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Review

Genetic factors underlying differential blood platelet sensitivity to inhibitors

Marcin Rozalski, Magdalena Boncler, Boguslawa Luzak, Cezary Watala

Department of Hemostasis and Hemostatic Disorders, Medical University of Łódź, Żeromskiego 113, PL 90-549 Łódź, Poland

Correspondence: Cezary Watala, e-mail: cwatala@csk.am.lodz.pl

Abstract:
Blood platelets are not only the primary defence mechanism involved in physiological hemostasis, but also their disorders constitute a crucial risk factor in arterial thrombosis. As arterial thrombi are composed of predominantly platelets formed under conditions of elevated shear stress at sites of atherosclerotic vascular injury and disturbed blood flow, the prevention of arterial thrombosis has been for years the main target for antiplatelet therapy. Individual differences in the rate of platelet activation and reactivity markedly influence normal hemostasis and the pathological outcome of thrombosis. Such an individual variability is largely determined by environmental and genetic factors. These are known to either hamper platelets' response to agonists, and thereby mimic the pharmacological modulation of platelet function or mask therapy effect and sensitize platelets. Some clinical studies have indicated that platelet glycoprotein polymorphisms are genetic factors contributing to arterial thrombosis. In spite of some discrepancies between different studies, there is substantial evidence that the integrin β_3 Pl^{A2} allele, the variants GPIbα Met^{145} and GPIbα ^{-5}C haplotype or the integrin α_2 haplotype 1 (^{807}T) each contribute to the risk for and morbidity of thrombotic disease. In this article, we reviewed a role of the aforementioned polymorphisms in modulating platelet function and platelet response to inhibitors. The paper focuses on the association between $Pl^{A1/A2}$ polymorphism and sensitivity (or resistance) to aspirin and the inhibitory efficacy of GPIIb-IIIa antagonists. Additionally, a potential role of $^{807}C/T$ polymorphism (GPIa), polymorphisms of GPIb and platelet purinoreceptor $P2Y_{12}$ in affecting platelet sensitivity to blocking agents is discussed.

Key words:
thrombosis, blood platelets, polymorphism, GPIIb-IIIa antagonists, aspirin