ASPIRIN METABOLIZERS
GLICOPROTEIN IIB/IIIA
(PLA1/A2, HPA-1A/B)

PATHOGENESIS	
	Glycoprotein IIIa (GPIIIa) belongs to the integrin family and is a membrane protein found on thrombocytes. During the blood clotting process, GPIIIa forms a complex with the GPIIb subunit, is activated and binds to fibrinogen and von Willebrand factor (vWF). This mechanism allows adjacent thrombocytes to bind together to form a clot. The gene encoding GPIIIa is polymorphic where a particular mutation (PlA2 or HPA1b) gives rise to a protein that has a different conformation than the non-mutated (wild-type) protein. This change in the structure of the protein results in an increase in the affinity between fibrinogen and GPIIIa, predisposing to an increase in the risk of thrombus formation. It has also been shown that this polymorphism is associated with an increased risk of contracting certain heart diseases, such as myocardial infarction, acute coronary events and coronary thrombosis.
PHARMACOGENETICS	
	Recent studies show that there is interference of the mutated allele (PlA2 or HPA1b) on GPIIIa with some drugs, both agonist and antagonist of GPIIIa. In particular, the platelets of individuals carrying the mutated PlA2 or HPA1b allele are less inhibited by the monoclonal antibody Abcximab (ReoPro®) resulting in increased platelet aggregation. This leads to interindividual variability in platelet function, which is considered an independent predictor for the risk of major secondary effects after Percutaneous Coronary Intervention. In aspirin therapy, carriers of the PlA2 or HPA1b mutation require a 10-fold lower dosage than normal (wild-type) individuals.
EPIDEMIOLOGY	
	The mutation (PlA2 or HPA1b) has a prevalence of 15% in Europe and reaches values of 25% in the United States.
TEST	
	PCR amplification of the gene and restriction analysis.
SAMPLE TAKING	
	Blood/EDTA, 5 ml.
EXECUTION	
	Daily.

Laboratorio di diagnostica molecolare

Further information or bibliographic references can be asked to the laboratory.