IDENTIFICATION OF GENE POLYMORPHISM
Dihydropyrimidine dehydrogenase (DPD): DPYD * 2A, DPYP * 13
2846 A> T
(Toxicity to fluoropyrimidine)

AMPLI SET DPYD REAL TIME Cat. 2.027RT

The dihydropyrimidine dehydrogenase (DPD) is the key enzyme involved in the catabolism of 5-fluorouracil (5-FU), the most widely used chemotherapy in the treatment of solid tumors, and of compounds of similar chemical structure, being responsible for the degradation of this pyrimidine analogue to its inactive metabolite diidrofluorouracile. The 80-90% of the administered 5-FU is degraded by the enzyme dihydropyrimidine dehydrogenase (DPYD) mainly in the liver. However, there is a great individual heterogeneity of enzyme activity can vary up to 8-21 times. Patients with low enzyme activity for the DPYD are not capable of inactivating efficiency with the 5-FU with the result of greater bioavailability of the drug that can cause severe hematologic toxicity, neurological and gastrointestinal. They have been highlighted many single nucleotide polymorphisms in the complex structure of the gene responsible for a DPYD inefficient metabolism of the drug resulting in increased risk of severe toxicity potentially fatal; among them the most frequent is the G → A point mutation in a splice site of exon 14 (IVS14 + 1G> A), which happens to be involved in the correct splicing of exon 14. If present, this nucleotide substitution results in loss exon itself and the formation of a protein product incomplete and devoid of enzymatic activity. Although a high percentage of the toxicity of 5-FU observed may be due to enzyme deficiencies distinct from the DPYD and that there are numerous mutations of the gene DPYD that can lead to the total absence of enzymatic activity, the presence of this allelic variant (also known as allele DPYD * 2A) is present in about 1% of the general population and accounts for approximately 50% of all the deficiencies of DPYD. In addition, to cause renal toxicity by enzymatic and 5-FU, it is sufficient the presence of the replacement of only one of the possible alleles. For these reasons, screening for this polymorphism in subjects in need of chemotherapy with a basis of 5-FU may be of particular interest in clinical oncology practice. The presence of the homozygous genotype DPYD * 2 causes a complete lack of the enzyme DPYD, while the heterozygous genotype results in a partial deficiency of the same. A less common mutation I560S position 1679T> G (also known as allele DPYD * 13) is associated with a decreased activity of DPYD and toxicity to 5-FU due to a change from isoleucine at amino acid serine at codon 560. The isoleucine in position 560 it is conserved in both 'man than in other species (mouse, rat, bovine and swine), suggesting its importance in maintaining the enzymatic activity of DPYD. The mutation DPYD * 13 was found in individuals with normal enzyme activity DPYD.
The kit allows the identification of the following mutations in the gene DPYD:
- DPYD * 2A (IVS14 + 1G> A rs 3918290);
- DPYD * 13 T> G in position c.1679 Ile560Ser (rs 55886062);

Principle: A) extraction of genomic DNA B) amplification C) detection through the use of the device real-time PCR
Applicability: on extracted and purified genomic DNA from whole blood samples.

KIT's CONTENT AND ITS CONSERVATION

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Primer-p
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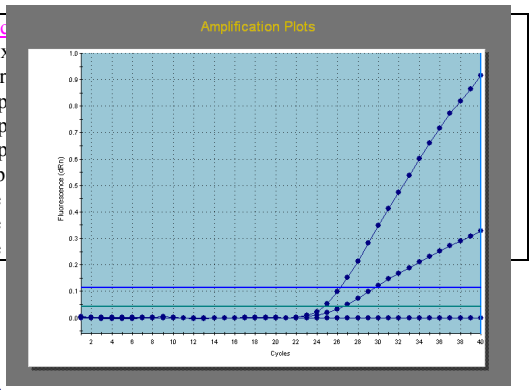

INTERPRETATION OF RESULTS

Analysis of the results will be carried out by a specific program (Allelic discrimination) Real-Time PCR previously set. However, it is always important to analyze the amplification plot graphs to ensure that the reaction has correctly taken place.

Biblioraphy:
Plos One (2013) 8;10 E780536
Pharmacogenomics(2011)10, 931-944
BJC (2013) 108 ,2505-2515
Ezzeldin HH, Lee AM, et al.
Clin Cancer Res. 11 ; 24: 8699-8705. (2005)