

UGT1A1 *6 GENETIC VARIANT

ORDERING INFORMATION

REF: FGC-014-25
Tests: 25
Reactions: 31
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for
Real-Time PCR amplification
*the reagents for the extraction of genomic
DNA are not supplied in the kit.



PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS- RESEARCH USE ONLY**. The FGC-014 kit allows the characterization of the genetic variant UGT1A1*6 (rs4148323) of the UGT gene through amplification with specific oligonucleotides and probes (allele-specific genotyping) and subsequent detection using qPCR-Real-time. Kit optimized for Real-time PCR instruments Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Thermofisher QuantStudio™ 5 Real-Time PCR System.

SCIENTIFIC BACKGROUND

UDP-glucuronosyltransferase (UGT) enzymes catalyze the covalent addition of sugars to a wide range of lipophilic molecules. This biotransformation plays a fundamental role in the elimination of multiple exogenous chemicals and products of endogenous metabolism. The most common allele UGT1A1*1 includes six repeats of the dinucleotide thymine-adenine (TA) in the promoter region (near the TATA box). The genetic polymorphisms in UGT1A1 profoundly influence this metabolic pathway, with two key variants - UGT1A1*28 (characterized by a TA repeat polymorphism in the promoter region) and UGT1A1*6 (a missense mutation in exon 1) - that show ethnicity-specific distributions and functional impacts. The UGT1A1*6 variant (G>A; rs4148323) present in exon 1 of region 39 is significantly associated with irinotecan toxicity. This polymorphism reduces the activity of the UGT1A1 enzyme, resulting in the substitution of glycine with arginine (Gly71Arg).

§ Correlation between UGT1A1 polymorphism and efficacy and toxicity of irinotecan in Chinese cancer patients *Front. Pharmacol.*, 18 March 2025 Sec. Pharmacoeconomics Volume 16 - 2025 | <https://doi.org/10.3389/fphar.2025.1563566>

§ *Physiol Rev.* 2019 Apr 1; 99 (2):1153-1222. Doi: 10.1152/physrev.00058.2017. The UDP-Glycosyltransferase (UGT) Superfamily: New Members, New Functions, and Novel Paradigms

§ *Dig Liver Dis.* 2019 Apr; 51 (4):579-583. doi: 10.1016/j.dld.2018.11.032. Epub 2018 Dec 10. A study of the association between UGT1A1*28 variant allele of UGT1A1 gene and colonic phenotype of sporadic colorectal cancer.

§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. *Clin Pharmacokinet.* 2017, Apr; 56 (4):317-337. doi: 10.1007/s40262-016-0450-z. Review.

§ Irinotecan Pathway Genotype Analysis to Predict Pharmacokinetics. *Clin Cancer Res.* 2003 Aug 15; 9 (9):3246-53.

§ Genetic testing of UGT1A1 in the diagnosis of Gilbert syndrome: The discovery of seven novel variants in the Chinese population. *Mol Genet Genomic Med.* 2022;10:e1958.

CLINICAL SIGNIFICANCE

Irinotecan-based chemotherapy is one of the most commonly used chemotherapies for patients with advanced gastric cancer, ovarian cancer, metastatic colorectal cancer, and other tumors. Irinotecan, which is a chemotherapeutic anticancer drug belonging to the class of camptothecins, is primarily transported to the liver and metabolized into the metabolite, SN-38, by a carboxylesterase. In turn, the molecule SN-38 is glucuronidated by uridine diphosphate (UDP)-glucuronosyltransferase (UGT) into an inactive form, SN-38G. Low glucuronidation rates lead to higher concentrations of SN-38, resulting in severe irinotecan-induced toxicity manifesting as diarrhea and neutropenia as the most common side effects, limiting its application. Recent studies have confirmed that UGT1A1 plays a vital role in the glucuronidation process. Patients with reduced UGT1A1 activity (e.g., homozygous for UGT1A1*28 or *6 variants, as in Gilbert's syndrome) have a higher risk of experiencing severe neutropenia and diarrhea following treatment with irinotecan. This risk increases with the dose of irinotecan.

The FGC-014 kit allows for the identification of the genetic variant UGT1A1*6 (rs4148323). The combination of the genotypes UGT1A1*1, UGT1A1*28, UGT1A1*6 (Clinical Pharmacogenetics Implementation Consortium (CPIC®)) allows us to classify the patient as "Normal Metabolizer," "Intermediate Metabolizer," and "Poor Metabolizer."

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-014-25	
Mix oligonucleotides and probes	Mix UGT1A1*6 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-014-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissues, cells
CONTROLS	Recombinant DNA for at least 3 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Thermofisher QuantStudio™ 5 Real-Time PCR System.
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 45 cycles at 95 °C (15 sec) + 63 °C (60 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 5 ng of genomic DNA
LIMIT OF BLANK (LOB)	>40 Cq
REPRODUCIBILITY	99,9%
SPECIFICITY / SENSITIVITY	99,9%/98%