

VKORC1 1639 G>A GENETIC VARIANT

ORDERING INFORMATION

REF: FGC-020-25
Tests: 25
Reactions: 31
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for
Real-Time PCR amplification
*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 1639 G>A (rs9923231) of the VKORC1 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

Warfarin is an anticoagulant that works by inhibiting the synthesis of vitamin K-dependent coagulation factors and is used in the prevention and treatment of various thrombotic disorders. Warfarin is a drug with a narrow therapeutic index; therefore, a small variation of its plasma levels can cause concentration-dependent adverse reactions or therapeutic failure. Therefore, the dose of warfarin should be customized for each patient based on their response, measured as INR (International Normalized Ratio), and the condition to be treated.

There is wide inter-individual variability in the dose of warfarin needed to achieve a good therapeutic response. About half of this variability is known to be caused by clinical or lifestyle factors (e.g., age, weight, BMI, sex, smoking status, existing conditions and concomitant drugs) and genetic factors such as variants in the VKORC1 and CYP2C9 genes).

§ J Pharm Pharm Sci. 2023 Jan 30;26:11136. The role of CYP2C9*2, CYP2C9*3 and VKORC1-1639 variants on the susceptibility of upper gastrointestinal bleeding: A full case-control study.

§ Front Cardiovasc Med. 2022 Jun 10;9:895169. Determination of Pleiotropic Effect of Warfarin in VKORC1 and CYP2C9 Genotypes in Patients With Heart Valve Replacement.

§ Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Pharmacogenetics-Guided Warfarin Dosing: 2017 Update

§ N Engl J Med. 2005 Jun 2;352(22):2285-93. Effect of VKORC1 haplotypes on transcriptional regulation and warfarin dose.

CLINICAL SIGNIFICANCE

Warfarin targets VKORC1, an enzyme involved in the recycling of vitamin K. A common non-coding variant, VKORC1, c.-1639G>A (rs9923231), is associated with increased sensitivity to warfarin and less need for dosing. Polymorphism occurs in the VKORC1 promoter region and is thought to alter the transcription factor binding site causing reduced protein expression.

The frequency of the VKORC1 allele, c.-1639G>A varies between different ethnic groups. It is the main allele (about 90%) in Asian populations and may be one of the factors contributing to the lower dose of warfarin often observed in patients of Asian origin. It is also common in Caucasians (about 40%) and African-Americans (about 14%).

An appropriate therapeutic dose of warfarin should therefore consider the genotype association for the rs1799853 (*2) and rs1057910 (*3) variants of the CYP2C9 gene and for the c.-1639G>A variant (rs9923231) of the VKORC1 gene. There are indications from the 2017 FDA (Food and Drug Administration) and The Dutch Pharmacogenetics Working Group (DPWG) that should be taken into account within the patient-specific clinical context.

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-020-25	
Mix oligonucleotides and probes	Mix 1639 G>A VKORC1 10X	1 x 62 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 310 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
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-020-25

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) + 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%