BioMol

LABORATORIES


EPSON

GENETICS

In vitro diagnostic devices belonging to the family
"REAL-TIME PCR QUALITATIVE GENOTYPING"

E.g. FV G1691A, FII G20210A, MTHFR C677T, ACE INS/DEL, HFE, PAI 4G/5G

PHARMACOGENETICS

In vitro diagnostic devices belonging to the family
«REAL-TIME QUALITATIVE PCR-PHARMACOGENETICS TEST»

*E.g. DPYD *2A, *13, Asp949Val, 1236G>A, HaB3 e 2194G>A, *6. GSTP1 A313G. ABCB1 C1236T, C3435T, G2677T/A*

ONCOHEMATOLOGY

In vitro diagnostic devices belonging to the family
"REAL-TIME PCR QUALITATIVE GENOTYPING"

E.g. BCR-ABL1. V617F JAK2. W515L/K MPL. DEL52bp INS5bp CALR

HLA

In vitro diagnostic devices belonging to the family
«REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS»

E.g. Ins/Del 14 bp HLA-G

INFECTIOUS DISEASES

In vitro diagnostic devices belonging to the family
«REAL-TIME QUALITATIVE PCR - INFECTIOUS DISEASES»

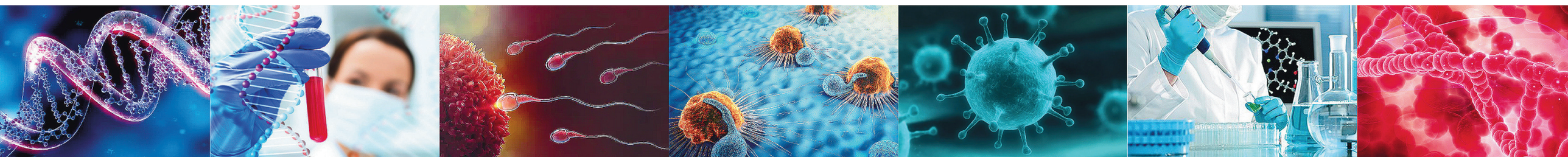
REPRODUCTION

In vitro diagnostic devices belonging to the family
«PCR END-POINT»
Optimized kit for any CE-IVD validated thermal cycler and agarose gel electrophoresis

DNA/RNA EXTRACTION

In vitro diagnostic devices for the extraction of nucleic acids (DNA/RNA) from whole blood, serum and cells. Kits optimized for Autopure 32 Allsheng, GenePure Pro BIOER and Nucleic Acid Purification System-16 BigFish and Auto-Pure Mini- Allsheng

Graphic & Print lithofer it



DNA/RNA EXTRACTION

DNA/RNA EXTRACTION KIT WITH MAGNETIC BEADS

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: EXT- 001-32 RDM Code: 2735760/R
Reactions: 32 (monotest strips)
REF: EXT- 002-32 RDM Code: 2734224/R
Reactions: 32 (2 plates of 16 tests)
CND Code: W0105900101
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for the extraction of DNA/RNA from various biological samples.

CONTENTS OF THE KIT

DESCRIPTION	LABEL	REACTIONS	STORAGE	
Strip monotest	DNA/RNA EXTRACTION KIT WITH MAGNETIC BEADS	32 reactions	RT	EXT-001-32
Tip combs		8 x 2	RT	
Plates	DNA/RNA EXTRACTION KIT WITH MAGNETIC BEADS	2 x 16 reactions	RT	EXT-002-32
Tip combs		2 x 2	RT	

PRODUCT CHARACTERISTICS

Automatic extraction with magnetic beads of DNA/RNA of bacteria or viruses from multiple biological samples (nasopharyngeal swab, vaginal swab, urine, stool supernatant, seminal fluid) in mono-sample pre-aliquoted strips/pre-aliquoted plates.

EXT-001-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.
EXT-002-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.

PRINCIPLE OF THE METHOD

The automatic extraction system using magnetic spheres provides, after the lysis phase in a specific buffer, the binding of the positively charged magnetic spheres to the negatively charged nucleic acid.
Subsequently, a magnetic piston attracts and retains the marbles to which the nucleic acid has bound. Finally, the magnetic marbles are subjected to quick washing in buffer to eliminate further contaminants and salts. Finally, the magnetic piston is moved away, and the nucleic acid is eluted with water.

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GENOMIC DNA EXTRACTION KIT WITH MAGNETIC BEADS

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: EXT - 011-32 Code RDM: 2724783/R
Reactions: 32 (monotest strips)
REF: EXT- 012-32 Code RDM: 2724797/R
Reactions: 32 (2 plates of 16 tests)
Code CND: W0105900101
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for genomic DNA extraction

CONTENTS OF THE KIT

DESCRIPTION	LABEL	REACTIONS	STORAGE	
Strip monotest	GENOMIC DNA EXTRACTION KIT WITH MAGNETIC BEADS	32 reactions	RT	EXT-011-32
Tip combs		8 x 2	RT	
Proteinase k (10 mg/ml)		750 µl	-20°C	
Plates	GENOMIC DNA EXTRACTION KIT WITH MAGNETIC BEADS	2 x 16 reactions	RT	EXT-012-32
Tip combs		2 x 2	RT	
Proteinase k (10 mg/ml)		750 µl	-20°C	

PRODUCT CHARACTERISTICS

Automatic magnetic beads extraction of genomic DNA from biological sample (whole blood, cell pellets and biological fluids) in mono-sample pre-aliquoted strips/pre-aliquoted plates.

EXT-011-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.
EXT-012-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.

PRINCIPLE OF THE METHOD

The automated extraction system using magnetic spheres provides, after the lysis phase in a specific buffer, the binding of the magnetic spheres to the nucleic acid.
Subsequently, a magnetic piston attracts and retains the beads to which the nucleic acid has bound. Finally, magnetic beads are subjected to a quick washing in buffer to eliminate further contaminants and salts. Finally, the magnetic piston is moved away, and the nucleic acid is eluted with water.

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TOTAL RNA EXTRACTION KIT WITH MAGNETIC BEADS

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: EXT- 013-32 Code RDM: 2725135/R
Reactions: 32 (strip monotest)
REF: EXT- 014-32 Code RDM: 2725136/R
Reactions: 32 (2 plates of 16 tests)
Code CND: W0105900101
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for genomic RNA extraction

CONTENTS OF THE KIT

DESCRIPTION	LABEL	REACTIONS	STORAGE	
Strip monotest	TOTAL RNA EXTRACTION KIT WITH MAGNETIC BEADS	32 reactions	RT	EXT-013-32
Tip combs		8 x 2	RT	
Proteinase k (10 mg/ml)		750 µl	-20°C	
Plates	TOTAL RNA EXTRACTION KIT WITH MAGNETIC BEADS	2 x 16 reactions	RT	EXT-014-32
Tip combs		2 x 2	RT	
Proteinase k (10 mg/ml)		750 µl	-20°C	

PRODUCT CHARACTERISTICS

Automatic magnetic beads extraction of total RNA from biological sample (whole blood, cell pellets and biological fluids) in mono-sample pre-aliquoted strips/pre-aliquoted plates.

EXT-013-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.

EXT-014-32: Validated for Autopure 32-Allsheng Nucleic Acid Purification System and Auto-Pure Mini-Allsheng instrumentation.

PRINCIPLE OF THE METHOD

The automatic extraction system using magnetic spheres provides, after the lysis phase in a specific buffer, the binding of the positively charged magnetic spheres to the negatively charged nucleic acid.
Subsequently, a magnetic piston attracts and retains the beads to which the nucleic acid has bound. Finally, magnetic beads are subjected to a quick washing in buffer to eliminate further contaminants and salts. Finally, the magnetic piston is moved away, and the nucleic acid is eluted with water.

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PHARMACOGENETICS

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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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.*

CONTENTS OF THE KIT

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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ABCB1 (MDR1) GENE VARIANT C1236T

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-003-25
RDM Code: 1875566/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.** Characterization of the genetic variant C1236T of the ABCB1 gene (rs1128503) 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, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Pharmacogenetic screening and/or drug-specific phenotyping of cancer patients eligible for treatment with chemotherapy drugs can identify patients susceptible or resistant to the proposed drugs. Similarly, identification of patients with an increased risk of developing toxicity allows for dose adaptation or application of other targeted therapies. Polymorphisms in genes encoding drug efflux transporters, such as P-glycoprotein, can affect the absorption and excretion of anticancer drugs. This contributes to interindividual variability in pharmacokinetics and, consequently, large differences in treatment response among cancer patients. P-gp is a member of the ABC superfamily of membrane transporters and is involved in the active transport of lipophilic and amphipathic molecules across lipid membranes. It is encoded by the multidrug resistance 1 (MDR1) gene (ABCB1, ATP-binding cassette transporter superfamily B member 1) located on chromosome 7q21. Numerous polymorphisms described in this gene significantly affect the pharmacokinetics of many anticancer drugs. There are three main polymorphisms affecting P-gp activity: the c.2677G>T/A polymorphism in exon 21 (rs2032582) which causes a substitution in the amino acid sequence Ala (G)/Ser (T) or Thr (A), with consequent possible increase in enzyme function. The second polymorphism is in exon 26, at position c.3435C>T (rs1045642), resulting in more than twofold expression of P-gp. The third C1236T polymorphism (rs1128503) in exon 12 does not directly affect P-gp expression but has an indirect effect as it alters the stability of the mRNA encoding the protein.

