

CYP2D6 *3 and *4 GENETIC VARIANTS

ORDERING INFORMATIONS

REF: FGC-018-25
Tests: 25
Reactions: 31 x 2
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 devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS- RESEARCH USE ONLY**. Detection of genetic variant *3 (rs35742686) and *4 (rs3892097) of the CYP2D6 gene by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with 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

Cytochrome P450 2D6 (CYP2D6) is a critical pharmacogene involved in the metabolism of ~20% of commonly used drugs across a broad spectrum of medical disciplines including psychiatry, pain management, oncology and cardiology. Nevertheless, CYP2D6 is highly polymorphic with single-nucleotide polymorphisms, small insertions/deletions and larger structural variants including multiplications, deletions, tandem arrangements, and hybridisations with non-functional CYP2D7 pseudogenes. The frequency of these variants differs across populations, and they significantly influence the drug-metabolising enzymatic function of CYP2D6. Importantly, altered CYP2D6 function has been associated with both adverse drug reactions and reduced drug efficacy.

§ CYP2D6 pharmacogenetics and phenoconversion in personalized medicine. Expert Opin Drug Metab Toxicol. 2022 November; 18(11): 769–785. doi: 10.1080/17425255.2022.2160317.
§ A Review of the Important Role of CYP2D6 in Pharmacogenomics. Genes 2020, 11, 1295; doi: 10.3390/genes11111295
§ Pharmacogenetics and individualized drug therapy. Annu. Rev. Med. 2005, 57, 119–156.
§ Cytochromes P450: A success story. Genome Biol. 2000, 1, reviews30031.

CLINICAL SIGNIFICANCE

The human CYP2D6 gene is relatively short, spanning just ~4.3 Kbps on the long arm of chromosome 22 (22q13.2), is encoded by nine exons, is translated into CYP2D6 protein that localises to the endoplasmic reticulum, and is highly expressed in liver, brain, intestinal tissue and lymphoid cells. CYP2D6*5 represents a whole allele deletion with a corresponding complete loss of function of the allele. Overall, this variant is present in 3–6% of African, European and East Asian populations. The CYP2D6*3 key variant is the frameshift-causing deletion at NC_000022.11:g.42128242 (rs35742686). The CYP2D6*4 key variant is the splicing defect/169frameshift-causing variant at NC_000022.11:g.42128945 (rs3892097).

Recent developments within pharmacogenetics and various guidelines from CPIC have promoted personalized therapy, ensuring drug safety and efficacy, especially for the medications metabolized by CYP2D6 (including tramadol, codeine, hydrocodone, atomoxetine, tamoxifen, paroxetine, fluoxetine, fluvoxamine, amitriptyline, nortriptyline, ondansetron and tropisetron).

The impact of CYP2D6 inhibitors on the efficacy and safety of CYP2D6-metabolized drugs and percentages of concomitant use of the CYP2D6 inhibitors can easily explain the need to implement phenoconversion along with CYP2D6 pharmacogenetics to lead to optimal therapeutic outcomes.

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-018-25	
Mix oligonucleotides and probes	Mix CYP2D6 *3 10X	1 x 62 µl	-20°C
Mix oligonucleotides and probes	Mix CYP2D6 *4 10X	1 x 62 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 5X	1 x 248 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2 CYP2D6*3	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2 CYP2D6*4	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-018-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissues, 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, 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) + 66 °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%