Detection Of IVS14+1G>A in Dihydropyrimidine Dehydrogenase Gene And 5-Fluorouracil Chemotherapy In Patients With Solid Malignancies

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The 5-fluorouracile (5-FU) is one of the most commonly anticancer drug for the treatment of solid malignancies including colorectal, breast, head and neck cancer.
Dihydropyrimidine dehydrogenase (DPD) is the initial and rate-limiting enzyme in the metabolism of 5-FU, and approximately 80%-85% of 5-FU is metabolized by DPD in the liver in dihydro5-FU, an inactive product. Patients with deficiency in DPD activity may suffer from serious toxicity after the administration of 5-FU, such as gastrointestinal and hematologic toxicities.
More than 30 polymorphisms in DPYD gene have been found, and one of the most common is G to A mutation in the splicing-recognition sequence of intron 14 (IVS14+1G>A), reported in approximately 3% of patients. This mutation leads to absence of exon 14, which results in partial or complete deficiency of DPD activity.
We investigated the frequency of IVS14+1G>A of DPYD in 70 (52 colorectal, 6 gastric,1 breast, 3 pancreatic and 2 head and neck cancer) consecutive patients from Campania before chemotherapy.
DNA extraction from peripheral blood sample, PCR and hybridization were performed using the kit PGX-5FU StripAssay (Vienna Lab).
We found the heterozygous mutation in 2/70 patient (2.8%). This polymorphism, one or two variant alleles, results in partial or complete lack of DPD activity. Therefore, the identification of IVS14+1G>A may help identify poor-metabolizer patients at risk of developing toxicities after standard doses of 5-FU. For patients with heterozygous DPD IVS14+1G>A mutation, 5-FU dose should be appropriately reduced to reduce adverse reactions, while the homozygous ones should avoid application of 5-FU and its derivatives.