CLINICAL SIGNIFICANCE

Evaluation of the Association of Polymorphisms With Palbociclib Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3 (ClinicalTrials.gov identifier: NCT01740427 and NCT01942135) paper revealed higher incidence of palbociclib-associated SAEs occurred among homozygous and heterozygous carriers of the c1236C>T variant compared to wild-type, 38% versus 23% (RR=1,65 95%CI 1,19–2,29, p=0,003) and 32% versus 23% (RR=1,37 95%CI 1,03–1,84, p=0,03).
An association between the ABCB1 C3435T (rs1045642), ABCB1 G2677T/A (rs2032582) polymorphism and
risk of adverse efects of docetaxel was found by meta-analysis. Namely, the TT homozygotes of the ABCB1 C3435T polymorphism may be associated with the risk of hematological toxicity. ABCB1 G2677T T(A)/T(A) genotype may be associated with the fuid retention.
Recently it has been demonstrated that 1236TT, 2677TT, and 3435TT carriers (also referred to as "TT-TT-TT" haplotype) need higher methadone doses to avoid withdrawal, probably associated with faster metabolism and consequent lower methadone plasma levels.

§ Clin Transl Sci. 2024 May;17(5):e13781. doi: 10.1111/cts.13781. A systematic review and meta-analysis of the impacts of germline pharmacogenomics on severe toxicity and symptom burden in adult patients with cancer
§ Int J Mol Sci. 2022 Nov 16;23(22):14125. doi: 10.3390/ijms232214125. The Impact of P-Glycoprotein on Opioid Analgesics: What's the Real Meaning in Pain Management and Palliative Care?
§ Cancer Chemother Pharmacol. 2022 Feb;89(2):173-181. doi: 10.1007/s00280-021-04374-3. Epub 2022 Jan 6 Association between gene polymorphism and adverse effects in cancer patients receiving docetaxel treatment: a meta-analysis
§ Oncologist. 2021 Jul;26(7):e1143-e1155. doi: 10.1002/onco.13811. Epub 2021 Jun 7. Evaluation of the Association of Polymorphisms With Palbociclib-Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3
§ Clinical utility of ABCB1 genotyping for preventing toxicity in treatment with irinotecan. Pharmacol Res. 2018 Oct; 136:133-139.doi:10.1016/j.phrs.2018.08.026. Epub 2018 Sep 11.
§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017, Apr; 56 (4):317-337. doi: 10.1007/ s40262-016-0450-z. Review.
§ Influence of the ABCB1 polymorphisms on the response to Taxane-containing chemotherapy: a systematic review and meta-analysis. Cancer Chemother Pharmacol. 2018, Feb; 81 (2):315-323.doi: 10.1007/s00280-017-3496-1. Epub 2017 Dec 5.
§ Are pharmacogenomic biomarkers an effective tool to predict taxane toxicity and outcome in breast cancer patients? Literature review. Cancer Chemother Pharmacol. 2015 Oct; 76 (4):679-90. doi: 10.1007/s00280-015-2818-4. Epub 2015 Jul 22.

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ABCB1 (MDR1) GENE VARIANT C1236T

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-003-25
RDM Code: 1875566/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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-003-25	
Mix oligonucleotides and probes	Mix 10X C1236T ABCB1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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-003-25	
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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BioMol LABORATORIES

GSTP1 GENE VARIANT A313G (I105V)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-004-25
RDM Code: 1875567/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-004 kit allows the characterization of the A313G genetic variant of the GSTP1 gene (rs1695) by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with qPCR-Real-time. Optimized kit for Biorad Real-Time PCR instrumentation CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The GSTP1 gene is located on chromosome 11q13 and has numerous polymorphisms. A single nucleotide substitution (rs1695) A/G causes an amino acid substitution from isoleucine to valine (I105V). This results in reduced substrate specificity, catalytic activity and thermal stability in the GSTP1 protein which is an isoenzyme with an important role in the detoxification of carcinogens, the metabolism of chemotherapeutic agents and the regulation of the cell cycle and apoptosis.

§ Association between Genetic Polymorphism of GSTP1 and Toxicities in Patients Receiving Platinum-Based Chemotherapy: A Systematic Review and Meta-Analysis. Pharmaceuticals (Basel) 2022 Apr 1;15(4):439.
§ Evaluating the role of GSTP1 genetic polymorphism (rs1695, 313A>G) as a predictor in cyclophosphamide-induced toxicities. Medicine 100(11): p e24423, March 19, 2021.
§ Glutathione S-transferasesP1 AA (105Ile) allele increases oral cancer risk, interacts strongly with c-Jun Kinase and weakly detoxifies areca-nut metabolites. Sci Rep 2020 Apr 7;10(1):6032 doi:10.1038/s41598-020-63034-3.
§ Predictive value of clinical toxicities of chemotherapy with fluoropyrimidines and oxaliplatin in colorectal cancer by DPYD and GSTP1 gene polymorphisms. World Journal of Surgical Oncology volume 18, Article number: 321 (2020).
§ GSTP1 and cancer: Expression, methylation, polymorphisms and signaling (Review). Int J Oncol 2020 Apr;56(4):867-878. doi: 10.3892/ijo.2020.4979.
§ Glutathione S-Transferase Pi 1 (GSTP1) Gene 313 A/G (rs1695) polymorphism is associated with the risk of urinary bladder cancer: Evidence from a systematic review and meta-analysis based on 34 case-control studies. Gene. 2019 Nov 30; 719: 144077. doi: 10.1016/j.gene.2019.144077. Epub 2019 Aug 24.
§ Relationship between GSTP1 rs1695 gene polymorphism and myelosuppression induced by platinum-based drugs: a meta-analysis. Int J Biol Markers. 2018 Sep 21:1724600818792897. doi: 10.1177/1724600818792897.
§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017, Apr; 56 (4):317-337. doi: 10.1007/ s40262-016-0450-z. Review.
§ Association of glutathione S-transferase T1, M1, and P1 polymorphisms in the breast cancer risk: a meta-analysis. Ther Clin Risk Manag. 2016 May 12; 12: 763-9. doi: 10.2147/TCRM.S104339. eCollection 2016.
§ Predictive potential role of glutathione S-transferase polymorphisms in the prognosis of breast cancer. Genet Mol Res. 2015 Aug 28; 14 (3):10236-41. doi: 10.4238/2015.August.28.7.

CLINICAL SIGNIFICANCE

Numerous studies in the literature have investigated the correlation between the GSTP1 rs1695 variant and various treatment outcomes, including survival and clinical response, in patients suffering from malignant tumors.
Recently, a significant correlation has been demonstrated between GSTP1 polymorphism and toxicity from platinum derivatives with symptoms such as vomiting and development of skin ulcers in patients affected by colorectal cancer (AA genotype for GSTP1 shows lower rates of severe vomiting (35.3 %) compared to patients with AG and GG genotypes (66,7% and 100%, respectively, p = 0,027).
A 2022 meta-analysis study showed that patients receiving platinum-based treatment with the rs1695 G allele had approximately 1,7 and 2.6 times higher haematological adverse events and neutropenia than those with the AA genotype, respectively. Hematological toxicity and neutropenia are serious adverse events leading to treatment discontinuation. In this context, the results of this study indicated that GSTP1 could serve as a potential marker and substantially influence treatment regimens (level 3, PHARMG KB).

