

## TheraGuide 5-FU™

TheraGuide 5-FU™ is the first and only comprehensive test for predisposition for 5-FU toxicity caused by variations in the *DPYD* and *TYMS* genes. It employs full sequencing of the *DPYD* gene and analysis of the *TYMS* gene.

### 1 in 4 individuals

carry variations in either the *DPYD* or *TYMS* genes that will increase their risk of dose-limiting toxicity.



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## Testing for 5-FU Toxicity: *TYMS* (TS)

As many as 1 in 3 patients receiving 5-FU related therapy experience dose limiting, and sometimes life-threatening, toxicity that is largely avoidable. The target enzyme for 5-FU is thymidylate synthase (TS), which is encoded by the gene *TYMS*. The following study evaluates the possibility of using *TYMS* analysis to predict patient toxicity to 5-FU-based chemotherapy.

Lecomte T, et al. Thymidylate synthase gene polymorphism predicts toxicity in colorectal cancer patients receiving 5-fluorouracil-based chemotherapy. *Clin Cancer Res.* 2004 Sep 1;10(17):5880-8.

**Purpose:** To evaluate the benefits of analyzing *TYMS* variants for use in predicting toxicity to 5-FU chemotherapy in colorectal cancer patients.

**Design and Methods:** Tissue obtained from 86 colorectal cancer patients treated with 5-FU based chemotherapy was analyzed for specific *TYMS* variations (2R/2R, 2R/3R, or 3R/3R) and toxicity. Clinical outcomes were evaluated for these patients and correlated with *TYMS* results.

**Results:** "Among colorectal cancer patients who received 5-FU-based chemotherapy, those possessing the 2R variant showed a significantly higher risk of severe toxicity to chemotherapy."

Genotype	Frequency	5-FU Toxicity Grade 3 or 4
2R/2R	14/86 (16%)	43%
2R/3R	44/86 (51%)	18%
3R/3R	28/86 (32%)	4%

**Bottom Line:** "This study demonstrated that *TYMS* analysis could be of help in predicting toxicity to 5-FU-based chemotherapy. *TYMS* analysis might make it possible to individualize treatment for patients with colorectal cancer." Other existing publications show findings similar to those outlined here. <sup>(1,2)</sup>

1. Pullarkat, S. T., J. Stoehlmacher, et al. Thymidylate synthase gene polymorphism determines response and toxicity of 5-FU chemotherapy. *Pharmacogenomics J* 2001.1(1): 65-70.
2. Ichikawa W, Takahashi T, Suto K, et al. Orotate phosphoribosyltransferase gene polymorphism predicts toxicity in patients treated with bolus 5-fluorouracil regimen. *Clin Cancer Res.* 2006 Jul 1;12(13):3928-34.



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