcγRIIB 232I/T polymorphism</th>
<th>Healthy controls, n = 193</th>
<th>Total ITP patients, n = 206</th>
<th>P, vs healthy controls</th>
<th>H pylori–infected ITP patients, n = 100*</th>
<th>P, vs healthy controls</th>
<th>H pylori–uninfected ITP patients, n = 82*</th>
<th>P, vs healthy controls</th>
<th>P pylori eradication therapy†</th>
<th>Responders, n = 21</th>
<th>Nonresponders, n = 21</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/I genotype</td>
<td>134 (69.4)</td>
<td>113 (54.8)</td>
<td>0.01‡</td>
<td>51 (51.0)</td>
<td>0.01‡</td>
<td>47 (57.3)</td>
<td>.2</td>
<td>7 (33.3)</td>
<td>18 (85.7)</td>
<td>.01‡</td>
<td></td>
</tr>
<tr>
<td>I/T genotype</td>
<td>56 (29.0)</td>
<td>84 (40.8)</td>
<td>44 (44.0)</td>
<td>33 (40.2)</td>
<td>12 (57.2)</td>
<td>3 (14.3)</td>
<td>0.053</td>
<td>7 (33.3)</td>
<td>18 (85.7)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>T/T genotype</td>
<td>3 (1.6)</td>
<td>9 (4.4)</td>
<td>5 (5.0)</td>
<td>2 (2.4)</td>
<td>2 (9.5)</td>
<td>0</td>
<td>0.053</td>
<td>7 (33.3)</td>
<td>18 (85.7)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Non-T carriers§</td>
<td>134 (69.4)</td>
<td>113 (54.8)</td>
<td>0.003</td>
<td>51 (51.0)</td>
<td>0.002</td>
<td>47 (57.3)</td>
<td>.053</td>
<td>7 (33.3)</td>
<td>18 (85.7)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>T carriers§</td>
<td>59 (30.6)</td>
<td>93 (45.2)</td>
<td>49 (49.0)</td>
<td>35 (42.7)</td>
<td>14 (66.7)</td>
<td>3 (14.3)</td>
<td>0.053</td>
<td>7 (33.3)</td>
<td>18 (85.7)</td>
<td>.001</td>
<td></td>
</tr>
</tbody>
</table>

Genotype distributions of the FcγRIIB 232I/T polymorphism in ITP patients and healthy controls, in *H pylori*–infected and –uninfected ITP patients, and in responders and nonresponders to *H pylori* eradication therapy. Genotype distributions were tested for statistical significance using the χ²-square or Fisher exact test where 1 or more variables was < .5.

*Of 182 patients with ITP evaluated for *H pylori* infection status, 100 were confirmed positive for *H pylori* infection based on a positive urea breath test and/or serum anti-*H pylori* antibodies measured by an enzyme-linked immunosorbent assay kit.
†Forty-two *H pylori*–infected ITP patients were administered amoxicillin (750 mg twice daily), clarithromycin (400 mg twice daily), and lansoprazole (30 mg twice daily) for 7 days. Twenty-one ITP patients were responders, defined as having a platelet count higher than 50 × 10⁹/L and doubling of the baseline level at 24 weeks after initiation of the eradication regimen.
‡The corrected P (Pcorr) values were calculated by multiplying the observed P value by the number of comparisons made. Pcorr = .05.
§FcγRIIB receptors encoded by FcγRIIB 232T are unable to interact with activating receptors and exert inhibitory activity.6,7 In addition, only few subjects were T/T genotype in this study. Therefore, we compared non-T carriers (I/I genotype) to T carriers (I/T + T/T genotype).
ITP patients (Table 1). ITP patients who were $F\gamma R\text{II}B$ 232T carriers contained significantly higher frequencies of responders than did noncarriers (66.7% vs 14.3%; $P = .001$; OR $= 12.0$; 95% CI, 2.62-54.99). Thus, more efficient eradication therapy in 232T carriers may improve $H$ pylori infection-related immunoregulatory systems, such as activating and inhibiting Fc-$\gamma$R balance, thereby interrupting phagocytosis and antigen presentation.

In summary, our data suggest that $F\gamma R\text{II}B$ 232I/T polymorphisms may play an important role in susceptibility to $H$ pylori–infected ITP and in platelet responses after $H$ pylori eradication in ITP patients.

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References


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