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GSTP1 GENE VARIANT A313G (I105V)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-004-25
RDM Code: 1875567/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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-004-25	
Mix oligonucleotides and probes	Mix 10X A313G GSTP1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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-004-25	
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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ED.1 REV.0 of 01/10/2024

BioMol LABORATORIES

GENETIC VARIANTS OF THE ENZYME CYTOCHROME P450 CYP2C9 (variants *2 and *3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-005-25
RDM Code: 1973964/R
CND Code: W0106030101
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
**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.** Detection of the genetic variants rs1799853 (*2) and rs1057910 (*3) of the CYP2C9 gene 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

Cytochromes P450s are a family of enzymes responsible for approximately 75% of all drug metabolism reactions. There are multiple isoforms of cytochrome P450 but most reactions are metabolised by CYP2C9, CYP2C19, CYP2D6 and CYP3A4. The CYP2C9 gene has been mapped to chromosome 10q24.2 and is highly variable; nucleotide sequencing has already identified nearly 60 alleles. Three alleles, namely CYP2C9 *1 (the wild-type allele with normal activity), CYP2C9 *2 and CYP2C9 *3 (both with reduced enzyme activity) are often identified in studies in the Caucasian population. Among the 60 variant CYP2C9 star (*) alleles listed on The Pharmacogene Variation Consortium website (https://www.pharmvar.org) at least 20 are reported to have in vivo and/or in vitro functional evidence of altered activity.

The CYP2C9 * 2 variant (rs1799853) has a C>T transition at position 430 of exon 3 coding for arginine, resulting in a substitution at position 144 (Arg144Cys) of the CYP2C9 protein, while the analysis of the CYP2C9 *3 variant (rs1057910) demonstrated an A>C transversion at position 1075 in exon 7 causing an isoleucine to leucine substitution at position 359 (Ile359Leu).

§ Mol Biol Rep. 2024 Jan 16;51(1):105.Genetic variation of CYP2C9 gene and its correlation with cardiovascular disease risk factors
§ Nucleosides Nucleotides Nucleic Acids. 2024;43(4):356-376. Identification of the effects of pathogenic genetic variations of human CYP2C9 and CYP2D6: an in silico approach.
§ Recommendations for Clinical CYP2C9 Genotyping Allele Selection: A Joint Recommendation of the Association for Molecular Pathology and College of American Pathologists.
The Journal of molecular diagnostics. JMD. 2019.
§ Polymorphisms of CYP2C9*2, CYP2C9*3 and VKORC1 genes related to time in therapeutic range in patients with atrial fibrillation using warfarin. Appl Clin Genet. 2019 Aug 2;12:1 51-159.
§ The Cytochrome P450 Slow Metabolizers CYP2C9*2 and CYP2C9*3 Directly Regulate Tumorigenesis via Reduced Epoxyeicosatrienoic Acid Production. Cancer Res. 2018 Sep 1; 78 (17):4865-4877.
§ CYP2C9 polymorphisms in epilepsy: influence on phenytoin treatment. Pharmgenomics Pers Med. 2018 Mar 29;11: 51-58.
§ Applications of CYP450 testing in the clinical setting. Mol Diagn Ther. 2013 Jun; 17(3):165-84.

CLINICAL SIGNIFICANCE

The cytochrome P450 superfamily is mainly expressed in the liver, small intestine and kidney. CYP P450 enzymes catalyze several types of oxidation and some reduction reactions.

Genetic polymorphisms in CYP genes are the major cause of inter-individual variation in drug metabolism. They cause variations in drug response ranging from adverse effects to lack of efficacy. In addition, CYP polymorphisms have been reported to confer susceptibility or reduced risk/protection from disease. CYP2C9 plays an important role in the phase I metabolism of xenobiotics and some endogenous compounds, for example, nonsteroidal anti-inflammatories, oral anticoagulants and oral hypoglycaemics. Individuals with low CYP2C9 catalytic activity (poor and/or intermediate metabolisers) develop adverse drug reactions particularly with substrates with a narrow therapeutic index, e.g. S-warfarin, phenytoin, glipizide and tolbutamide. The combination of genotypes (www.pharmgkb.org) allows to define the patient as "Normal Metabolizer" (Homozygous CYP2C9*1), "Intermediate Metabolizer" (Heterozygous CYP2C9*2 and *3) and "Poor Metabolizer" (Homozygous or Double CYP2C9 heterozygous *2 and *3).

Recently, the importance of CYP2C9 in the metabolism of Siponimod, an orally available immunomodulatory drug used to treat relapsing forms of multiple sclerosis, has been demonstrated. Indeed, the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) indicate that molecular characterization is necessary before starting treatment (CYP2C9 *3/*3 patients should not be subjected to pharmacological treatment).

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BioMol LABORATORIES

GENETIC VARIANTS OF THE ENZYME CYTOCHROME P450 CYP2C9 (variants *2 and *3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-005-25
RDM Code: 1973964/R
CND Code: W0106030101
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
**the reagents for the extraction of genomic DNA are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-005-25	
Mix oligonucleotides and probes	Mix 10X CYP2C9 *2	1 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X CYP2C9 *3	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA Control 1	Control 1 Homozygous **CC CYP2C9 C430T** Homozygous **AA CYP2C9 A1075C**	1 x 30 µl	-20°C
Genomic DNA or recombinant DNA Control 2	Control 2 Heterozygous **CT CYP2C9 C430T *2** Heterozygous **AC CYP2C9 A1075C *3**	1 x 30 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-005-25

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 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
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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BioMol LABORATORIES

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/ 138161207901126835.
§ 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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BioMol LABORATORIES

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.*

CONTENTS OF THE KIT

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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BioMol LABORATORIES

ABCB1 (MDR1) GENE VARIANT C3435T

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-008-25
RDM Code: 2159865/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-GENETIC VARIANTS.**
The FGC-008 kit allows the characterization of the C3435T genetic variant of the ABCB1 gene (rs1045642) 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, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Pharmacogenetic screening and/or drug-specific phenotyping of cancer patients eligible for treatment with chemotherapy drugs can identify patients likely to be reactive or resistant to proposed drugs. Similarly, identification of patients with an increased risk of developing toxicity allows for dose adaptation or application of other targeted therapies. Polymorphisms in genes encoding drug efflux transporters, such as P-glycoprotein, can affect the absorption and excretion of anticancer drugs. This contributes to interindividual variability in pharmacokinetics and, consequently, large differences in treatment response among cancer patients. P-gp is a member of the ABC superfamily of membrane transporters and is involved in the active transport of lipophilic and amphipathic molecules across lipid membranes. It is encoded by the multidrug resistance 1 (MDR1) gene (ABCB1, ATP-binding cassette transporter superfamily B member 1) located on chromosome 7q21. There are three main polymorphisms affecting P-gp activity: the first polymorphism c.2677G>T/A (rs2032582) in exon 21 which causes a substitution in the amino acid sequence Ala (G)/Ser (T) or Thr (A), resulting in a possible increase in enzyme function. The second polymorphism is in exon 26 at position c.3435C>T (rs1045642), resulting in more than twofold expression of P-gp. The third polymorphism C1236T (rs1128503) in exon 12 does not directly affect P-gp expression but has an indirect effect as it alters the stability of the mRNA encoding the protein.

CLINICAL SIGNIFICANCE

Evaluation of the Association of Polymorphisms With Palbociclib Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3 (ClinicalTrials.gov identifier: NCT01740427 and NCT01942135) paper revealed higher incidence of palbociclib-associated SAEs occurred among homozygous and heterozygous carriers of the c1236C>T variant compared to wild-type, 38% versus 23% (RR=1,65 95%CI 1,19–2,29, p=0,003) and 32% versus 23% (RR=1,37 95%CI 1,03–1.84, p=0,03). An association between the ABCB1 C3435T (rs1045642), ABCB1 G2677T/A (rs2032582) polymorphism and risk of adverse efects of docetaxel was found by meta-analysis. Namely, the TT homozygotes of the ABCB1 C3435T polymorphism may be associated with the risk of hematological toxicity. ABCB1 G2677T T(A)/T(A) genotype may be associated with the fuid retention. Recently it has been demonstrated that 1236TT, 2677TT, and 3435TT carriers (also referred to as “TT-TT-TT” haplotype) need higher methadone doses to avoid withdrawal, probably associated with faster metabolism and consequent lower methadone plasma levels.

§ Clin Transl Sci. 2024 May;17(5):e13781. doi: 10.1111/cts.13781. A systematic review and meta-analysis of the impacts of germline pharmacogenomics on severe toxicity and symptom burden in adult patients with cancer
§ Int J Mol Sci. 2022 Nov 16;23(22):14125. doi: 10.3390/ijms232214125. The Impact of P-Glycoprotein on Opioid Analgesics: What's the Real Meaning in Pain Management and Palliative Care?
§ Cancer Chemother Pharmacol. 2022 Feb;89(2):173-181. doi: 10.1007/s00280-021-04374-3. Epub 2022 Jan 6 Association between gene polymorphism and adverse effects in cancer patients receiving docetaxel treatment: a meta-analysis
§ Oncologist. 2021 Jul;26(7):e1143-e1155. doi: 10.1002/onco.13811. Epub 2021 Jun 7. Evaluation of the Association of Polymorphisms With Palbociclib-Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3
§ Clinical utility of ABCB1 genotyping for preventing toxicity in treatment with irinotecan. Pharmacol Res. 2018 Oct; 136:133-139.doi:10.1016/j.phrs.2018.08.026. Epub 2018 Sep 11.
§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017, Apr; 56 (4):317-337. doi: 10.1007/s40262-016-0450-z. Review.
§ Influence of the ABCB1 polymorphisms on the response to Taxane-containing chemotherapy: a systematic review and meta-analysis. Cancer Chemother Pharmacol. 2018, Feb; 81 (2):315-323.doi: 10.1007/s00280-017-3496-1. Epub 2017 Dec 5.
§ Are pharmacogenomic biomarkers an effective tool to predict taxane toxicity and outcome in breast cancer patients? Literature review. Cancer Chemother Pharmacol. 2015 Oct; 76 (4):679-90. doi: 10.1007/s00280-015-2818-4. Epub 2015 Jul 22.

