Gene test information

5-FU TOXICITY (DPYD MUTATIONS)

- **Background**

  5-Fluorouracil (5-FU) is one of the most commonly prescribed anti-cancer agents and used for a wide variety of malignancies, including colorectal, gastric, pancreatic, head, neck, breast, ovarian, and cervical cancers.

  Dihydropyrimidine dehydrogenase (DPYD) is a key enzyme in the breakdown of 5-FU, and DPYD deficiency is an important determinant for severe adverse reactions from 5-FU treatment. Individuals with diminished DPYD activity cannot effectively inactivate 5-FU, which leads to toxic levels of 5-FU and to severe-to-lethal hematological, gastrointestinal, or neurological reactions, including stomatitis, diarrhea, dermatitis, fever, leukopenia, therombocytopenia, myelosuppression, and even death.

  More than 40 mutations in the gene that codes for DPYD have been described and the most common three of them (DPYD*2A, p.I560S, p.D949V) account for more than 50% of the patients with a complete or nearly complete DPD deficiency.

- **Indications for testing**

  - Estimation of individual risk for 5-FU toxicity
  - Analysis of the molecular cause for previous 5-FU toxicities

  Factors other than DPYD mutation can influence drug response. A negative result (no mutant DPYD allele detected) on this test does not completely exclude toxicities in patients treated with 5-FU.

References:

Morel A et al. Clinical relevance of different dihydropyrimidine dehydrogenase gene single nucleotide polymorphisms on 5-fluorouracil tolerance. Mol Cancer Ther. 2006;5:2895-904.

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