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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

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

	No. (%)			No. (%)		No. (%)		No. (%)		
								H pylori eradication therapy†		
***FcγRIIB* 232I/T polymorphism**	**Healthy controls, n = 193**	**Total ITP patients, n = 206**	***P*, vs healthy controls**	***H pylori*–infected ITP patients, n = 100***	***P*, vs healthy controls**	***H pylori*–uninfected ITP patients, n = 82***	***P*, vs healthy controls**	**Responders, n = 21**	**Nonresponders, n = 21**	***P***
I/I genotype	134 (69.4)	113 (54.8)	.01‡	51 (51.0)	.01‡	47 (57.3)	.2	7 (33.3)	18 (85.7)	.01‡
I/T genotype	56 (29.0)	84 (40.8)		44 (44.0)		33 (40.2)		12 (57.2)	3 (14.3)	
T/T genotype	3 (1.6)	9 (4.4)		5 (5.0)		2 (2.4)		2 (9.5)	0	
Non-T carriers§	134 (69.4)	113 (54.8)	.003	51 (51.0)	.002	47 (57.3)	.053	7 (33.3)	18 (85.7)	.001
T carriers§	59 (30.6)	93 (45.2)		49 (49.0)		35 (42.7)		14 (66.7)	3 (14.3)	

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 χ-square or Fisher exact test when 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 50×10^9/L and doubling of the baseline level at 24 weeks after initiation of the eradication regimen.

‡The corrected *P* (P_{corr}) values were calculated by multiplying the observed *P* value by the number of comparisons made. $P_{corr} = .03$.

§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 *FcγRIIB* 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 FcγR balance,[3] thereby interrupting phagocytosis and antigen presentation.

In summary, our data suggest that *FcγRIIB* 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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