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BioMol LABORATORIES

ABCB1 (MDR1) GENE VARIANT C3435T

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-008-25
RDM Code: 2159865/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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-008-25	
Mix oligonucleotides and probes	Mix 10X C3435T ABCB1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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-008-25

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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BioMol LABORATORIES

ABCB1 (MDR1) GENE VARIANT G2677T/A

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-009-25
RDM Code: 2190182/R
CND Code: W010699
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
**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.** Detection of genetic variant G2677T; G>T / G2677A; G>A) of the gene ABCB1 (rs2032582) 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

Pharmacogenetic screening and/or drug-specific phenotyping of cancer patients eligible for treatment with chemotherapy drugs can identify patients susceptible or resistant to the proposed drugs. Similarly, identification of patients with an increased risk of developing toxicity allows for dose adaptation or application of other targeted therapies.Polymorphisms in genes encoding drug efflux transporters, such as P-glycoprotein, can affect the absorption and excretion of anticancer drugs. This contributes to interindividual variability in pharmacokinetics and, consequently, large differences in treatment response among cancer patients. P-gp is a member of the ABC superfamily of membrane transporters and is involved in the active transport of lipophilic and amphipathic molecules across lipid membranes. It is encoded by the multidrug resistance 1 (MDR1) gene (ABCB1, ATP-binding cassette transporter superfamily B member 1) located on chromosome 7q21. Numerous polymorphisms described in this gene significantly affect the pharmacokinetics of many anticancer drugs. There are three main polymorphisms affecting P-gp activity: the c.2677G>T/A polymorphism in exon 21 (rs2032582) which causes a substitution in the amino acid sequence Ala (G)/Ser (T) or Thr (A), with consequent possible increase in enzyme function. The second polymorphism is in exon 26, at position c.3435C>T (rs1045642), resulting in more than twofold expression of P-gp. The third C1236T polymorphism (rs1128503) in exon 12 does not directly affect P-gp expression but has an indirect effect as it alters the stability of the mRNA encoding the protein.

CLINICAL SIGNIFICANCE

Evaluation of the Association of Polymorphisms With Palbociclib Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3 (ClinicalTrials.gov identifier: NCT01740427 and NCT01942135) paper revealed higher incidence of palbociclib-associated SAEs occurred among homozygous and heterozygous carriers of the c1236C>T variant compared to wild-type, 38% versus 23% (RR=1,65 95%CI 1,19–2.29, p=0,003) and 32% versus 23% (RR=1,37 95%CI 1,03–1,84, p=0,03). An association between the ABCB1 C3435T (rs1045642), ABCB1 G2677T/A (rs2032582) polymorphism and risk of adverse efects of docetaxel was found by meta-analysis. Namely, the TT homozygotes of the ABCB1 C3435T polymorphism may be associated with the risk of hematological toxicity. ABCB1 G2677T T(A)/T(A) genotype may be associated with the fuid retention.
Recently it has been demonstrated that 1236TT, 2677TT, and 3435TT carriers (also referred to as "TT-TT-TT" haplotype) need higher methadone doses to avoid withdrawal, probably associated with faster metabolism and consequent lower methadone plasma levels.

§ Clin Transl Sci. 2024 May;17(5):e13781. doi: 10.1111/cts.13781. A systematic review and meta-analysis of the impacts of germline pharmacogenomics on severe toxicity and symptom burden in adult patients with cancer
§ Int J Mol Sci. 2022 Nov 16;23(22):14125. doi: 10.3390/ijms232214125. The Impact of P-Glycoprotein on Opioid Analgesics: What's the Real Meaning in Pain Management and Palliative Care?
§ Cancer Chemother Pharmacol. 2022 Feb;89(2):173-181. doi: 10.1007/s00280-021-04374-3. Epub 2022 Jan 6 Association between gene polymorphism and adverse effects in cancer patients receiving docetaxel treatment: a meta-analysis
§ Oncologist. 2021 Jul;26(7):e1143-e1155. doi: 10.1002/onco.13811. Epub 2021 Jun 7. Evaluation of the Association of Polymorphisms With Palbociclib-Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3
§ Clinical utility of ABCB1 genotyping for preventing toxicity in treatment with irinotecan. Pharmacol Res. 2018 Oct; 136:133-139.doi:10.1016/j.phrs.2018.08.026. Epub 2018 Sep 11.
§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017, Apr; 56 (4):317-337. doi: 10.1007/ s40262-016-0450-z. Review.
§ Influence of the ABCB1 polymorphisms on the response to Taxane-containing chemotherapy: a systematic review and meta-analysis. Cancer Chemother Pharmacol. 2018, Feb; 81 (2):315-323.doi: 10.1007/s00280-017-3496-1. Epub 2017 Dec 5.
§ Are pharmacogenomic biomarkers an effective tool to predict taxane toxicity and outcome in breast cancer patients? Literature review. Cancer Chemother Pharmacol. 2015 Oct; 76 (4):679-90. doi: 10.1007/s00280-015-2818-4. Epub 2015 Jul 22.

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ABCB1 (MDR1) GENE VARIANT G2677T/A

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-009-25
RDM Code: 2190182/R
CND Code: W010699
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
**the reagents for the extraction of genomic DNA are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-009-25	
Mix oligonucleotides and probes	Mix 10X G2677T ABCB1 G>T	1 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X G2677A ABCB1 G>A	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1 Homozygous G2677G ABCB1	1 x 40 µl	-20°C
Genomic DNA or recombinant DNA	Control 2 Heterozygous G2677T ABCB1	1 x 40 µl	-20°C
Genomic DNA or recombinant DNA	Control 3 Homozygous T2677T ABCB1	1 x 40 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-009-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissues, 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 at (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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BioMol LABORATORIES

GENETIC VARIANTS OF THE ENZYME DIHYDROPYRIMIDINE DEHYDROGENASE (DPYD) (DPYD *2A, *13, Asp949Val, 1236 G>A, HapB3 and 2194 G>A, *6)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-010-25 RDM Code: 2256421/R
Tests: 25 Reactions: 31 x 5
REF: FGC-010-50 RDM Code: 2256529/R
Tests: 50 Reactions: 62 x 5
CND Code: W0106010499
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.** Detection of genetic variants *2A (rs3918290, 1905 +1G>A, IVS14 +1 G>A), *13 (rs55886062, 1679 T>G), Asp949Val, (rs67376798, 2846 A>T), 1236 G>A (rs 56038477, HapB3) and *6 (2194 G>A, rs 1801160) of the gene DPYD 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, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The treatment of neoplastic pathologies has become increasingly personalized in relation to the large inter-individual differences that exist in the effect of therapy and its toxicity. Polymorphisms in genes encoding proteins responsible for drug metabolism can significantly influence the absorption, metabolism and elimination of anticancer drugs. As a result, different pharmacokinetics can significantly influence the efficacy and toxicity of drugs.
Pharmacogenetic screening and/or drug-specific phenotyping of cancer patients eligible for treatment with chemotherapy drugs can identify patients likely to be reactive or resistant to the proposed drugs. Likewise, identifying patients with an increased risk of developing toxicity allows for dose adaptation or the application of other targeted therapies.

