GENETIC VARIANTS OF SLCO1B1 GENE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-007-25
RDM Code: 2248810/R
CND Code: W010699
Tests: 25
Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for Real-Time PCR amplification
**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**. Detection of genetic variants SLCO1B1 c.521 T>C (rs4149056, V174A), SLCO1B1 c.388 A>G (rs2306283, N130D), SLCO1B1 g.-11187 G>A (rs4149015) of the gene SLCO1B1 by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with qPCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

SLCO1B1 encodes a liver-specific member of the organic anion transporter family. The encoded protein is a transmembrane receptor that mediates the sodium-independent uptake of numerous endogenous compounds including bilirubin, 17-beta-glucuronosyl estradiol and leukotriene C4. In addition, this drug transporter contributes to the hepatic uptake of many clinically used drugs, including statins (e.g., atorvastatin, pravastatin, rosuvastatin, simvastatin), methotrexate, angiotensin-converting enzyme (ACE) inhibitors (e.g., enalapril, temocapril), the angiotensin II receptor blockers (e.g., olmesartan, valsartan), endothelin receptor antagonists (e.g., bosentan).
Genetic variation in SLCO1B1 can result in lower amounts of OATP1B1 protein on the basolateral surface of human hepatocytes, or decreased function resulting in diminished hepatocellular uptake. This, in turn, can limit hepatic clearance and cause increased systemic exposure to drug substrates, which can lead to increased risk for systemic drug toxicity and adverse events.

CLINICAL SIGNIFICANCE

Identifying the clinical and genetic risk factors associated with hepatotoxicity is essential for preventing adverse drug events (ADEs) in patients receiving statin therapy. Polymorphisms of the SLCO1B1 gene reduce the functionality of OATP1B1 causing adverse drug reactions (ADRs).
SLCO1B1 is therefore classified as 'very important' on the pharmacogenetics review site PharmGKB. The common variants SLCO1B1*5 (rs4149056, c.521 T>C, V174A) and SLCO1B1*1B or *37 (rs2306283, c.388 A>G, N130D) have European allele frequencies of ~2% and 40%. These variants, together SLCO1B1*15 (*5 and *37 inherited together), affect statin pharmacokinetics.
The characterization of haplotypes with reduced functionality (**SLCO1B1*37**, **SLCO1B1*5**, **SLCO1B1*15** SLCO1B1*9, SLCO1B1*23 and SLCO1B1*31) allows the optimization of therapy (Level 1A, PharmGKB).
In addition, recently SLC01B1 rs4149015 GA was associated with lower overall survival probabilities after chemotherapy.

§ Cardiovasc Drugs Ther. 2024 May 29. doi: 10.1007/s10557-024-07580-2. Transporter Genes and statin-induced Hepatotoxicity
§ Clin Pharmacol Ther. 2023 Apr;113(4):782-793. doi: 10.1002/cpt.2705. Epub 2022 Jul 27. PharmVar GeneFocus: SLCO1B1
§ Na Nakorn C, Waisayarat J, Dejthevaporn C, Srisawasdi P, Wongwaisayawan S, Sukasem C. Genetic Variations and Frequencies of the Two Functional Single Nucleotide Polymorphisms of SLCO1B1 in the Thai Population. Front Pharmacol. 2020 Jun 5; 11: 728. doi: 10.3389/fphar.2020.00728. eCollection 2020. PMID: 32581780.
§ SLCO1B1 and ABCG2 Gene Polymorphisms in a Thai Population. Pharmgenomics Pers Med. 2020 Oct 22; 13: 521-530. doi: 10.2147/PGPM.S268457. eCollection 2020.
§ Gong, I. Y., and Kim, R. B. (2013). Impact of genetic variation in OATP transporters to drug disposition and response. Drug Metab. Pharmacokinet. 28(1), 4–18. doi: 10.2133/dmpk.DMPK-12-RV-099.
§ Franke RM, Gardner ER, Sparreboom A. Pharmacogenetics of Drug Transporters. Curr Pharm Des. 2010; 16 (2):220–230. doi: 10.2174/ 138161210790112683 5.
§ Mizuno N, Sugiyama Y. Drug transporters: their role and importance in the selection and development of new drugs. Drug Metab Pharmacokinet. 2002; 17 (2):93–108. doi:10.2133/dmpk.17.932.

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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-007-25	
Mix oligonucleotides and probes	Mix 10X SLCO1B1 c.521 T>C **Mix 1**	1 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X SLCO1B1 c.388 A>G **Mix 2**	1 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X SLCO1B1 g.-11187 G>A **Mix 3**	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 1162,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	**Control 1** Homozygous **TT SLCO1B1 c.521** Homozygous **AA SLCO1B1 c.388** Homozygous **GG SLCO1B1 g.-11187**	1 x 40 µl	-20°C
Genomic DNA or recombinant DNA	**Control 2** Heterozygous **TC SLCO1B1 c.521**	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	**Control 3** Heterozygous **AG SLCO1B1 c.388**	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	**Control 4** Heterozygous **GA SLCO1B1 g.-11187**	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-007-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, 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
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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