GENETIC VARIANTS UGT1A1*1 AND UGT1A1*28

For in vitro diagnostic use

CE IVD

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.*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS.** 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).

§ Clinical Benefits and Utility of Pretherapeutic DPYD and UGT1A1 Testing in Gastrointestinal Cancer. JAMA Network Open. 2024;7(12): e2449441. doi:10.1001/jamanetworkopen.2024.49441
§ Correlation of UGT1A1 Gene Polymorphisms or Prior Irinotecan Treatment and Treatment Outcomes of Nanoliposomal-Irinotecan plus 5-Fluorouracil/Leucovorin for Pancreatic Ductal Adenocarcinoma: A Multicenter, Retrospective Cohort Study (HGCSG2101). J Clin Med. 2023 Feb 17;12(4):1596. doi: 10.3390/jcm12041596.
§ J Pers Med. 2022 Feb 2;12(2):204. doi: 10.3390/jpm12020204.
§ JCO Oncol Pract. 2022 Apr;18(4):270-277.
§ JCO Oncol Pract. 2022 Apr;18(4):278-280.
§ Cancers (Basel). 2021 Mar 29;13(7):1566.
§ JGH Open. 2019 Feb 8; 3 (5):361-369. 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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ISO 9001 :2015
ISO 13485:2021

ED.1 REV.0 of 01/10/2024

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-002-25	
Mix oligonucleotides and probes	Mix 10X UGT1A1*1/*28	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 5X	1 x 155 µl	-20°C
Deionized H_20	Deionized H_20	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
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 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
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
LIMIT OF DETECTION (LOD)	≥ 0,016 ng of genomic DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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