§ 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
§ J Mol Diagn. 2024 Oct;26(10):851-863. doi: 10.1016/j.jmoldx.2024.05.015.Review
§ ESMO Open. 2023 Apr;8(2):101197. doi: 10.1016/j.esmoop.2023.101197. Epub 2023 Mar 28.PMID: 36989883
§ Cancers (Basel). 2022 Jun 30;14(13):3207. doi: 10.3390/cancers14133207. Testing for Dihydropyrimidine Dehydrogenase Deficiency to Individualize 5-Fluorouracil Therapy.
§ Oncologist. 2021 Apr;26(4):e597-e602. doi: 10.1002/onco.13626. Epub 2020 Dec 23. Implementing DPYD*2A Genotyping in Clinical Practice: The Quebec, Canada, Experience
§ EMA recommendations on DPD testing prior to treatment with fluorouracil, capecitabine, tegafur and flucytosine. 30 April 2020
§ Br J Cancer. 2019 Apr; 120(8):834-839. doi: 10.1038/s41416-019-0423-8. Epub 2019 Mar 12. The Clinical Relevance of Multiple DPYD Polymorphisms on Patients Candidate for Fluoropyrimidine Based-Chemotherapy. An Italian Case-Control Study
§ Curr Ther Res Clin Exp. 2018 Oct 31; 90:1-7. doi: 10.1016/j.curtheres.2018.10.001. eCollection 2019. Evolution of Dihydropyrimidine Dehydrogenase Diagnostic Testing in a Single Center during an 8-Year Period of Time.
§ Int J Cancer. 2015 Dec 15; 137(12):2971-80. doi: 10.1002/ijc.29654. Epub 2015 Jul 14. Clinical validity of a DPYD-based pharmacogenetic test to predict severe toxicity to fluoropyrimidines.

CLINICAL SIGNIFICANCE

The main chemotherapeutic agents used in many types of cancer are fluoropyrimidines, namely 5-fluorouracil (5-FU), capecitabine and various derivatives. Treatment with these agents is not well tolerated in a subgroup of patients as moderate to severe (fatal) toxicity occurs in 20% to 40% of cases, manifested by nausea and vomiting, diarrhea, mucositis/stomatitis, myelosuppression and syndrome hand-foot.
The main degradation pathway of fluoropyrimidines is the enzyme dihydropyrimidine dehydrogenase (DPYD). The reduced functionality of this enzyme causes increased exposure to active metabolites, which can lead to varying degrees of toxicity. The DPYD gene is on chromosome 1p22 and has 23 exons. More than 100 variants have been reported. Among these, three have been associated with toxicity and decreased activity of the enzyme: DPYD *2A (c.1905 + 1G>A; rs3918290), DPYD *13 (c .1679 T>G p. [Ile560Ser], rs55886062) and c .2846A> T p. (Asp949Val), rs67376798.
As reported in the 2018 CPIC (Clinical Pharmacogenetics Implementation Consortium (CPIC®) guidelines and in the 2019 AIOM (Italian Association of Medical Oncology), SIF (Italian Society of Pharmacology) and EMA (European Medicines Agengy) recommendations, the DPYP pharmacogenetic analysis it is recommended to optimize the therapeutic dose and possibly define a reduction in the drug dose (25-50%) for Intermediate Metabolizers patients and the evaluation of an alternative therapy for Poor Metabolizers.

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GENETIC VARIANTS OF THE ENZYME DIHYDROPYRIMIDINE DEHYDROGENASE (DPYD) (DPYD *2A, *13, Asp949Val, 1236 G>A, HapB3 and 2194 G>A, *6)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-010-25 RDM Code: 2256421/R
Tests: 25 Reactions: 31 x 5
REF: FGC-010-50 RDM Code: 2256529/R
Tests: 50 Reactions: 62 x 5
CND Code: W0106010499
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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		FGC-010-25	FGC-010-50	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD *2A	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD *13	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD Asp949Val	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD 1236 G>A	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD *6	1 x 77,5 µl	2x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	2 x 969 µl	4 x 969 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 60 µl	2 x 60 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 60 µl	2 x 60 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-010-25 / COD. FGC-010-50

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 (FGC-010-25) Recombinant DNA for at least 6 analytical sessions (FGC-010-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx ,Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP
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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BioMol LABORATORIES

GENETIC VARIANT ARG399GLN OF THE XRCC1 GENE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-011-25
RDM Code: 2259495/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.** Determination of the ARG399GLN polymorphism of the XRCC1 gene (G>A; ARG399GLN; rs25487) 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, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Radiation therapy is a potentially curative and important treatment option in the early stages of localized cancer. Radiation therapy and cytotoxic treatment destroy cancer cells by inducing DNA damage. Therefore, the outcome of these treatments depends on the effectiveness of the DNA repair systems. The XRCC1 (X-Ray repair cross complementing group 1) protein is essentially involved in both single-strand break repair and base excision repair. The single nucleotide polymorphism (SNPs) of the XRCC1(rs25487) gene identifies the G>A substitution that causes the variation of codon 399 of the amino acid arginine (Arg) to the amino acid glutamine (Gln).

§ Mol Cells. 2025 Jan 17:100186. doi: 10.1016/j.mocell.2025.100186. Online ahead of print. Cancer prognosis using base excision repair genes
§ Biomol Biomed. 2024 Dec 13. doi: 10.17305/bb.2024.11314. Online ahead of print. The association of rs25487 of the XRCC1 gene and rs13181 of the ERCC2 gene polymorphisms with the ovarian cancer risk
§ Front Pharmacol. 2024 Aug 21:15:1445328. doi: 10.3389/fphar.2024.1445328. eCollection 2024.Genetic polymorphisms and platinum-induced hematological toxicity: a systematic review
§ BMC Cancer. 2024 Jan 15;24(1):78. Novel model integrating computed tomography-based image markers with genetic markers for discriminating radiation pneumonitis in patients with unresectable stage III non-small cell lung cancer receiving radiotherapy: a retrospective multi-center radiogenomics study
§ Reprod Sci. 2023 Apr;30(4):1118-1132.Elucidation of Increased Cervical Cancer Risk Due to Polymorphisms in XRCC1 (R399Q and R194W), ERCC5 (D1104H), and NQO1 (P187S)
§ Nucleosides Nucleotides Nucleic Acids. 2022;41(5-6):530-554. Association of genetic polymorphisms in DNA repair genes ERCC2 Asp312Asn (rs1799793), ERCC2 Lys 751 Gln (rs13181), XRCC1 Arg399 Gln (rs25487) and XRCC3 Thr 241Met (rs861539) with the susceptibility of lung cancer in Saudi population
§ Front Oncol. 2021 May 19:11:654784. Significant Association Between XRCC1 Expression and Its rs25487 Polymorphism and Radiotherapy-Related Cancer Prognosis
§ J Cell Biochem. 2017 Dec;118(12):4782-4791. Evaluation of Prediction of Polymorphisms of DNA Repair Genes on the Efficacy of Platinum-Based Chemotherapy in Patients With Non-Small Cell Lung Cancer: A Network Meta-Analysis
§ XRCC1 rs25487 Polymorphism Predicts the Survival of Patients After Postoperative Radiotherapy and Adjuvant Chemotherapy for Breast Cancer ANTICANCER RESEARCH 34: 3031-3038 (2014)
§ Genetic polymorphisms in XRCC1 associated with radiation therapy in prostate cancer Cancer Biology & Therapy 10:1, 13-18; July 1, 2010.
§ Functional characterization of polymorphisms in DNA repair genes using cytogenetic challenge assays. Environ Health Perspect 111: 1843-1850, 2003. ANTICANCER RESEARCH 34: 3031-3038 (2014) 3036

CLINICAL SIGNIFICANCE

Studies have been conducted on the functional effects of the amino acid substitution Arg399Gln, suggesting that the genotype of the AA variant is associated with a 3- to 4-fold reduced DNA repair capacity.
In addition, it has also been associated with an increase in chromosomal deletions, increasing the risk of cancer. Recent meta-analysis studies have shown that polymorphisms in the DNA damage repair genes XRCC1 (rs25487 and rs1799782), ERCC5 (rs17655) and the oxidative stress-related NQO1 gene (rs1800566) are significantly associated with an increased risk of developing cancer. Recently, an increased risk of developing ovarian cancer has been demonstrated in subjects carrying the GA and AA genotypes of the rs25487 polymorphism.
DNA repair genes increase susceptibility to lung cancer (LC) occurrence in the Saudi population through gene-gene interaction rather than through independent variants.
On the other hand, the data indicate that in terms of overall response ratio (ORR), ERCC1 (rs11615), XRCC1 (rs25487, rs1799782), and XPD (rs13181) polymorphisms are associated with the efficacy of platinum-based chemotherapy in non-small cell lung cancer (NSCLC).

