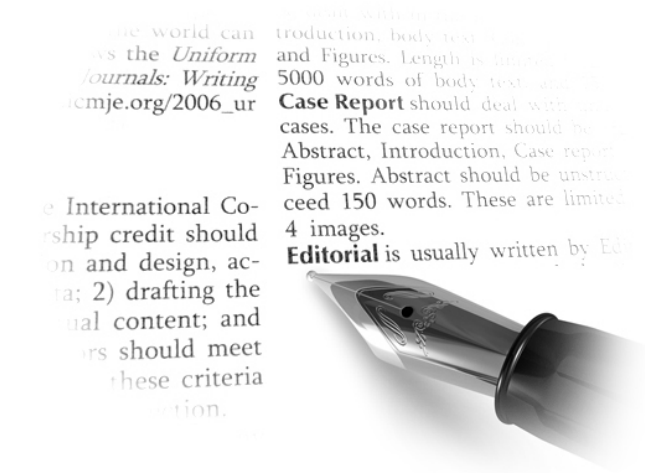

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Editorial

IL-1B-31 and *IL-1Ra* polymorphisms associated with increased host susceptibility to immune thrombocytopenia

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Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder in which the platelet autoantigens activate the immune system of the patient causing immune-mediated platelet destruction and/or suppression of platelet production. ITP can be either primary or secondary to other disorders, but the primary cause of the disease is still not well known. Meanwhile, many reports on genetic factors of ITP described several single nucleotide polymorphisms (SNPs), mostly inflammatory cytokine polymorphisms, associated with increased risk of ITP [1]. These SNPs may cause disturbance in the Th1 and Th2 cell balance leading to overproduction of inflammatory cytokines [2]. The SNPs in TNF-α gene are associated with increased phagocytic activity of macrophages and T-cytotoxic cells leading to the destruction of platelets via activation of apoptotic pathways [3]. Furthermore, TNF-α and -β are associated with increased serum level of cytokines which plays a crucial role in the regulation of immune systems. Of note, the patient with *TNF-β* +252GG genotype was shown to be associated with platelet recovery in ITP patients after the eradication of *Helicobacter pylori* [4]. Moreover, the *IFN-γ* +874TT was found as a genotype that is associated with increased cytokine production which in turn causes increment of antibody production leading to increased platelet destruction [5].

In this issue of the **Blood Research**, Yadav *et al.* [6] evaluated the association of polymorphisms in interleukin *(IL)-1B-31*, *IL-1B-511*, and *IL-1Ra* with ITP, and revealed that *IL-1B-31* and *IL-1Ra* were significantly associated with ITP whereas *IL-1B-511* failed to show association with ITP. Notably, a significant association of homozygous variant genotypes of *IL-1B-31* was observed with severe ITP when compared with healthy controls and showed significant risk association with severe ITP, whereas *IL-1Ra* failed to show significant difference. Three polymorphisms in the promoter region of *IL-1B*, i.e. *IL-1B*-1464 (G/C; rs1143623; previously known as -1476), *IL-1B*-511 (C/T; rs16944), and *IL-1B*-31 (T/C; rs1143627), have been widely investigated, especially in association with gastric cancer risk and *H. pylori* infection. The IL-1β is a potent pro-inflammatory cytokine involved in a variety of cellular activities, including cell proliferation, differentiation and apoptosis [7]. Moreover, IL-1β is important in amplifying immune response to infection, and is a potent inhibitor of gastric acid secretion [8]. Although association studies of *IL-1B* polymorphism and autoimmune or immune-inflammatory diseases have been carried out, only few reports in relation to ITP are found. Wu *et al.* [9] described *IL-1Ra* but not *IL-1B* exon 5 polymorphism was associated with childhood ITP. Lack of the *IL-1B-511T* allele was associated with *H. pylori* infection in patients with early-onset ITP but not in those with late-onset ITP [10]. Most of the previously reported cases of IL-1B polymorphism in ITP were in relation to *H. pylori* infection. In the report by Yadav *et al.*, in order to rule out ITP associated with secondary causes, patients with human immune deficiency virus, systemic lupus erythematous, and

H. pylori were excluded from the study. Thus, direct association between ITP and *IL-1B* polymorphisms could be elucidated. Although the regulation of cytokine production is known to play a major role in the development of ITP, not many studies have focused on the host genetic factor as a potential triggering factor of the disease. The possible role of the *IL-1B* genotype in the development of ITP could be applied to determine the underlying etiology. However, the risk allele of *IL-1B* should be confirmed in other ethnic groups and should also be validated in larger cohort of patients before applying the concept since some instances the allele flips are observed in *IL-1B* depending on the pathogenesis of disease.

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