

GENETIC VARIANTS UGT1A1*1 AND UGT1A1*28 (UDP-GLYCOSYLTRANSFERASE)

ORDERING INFORMATIONS

REF: FGC-002-25
 RDM Code: 1875564/R
 CND Code: W0106010499
 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.

For in vitro diagnostic use



PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-PHARMACOGENETICS TEST**. The FGC-002 kit allows the characterization of the genetic variants UGT1A1*1 and UGT1A1*28 of the UGT gene by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with qPCR-Real-time. Optimized kit for Real Time PCR instrumentation Biorad CFX96, Biorad Opus DX, Agilent AriaDx

SCIENTIFIC BACKGROUND

UDP-glycosyltransferase (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. In mammals the superfamily includes four families: UGT1, UGT2, UGT3 and UGT8. The UGT1 and UGT2 enzymes have important roles in pharmacology and toxicology. The UGT1A1 gene has over 60 different genetic polymorphisms. The most common allele **UGT1A1*1** comprises six thymine-adenine dinucleotide (TA) repeats in the promoter region (near the TATA box). The other alleles have a number of TA repeats from five (UGT1A1*36) to eight (UGT1A1*37, deficient allele) and the enzymatic activity is inversely proportional to the number of repeats. The **UGT1A1*28** variant contains 7 TA repeats and is a variant associated with **Gilbert syndrome** in the Caucasian population. The most common variants in the Caucasian population are UGT1A1*1 (0.682) and UGT1A1*28 (0.316).

- § J Pers Med. 2022 Feb 2;12(2):204. doi: 10.3390/jpm12020204.
- § JCO Oncol Pract. 2022 Apr;18(4):270-277. doi: 10.1200/OP.21.00624. Epub 2021 Dec 3.
- § JCO Oncol Pract. 2022 Apr;18(4):278-280. doi: 10.1200/OP.21.00858. Epub 2022 Jan 21.
- § Cancers (Basel). 2021 Mar 29;13(7):1566. doi: 10.3390/cancers13071566.
- § JGH Open. 2019 Feb 8; 3 (5):361-369. doi: 10.1002/jgh3.12153. eCollection 2019 Oct. Review.
- § 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.

CLINICAL SIGNIFICANCE

Irinotecan-based chemotherapy is one of the most widely used chemotherapies for patients with advanced gastric cancer, ovarian cancer, metastatic colorectal cancer and other cancers. Irinotecan, which is an antineoplastic chemotherapy drug belonging to the camptothecin class, is primarily transported to the liver and metabolized to the metabolite, SN-38, by a carboxylesterase. In turn, the SN-38 molecule is glucuronidated by uridiniphosphate (UDP)-glucuronosyltransferase (UGT) to an inactive form, SN-38G. Low rates of glucuronidation lead to higher concentrations of SN-38, resulting in severe irinotecan-induced toxicity manifesting with 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.

The kit allows the identification of the UGT1A1*1 and UGT1A1*28 alleles. The combination of the UGT1A1*1 and UGT1A1*28 genotypes (Clinical Pharmacogenetics Implementation Consortium (CPIC®)) allows the patient to be defined as "Normal Metabolizer", "Intermediate Metabolizer" and "Poor Metabolizer".

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-002-25	
Mix oligonucleotides and probes	Mix 10X UGT1A1*1/*28	1 x 85 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 5X	1 x 170 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	2 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
Genomic DNA or recombinant DNA	Control +3	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-002-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
POSITIVE CONTROL	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 e Agilent AriaDx
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 45 cycles at 95 °C (15 sec) + 60 °C (60 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY: LIMIT OF DETECTION (LOD)	≥ 0,016 ng of genomic DNA
ANALYTICAL SENSITIVITY: LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%