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GENETIC VARIANT ARG399GLN OF THE XRCC1 GENE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-011-25
RDM Code: 2259495/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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-011-25	
Mix oligonucleotides and probes	Mix 10X Arg399Gln XRCC1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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-011-25	
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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GENETIC VARIANTS 197 G>T and 19007 T>C OF THE ERCC1 GENE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-012-25
RDM Code: 2259502/R
CND Code: W0106010499
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
**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.** Determination of the genetic variants 197 G>T (rs3212986) and 19007 T>C (Asn118Asn; NM_001369414.1: c.354T>C, rs11615) of the ERCC1 gene 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, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

DNA repair systems play a critical role in maintaining the integrity and fidelity of the genome, and DNA repair capacity is an important source of interindividual variability in relation to cancer development. In particular, polymorphisms in DNA repair genes can influence repair capacity.
The ERCC1 (*Excision repair cross-complementation group 1*) protein is a 297 amino acid protein encoded by a gene located on chromosome 19q13.
ERCC1 contributes to the elimination of DNA adducts, altered forms of DNA that result from exposure to chemical carcinogens (UV light, ROS, environmental mutagens, and chemotherapy drugs). Furthermore, the protein also plays a role in preserving chromosomal stability and telomere integrity. High levels of ERCC1 have been associated with resistance to therapy with platinum derivatives, while cells deficient in this protein appear to be highly sensitive to alkylating agents.
The best characterized single nucleotide polymorphisms (SNPs) of ERCC1 include the T19007C variant (Asn118Asn; rs11615) and the HGVS variant: c.*197G>T, SNP n.8092 C>A (3' UTR; rs3212986).

§ Pharmaceutics 2024, 16, 1121. ERCC1 and ERCC2 Polymorphisms Predict the Effcacy and Toxicity of Platinum-Based Chemotherapy in Small Cell Lung Cancer
§ Front. Pharmacol., 21 August 2024Sec. Pharmacogenetics and Pharmacogenomics Volume 15 - 2024 |
§ PHARMACOVIGILANCE, DRUG INTERACTIONS, PHARMACOGENETICS AND THERAPEUTIC DRUG MONITORING OF ANTICANCER AGENTS: A VALUABLE SUPPORT FOR CLINICAL PRACTICE. Volume 3, issue 3, 2021: 548-67 Doi: 10.36118/pharmadvances.2021.15
§ SNPs in predicting clinical efficacy and toxicity of chemotherapy: walking through the quicksand. Oncotarget, 2018, Vol. 9, (No. 38), pp: 25355-25382
§ ERCC1 rs11615 polymorphism increases susceptibility to breast cancer: a meta-analysis of 4547 individuals. Bioscience Reports (2018) 38 BSR20180440 https://doi.org/10.1042/BSR20180440

CLINICAL SIGNIFICANCE

The ERCC1 T19007C variant (Asn118Asn; NM_001369414.1: c.354T>C, rs11615), although it does not cause a change at the amino acid level, results in reduced stability of the protein. On the other hand, reduced expression of ERCC1, as a result of the C allele, has been shown to correlate with better responses to platinum-based therapies, such as FOLFOX (chemotherapeutic combination composed of folinic acid, fluorouracil and oxaliplatin), in NSCLC (*non-small cell lung cancer*) patients, while the T allele was found to be more correlated with platinum resistance in gastric, ovarian and cervical cancers. Furthermore, the presence of the C allele increases genotoxicity to platinum derivatives.
Another ERCC1 variant is C8092A, located in the 3'UTR of the gene and can alter polyadenylation, translation efficiency, localization and stability of the mRNA.
In particular, the presence of the A allele reduces the stability of the mRNA causing a lower expression of the protein, and an increase in sensitivity to genotoxic chemotherapies.
In a recent study, it was demonstrated that, in NSCLC patients treated with platinum-based chemotherapy, AA/CA genotypes of the C8092A variant were associated with increased genotoxicity.

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BioMol LABORATORIES

GENETIC VARIANTS 197 G>T and 19007 T>C OF THE ERCC1 GENE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-012-25
RDM Code: 2259502/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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-012-25	
Mix oligonucleotides and probes	Mix 10X 197 G>T ERCC1	1 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix 10X 19007 T>C ERCC1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase	Mix Real-Time PCR 2X	1 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1 Homozygous GG 197 G>T ERCC1 Homozygous TT 19007 T>C ERCC1	1 x 40 µl	-20°C
Genomic DNA or recombinant DNA	Control 2 Heterozygous GT 197 G>T ERCC1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3 Heterozygous TC 19007 T>C ERCC1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 4 Homozygous TT 197 G>T ERCC1 Homozygous CC 19007 T>C ERCC1	1 x 40 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-012-25

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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BioMol LABORATORIES

GENETICS

FV LEIDEN G1691A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-001-25 RDM Code: 1718429/R
Tests: 25 Reactions: 31
REF: GEN-001-50 RDM Code: 2255477/R
Tests: 50 Reactions: 62
CND Code: W0106010103
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 the G1691A FV Leiden polymorphism by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Venous thromboembolism (VTE), usually involving deep vein thrombosis, pulmonary embolism, or both, is a complex, multifactorial disorder in which a number of conditions interact and contribute to increased individual risk culminating in the development of venous occlusives. Thrombophilia is commonly defined as a propensity to develop venous thromboembolism based on a hypercoagulable condition attributable to inherited or acquired disorders involving blood clotting or fibrinolysis.

Among the environmental risk factors, some can lead to increased hypercoagulability, for example cancer, surgery, trauma or fracture, immobilisation, pregnancy and the postpartum period, long-distance travel, hospitalization, catheterization and acute infection and others may be considered as predisposing conditions, such as age, gender, race/ethnicity, body mass index and obesity, use of oral contraceptive or hormone therapy, corticosteroids or statins, diet, physical activity, sedentary weather and air pollution.

CLINICAL SIGNIFICANCE

Venous thromboembolism has a strong genetic basis, with approximately 50-60% of the variance in incidence attributable to genetic effects. Some genetic susceptibility variants that contribute to risk have been identified in candidate genes, such as factor V Leiden and prothrombin.

The identification of the factor V Leiden (G1691A) missense mutation (Arg506Gln) causing factor V resistance to the anticoagulant action of activated protein C represents a landmark in understanding the basis of hereditary thrombotic risk. The FVL mutation is, in fact, the most common hereditary defect that predisposes to venous thrombosis

§ Int J Mol Sci. 2024 May 11;25(10):5228. doi: 10.3390/ijms25105228.The Etiology of the Thrombotic Phenomena Involved in the Process of Coronary Artery Disease-What Is the Role of Thrombophilic Genes in the Development of This Pathology?

§ J Hum Reprod Sci. 2023 Oct-Dec;16(4):352-357.doi: 10.4103/jhrs.jhrs_137_23. Epub 2023 Dec 29. Combined Parental Thrombophilia Gene Mutation Defects in Couples with Repeated Pregnancy Loss

§ Ann Hematol. 2024 Aug 21. doi: 10.1007/s00277-024-05926-2. Online ahead of print. Venous thromboembolism risk in adults with hereditary thrombophilia: a systematic review and meta-analysis

§Thrombophilia Screening: Not So Straightforward. Moore GW. Semin Thromb Hemost. 2024 May 11. doi: 10.1055/s-0044-1786807.

§ Turk J Med Sci. 2024 Jun 12;54(4):682-687. doi: 10.55730/1300-0144.5837. eCollection 2024. Can prothrombotic gene variants and Apoa1 rs5069 polymorphism be the predictors of early myocardial infarctions?

§ Laboratory biomarkers for venous thromboembolism risk in patients with hematologic malignancies: A review. Thromb Res. 2018 Mar; 163:138-145. doi: 10.1016/j.thromres.2018.01.037. Epub 2018 Jan 31.

§ Pregnancy, thrombophilia, and the risk of a first venous thrombosis: systematic review and bayesian meta-analysis. Croles FN, Nasserinejad K, Duvekot JJ, Kruip MJ, Meijer K, Leebeek FW. BMJ 2017; 359 doi: https://doi.org/10.1136/bmj.j4452

§ J Res Med Sci. 2015 Jun; 20 (6):554-62. Factor V Leiden, factor V Cambridge, factor II GA20210, and methylenetetrahydrofolate reductase in cerebral venous and sinus thrombosis: A case-control study.

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BioMol LABORATORIES

FV LEIDEN G1691A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-001-25 RDM Code: 1718429/R
Tests: 25 Reactions: 31
REF: GEN-001-50 RDM Code: 2255477/R
Tests: 50 Reactions: 62
CND Code: W0106010103
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-001-25	GEN-001-50	
Mix oligonucleotides and probes	Mix G1691A FV Leiden 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-001-25 / COD. GEN-001-50

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 (GEN-001-25), Recombinant DNA for at least 6 analytical sessions (GEN-001-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

FII PROTHROMBIN G20210A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-002-25 RDM Code: 1718459/R
Tests: 25 Reactions: 31
REF: GEN-002-50 RDM Code: 2255478/R
Tests: 50 Reactions: 62
CND Code: W0106010114
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 the G20210A FII Prothrombin polymorphism by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Venous thromboembolism (VTE), which usually involves deep vein thrombosis, pulmonary embolism, or both, is a complex, multifactorial disorder in which a number of conditions interact and contribute to increasing individual risk culminating in the development of venous occlusive disorders. Thrombophilia is commonly defined as a propensity to develop venous thromboembolism based on a hypercoagulable condition attributable to inherited or acquired disorders involving blood clotting or fibrinolysis. Among environmental risk factors, some can cause increased hypercoagulability, such as cancer, surgery, trauma or fractures, pregnancy and the postpartum period, long-distance travel, hospitalization, catheterization, and acute infection and others may be considered as predisposing conditions, such as age, sex, race/ethnicity, body mass index and obesity, use of oral contraceptive or hormone therapy, corticosteroids or statins, diet, physical activity, sedentary weather, and air pollution.

