RESISTANCE TO ANTI-AGGREGATION DRUG PLAVIX (RECEPTOR POLYMORPHISM P2Y12)

PATHOGENESIS

The Plavix is a platelet anti-aggregate medicament normally used to prevent cardiovascular pathologies. In some cases, there was a medicament resistance, which is subjective and characterized by a multi-factors nature. Among possible causes, there are genetic polymorphisms which involved the receptor P2Y12. Another relevant factor for the resistance is about genetic polymorphisms which are at the same level as the main metabolizer of the medicament, the cytochrome P450, and in particular the isozyme CYP3A4. The presence of alleles varieties on the gene which codifies for the CYP3A4 can determinate a different efficiency of its enzymatic activity. Recent studies demonstrated that Plavix's interaction with others medicaments or the presence of a competitive situation between the medicament and others substances (such as CYPA4) can contribute to create a resistance, which takes to the inefficacy of the treatment. Every mutations regarding the coded gene of the receptor P2Y12 are involved in congenital disorders of the coagulation. The receptor P2Y12 represents the target of efficient antithrombotic agents, such as ticlopidine, Plavix and AR-C66096. Carriers' platelets have problems in the mechanism that take to the ability of conformational change of thrombocytes, as a consequence of the ADP link. This receptor has a fundamental role in platelets' aggregation. For this reason, sequence's variations of the gene (it codifies for the receptor P2Y12) are considered.

EPIDEMIOLOGY

Polymorphisms i-C139T, i-T744C, i-ins801A and G52T are the linkage disequilibrium in Caucasian population. It's now possible to discriminate two different haplotypes: haplotype H1 and haplotype H2. Haplotype H1 represents the major haplotype, with a frequency of 86% in the population. H2 results to be the minor haplotype and it has a frequency of 14%. H2 was associated to a maximal platelets aggregation as a response to the ADP.

TEST

The gene that codifies the receptor is made by two separate exons of one intron. In gene's sequence 5 polymorphisms were located. Polymorphisms consist in four different substitutions of one nucleotide (SNPs) and of a mononucleotide insertion

SAMPLE TAKING

Blood/EDTA, 2 ml.

EXECUTION

Daily.

COST

Upon request.

Laboratorio di diagnostica molecolare

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