CLINICAL SIGNIFICANCE

Venous thromboembolism also has a strong genetic basis, with about 50-60% of the variance in incidence attributable to genetic effects. Certain genetic susceptibility variants that contribute to risk have been identified in candidate genes, such as factor V Leiden and prothrombin. The G20210A FII gene variant is a G>A substitution in the 3'-untranslated region of the gene and has been associated with an increased concentration of FII in plasma and has a frequency between 1-6% in Caucasian populations. The risk of thrombosis is 2 to 3 times greater in carriers of this mutation than in controls.

§ Int J Mol Sci. 2024 May 11;25(10):5228. doi: 10.3390/ijms25105228.The Etiology of the Thrombotic Phenomena Involved in the Process of Coronary Artery Disease-What Is the Role of Thrombophilic Genes in the Development of This Pathology?

§ J Hum Reprod Sci. 2023 Oct-Dec;16(4):352-357.doi: 10.4103/jhrs.jhrs_137_23. Epub 2023 Dec 29. Combined Parental Thrombophilia Gene Mutation Defects in Couples with Repeated Pregnancy Loss

§ Ann Hematol. 2024 Aug 21. doi: 10.1007/s00277-024-05926-2. Online ahead of print. Venous thromboembolism risk in adults with hereditary thrombophilia: a systematic review and meta-analysis

§Thrombophilia Screening: Not So Straightforward. Moore GW. Semin Thromb Hemost. 2024 May 11. doi: 10.1055/s-0044-1786807.

§ Turk J Med Sci. 2024 Jun 12;54(4):682-687. doi: 10.55730/1300-0144.5837. eCollection 2024. Can prothrombotic gene variants and Apoa1 rs5069 polymorphism be the predictors of early myocardial infarctions?

§ Laboratory biomarkers for venous thromboembolism risk in patients with hematologic malignancies: A review. Thromb Res. 2018 Mar; 163:138-145. doi: 10.1016/j.thromres.2018.01.037. Epub 2018 Jan 31.

§ Pregnancy, thrombophilia, and the risk of a first venous thrombosis: systematic review and bayesian meta-analysis. Croles FN, Nasserinejad K, Duvekot JJ, Kruip MJ, Meijer K, Leebeek FW. BMJ 2017; 359 doi: https://doi.org/10.1136/bmj.j4452

§ J Res Med Sci. 2015 Jun; 20 (6):554-62. Factor V Leiden, factor V Cambridge, factor II GA20210, and methylenetetrahydrofolate reductase in cerebral venous and sinus thrombosis: A case-control study.

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BioMol LABORATORIES

FII PROTHROMBIN G20210A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-002-25 RDM Code: 1718459/R
Tests: 25 Reactions: 31
REF: GEN-002-50 RDM Code: 2255478/R
Tests: 50 Reactions: 62
CND Code: W0106010114
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-002-25	GEN-002-50	
Mix oligonucleotides and probes	Mix G20210A FII 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-002-25 / COD. GEN-002-50

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 (GEN-002-25), Recombinant DNA for at least 6 analytical sessions (GEN-002-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

MTHFR C677T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-003-25 RDM Code: 1718916/R
Tests: 25 Reactions: 31
CND Code: W0106010499
REF: GEN-003-50 RDM Code: 2255479/R
Tests: 50 Reactions: 62
CND Code: W0106010199

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 the C677T polymorphism of the MTHFR gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The MTHFR enzyme gene (5, 10-methylenetetrahydrofolate reductase) is located at the end of the short arm of chromosome 1 (1p36.3). The DNA sequence of the gene is approximately 2.2 kilobases (kb), comprising 11 exons. Two polymorphisms have been described in detail for the MTHFR gene: C677T (rs1801133) and A1298C (rs1801131). The C677T polymorphism is located in exon 4 and results in a conversion of alanine to valine at codon 222 (A222V) in a protein region that is the binding site for the cofactor of MTHFR, flavin adenine dinucleotide (FAD). It is reported in the literature that the MTHFR 677T genotype decreases MTHFR enzyme activity by 30% in vitro compared to the wild-type type. Folate is one of the most important precursor substrates for cellular metabolism. One of folate's jobs is to act as a carrier of individual carbon fragments. This reaction is required for the synthesis of purine-pyrimidines, DNA, RNA and protein methylation. Previous research has shown that low folate levels result in uracil disincorporation during DNA replication, which causes increased double-strand breaks during uracil remnant excision repair.

§ Thrombophilia Screening: Not So Straightforward. Moore GW. Semin Thromb Hemost. 2024 May 11. doi: 10.1055/s-0044-1786807.
§ Arch Dermatol Res. 2024 May 21;316(5):184. doi: 10.1007/s00403-024-02905-5. Association between Psoriasis and MTHFR polymorphisms: a systematic review and meta-analysis
§ Mol Biol Rep. 2024 Sep 26;51(1):1014. doi: 10.1007/s11033-024-09948-x.
§ J Hum Reprod Sci. 2023 Oct-Dec;16(4):352-357. Combined Parental Thrombophilia Gene Mutation Defects in Couples with Repeated Pregnancy Loss
§ Associations of meth ylenetetrahydrofolate reductase gene (MTHFR) rs1801131 and rs1801133 polymorphisms with susceptibility to vitiligo: a meta-analysis. J Cosmet Dermatol 20(7):2359–2368. (2021)
§ MTHFR C677T and A1298C polymorphisms in breast cancer, gliomas and gastric cancer: a review. Genes 12(4):587. (2021)
§ Association between MTHFR gene polymorphism and susceptibility to autism spectrum disorders: systematic review and meta-analysis. Res Autism Spectr Disord 70:101473. (2020)
§ Effects of MTHFR C677T polymorphism on vitamin D, homocysteine and natural killer cell cytotoxic ity in women with recurrent pregnancy losses. Hum Reprod 35(6):1276–1287. (2020)
§ Two Common MTHFR Gene Polymorphisms (C677T and A1298C) and Fetal Congenital Heart Disease Risk: An Updated Meta-Analysis with Trial Sequential Analysis. Cell Physiol Biochem. 2018 Mar 15;45(6):2483-2496.
§ The methylenetetrahydrofolate reductase 677T-1298C haplotype is a risk factor for acute lymphoblastic leukemia in children. Medicine (Baltimore). 2017 Dec;96(51):e9290.
§ Folate metabolism genetic polymorphisms and meningioma and glioma susceptibility in adults. Oncotarget. 2017 Jul 4;8(34):57265-57277.
§ J Res Med Sci. 2015 Jun; 20 (6):554-62. Factor V Leiden, factor V Cambridge, factor II GA20210, and methylenetetrahydrofolate reductase in cerebral venous and sinus thrombosis: A case-control study.

CLINICAL SIGNIFICANCE

Because of the importance of the folate pathway and the potentially deleterious effects of hyperhomocysteinemia, the role of MTHFR mutations including C677T and A1298C has been investigated in conditions varying from autism, recurrent pregnancy loss, coronary artery disease, stroke, breast and gastric cancers, and skin conditions such as vitiligo. Additionally, patients with psoriasis have been shown to demonstrate elevated levels of serum homocysteine, a known risk factor for cardiovascular disease.

Folate deficiency, therefore, has also been associated with an increased risk for a number of cancers and other disease risks such as cardiovascular disease, diabetes, birth defects, ischemia, venous thrombosis, hypotonia, leukemia, migraine, schizophrenia, depression, preeclampsia, Alzheimer's disease, birth defects of the heart, Down syndrome and cleft palate.

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BioMol LABORATORIES

MTHFR C677T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-003-25 RDM Code: 1718916/R
Tests: 25 Reactions: 31
CND Code: W0106010499
REF: GEN-003-50 RDM Code: 2255479/R
Tests: 50 Reactions: 62
CND Code: W0106010199

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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-003-25	GEN-003-50	
Mix oligonucleotides and probes	Mix C677T MTHFR 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-003-25 / COD. GEN-003-50

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 (GEN-003-25), Recombinant DNA for at least 6 analytical sessions (GEN-003-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

MTHFR A1298C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-004-25 RDM Code: 1718917/R
Tests: 25 Reactions: 31
CND Code: W0106010499
REF: GEN-004-50 RDM Code: 2255480/R
Tests: 50 Reactions: 62
CND Code: W0106010199
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 the A1298C polymorphism of the MTHFR gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The MTHFR enzyme gene (5,10-methylenetetrahydrofolate reductase) is located at the end of the short arm of chromosome 1 (1p36.3). The DNA sequence of the gene is approximately 2,2 kilobases (kb), comprising 11 exons. Two polymorphisms have been described in detail for the MTHFR gene: C677T (rs1801133) and A1298C (rs1801131). The C677T polymorphism is located in exon 4 and results in a conversion of alanine to valine at codon 222 (A222V) in a protein region that is the binding site for the cofactor of MTHFR, flavin adenine dinucleotide (FAD). It is reported in the literature that the MTHFR 677T genotype decreases MTHFR enzyme activity by 30% in vitro compared to the wild-type type. Folate is one of the most important precursor substrates for cellular metabolism. The second polymorphism of the MTHFR gene is A1298C, located in exon 7 and resulting in a substitution of a glutamic acid residue to alanine at codon 429 (E429A). This polymorphism is located in the regulatory domain of the enzyme S-adenosyle methionine (SAM) and causes conformational changes within the MTHFR enzyme that alter its enzymatic activity.

§ Thrombophilia Screening: Not So Straightforward. Moore GW. Semin Thromb Hemost. 2024 May 11. doi: 10.1055/s-0044-1786807.
§ Arch Dermatol Res. 2024 May 21;316(5):184. doi: 10.1007/s00403-024-02905-5. Association between Psoriasis and MTHFR polymorphisms: a systematic review and meta-analysis
§ Mol Biol Rep. 2024 Sep 26;51(1):1014. doi: 10.1007/s11033-024-09948-x.
§ J Hum Reprod Sci. 2023 Oct-Dec;16(4):352-357. Combined Parental Thrombophilia Gene Mutation Defects in Couples with Repeated Pregnancy Loss
§ Associations of meth ylenetetrahydrofolate reductase gene (MTHFR) rs1801131 and rs1801133 polymorphisms with susceptibility to vitiligo: a meta-analysis. J Cosmet Dermatol 20(7):2359–2368. (2021)
§ MTHFR C677T and A1298C polymorphisms in breast cancer, gliomas and gastric cancer: a review. Genes 12(4):587. (2021)
§ Association between MTHFR gene polymorphism and susceptibility to autism spectrum disorders: systematic review and meta-analysis. Res Autism Spectr Disord 70:101473. (2020)
§ Effects of MTHFR C677T polymorphism on vitamin D, homocysteine and natural killer cell cytotoxic ity in women with recurrent pregnancy losses. Hum Reprod 35(6):1276–1287. (2020)
§ Two Common MTHFR Gene Polymorphisms (C677T and A1298C) and Fetal Congenital Heart Disease Risk: An Updated Meta-Analysis with Trial Sequential Analysis. Cell Physiol Biochem. 2018 Mar 15;45(6):2483-2496.
§ The methylenetetrahydrofolate reductase 677T-1298C haplotype is a risk factor for acute lymphoblastic leukemia in children. Medicine (Baltimore). 2017 Dec;96(51):e9290.
§ Folate metabolism genetic polymorphisms and meningioma and glioma susceptibility in adults. Oncotarget. 2017 Jul 4;8(34):57265-57277.
§ J Res Med Sci. 2015 Jun; 20 (6):554-62. Factor V Leiden, factor V Cambridge, factor II GA20210, and methylenetetrahydrofolate reductase in cerebral venous and sinus thrombosis: A case-control study.

CLINICAL SIGNIFICANCE

One of folate's jobs is to act as a carrier of individual carbon fragments. This reaction is required for the synthesis of purine-pyrimidines, DNA, RNA and protein methylation. Previous research has shown that low folate levels result in uracil disincorporation during DNA replication, which causes increased double-strand breaks during uracil remnant excision repair.

Because of the importance of the folate pathway and the potentially deleterious effects of hyperhomocysteinemia, the role of MTHFR mutations including C677T and A1298C has been investigated in conditions varying from autism, recurrent pregnancy loss, coronary artery disease, stroke, breast and gastric cancers, and skin conditions such as vitiligo. Additionally, patients with psoriasis have been shown to demonstrate elevated levels of serum homocysteine, a known risk factor for cardiovascular disease.

Folate deficiency, therefore, has also been associated with an increased risk for a number of cancers and other disease risks such as cardiovascular disease, diabetes, birth defects, ischemia, venous thrombosis, hypotonia, leukemia, migraine, schizophrenia, depression, preeclampsia, Alzheimer's disease, birth defects of the heart, Down syndrome and cleft palate.

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MTHFR A1298C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-004-25 RDM Code: 1718917/R
Tests: 25 Reactions: 31
CND Code: W0106010499
REF: GEN-004-50 RDM Code: 2255480/R
Tests: 50 Reactions: 62
CND Code: W0106010199
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-004-25	GEN-004-50	
Mix oligonucleotides and probes	Mix A1298C MTHFR 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-004-25 / COD. GEN-004-50

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 (GEN-004-25), Recombinant DNA for at least 6 analytical sessions (GEN-004-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

PAI-1 4G/5G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-005-25 RDM Code: 2255481/R
Tests: 25 Reactions: 31 x 2
REF: GEN-005-50 RDM Code: 1730063/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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 the polymorphism – 675 4G/5G of the PAI-1 gene by Real-Time PCR technique. Kit optimized for Real-time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The PAI-1 gene encodes the protein PAI-1 (plasminogen activator inhibitor-1), a member of the serine protease inhibitor superfamily (located on chr.7q21.3). The PAI-1 protein inhibits plasminogen activators, including tissue plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA), which catalyze one of the reactions of fibrinolysis by the conversion of plasminogen to plasmin. Following the formation of a fibrin clot, the fibrinolytic system is activated through PAI-1-mediated regulation. The gene encoding PAI-1 (SERPINE1) is located on the short arm of chromosome 7 and contains 9 exons (NM_000602). Genetic polymorphisms (−844 A>G, −675 4G>5G, 43 G>A, 9785 A>G, and 11053 T>G) can vary serum PAI-1 concentrations and its activity resulting in hypofibrinolysis and/or thrombosis. In fact, it has been demonstrated that some polymorphisms of the PAI-1 gene are related to changes in the uteroplacental unit and to a high risk for recurrent spontaneous abortions. An increase in the secretion of PAI-1 by endothelial cells, in fact, causes the formation of thrombi in the spiral arteries. Furthermore, polymorphisms of the PAI-1 gene may also be correlated with the development of preeclampsia, hyper-gestational tension, intrauterine growth restriction or fetal death.

§ Medicina 2024, 60, 521. https://doi.org/10.3390/medicina60040521
§ Int J Mol Sci. 2024 May 11;25(10):5228. doi: 10.3390/ijms25105228.The Etiology of the Thrombotic Phenomena Involved in the Process of Coronary Artery Disease-What Is the Role of Thrombophilic Genes in the Development of This Pathology?
§ Thrombosis Journal (2024) 22:44 https://doi.org/10.1186/s12959-024-00612-9
§ Genetic and non-genetic risk factors for pre-eclampsia: umbrella review of systematic reviews and meta-analyses of observational studies. Ultrasound Obstet Gynecol. 2017 Nov 16. Review.
§ Role of Plasminogen Activator Inhibitor Type 1 in Pathologies of Female Reproductive Diseases. Int J Mol Sci. 2017 Jul 29; 18 (8). pii: E1651. doi: 10.3390/ijms18081651. Review.
§ The Plasminogen Activator Inhibitor 1 4G/5G Polymorphism and the Risk of Alzheimer's Disease. Am J Alzheimers Dis Other Demen. 2017 Sep;32 (6):342-346. 3.

CLINICAL SIGNIFICANCE

Proper functioning of the fibrinolytic system provides vessel elasticity eliminating thrombosis, dismantling the extracellular matrix and causing tissue remodeling, cell adhesion and cell migration.

The rs1799889 gene polymorphism is localized in the promoter region of the PAI-1 gene and consists in the deletion of a guanine residue in nucleotide position -675 with respect to the transcription start site. The PAI-1 -675 4G allele has higher transcriptional activity than the PAI-1 -675 5G allele, and the homozygous -675 4G variant is associated with higher plasma levels of PAI-1 (approximately 25% higher high compared to subjects with 5G/5G genotype). Homozygosity for the 4G allele is therefore associated with an increased thrombotic risk.

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BioMol LABORATORIES

PAI-1 4G/5G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-005-25 RDM Code: 2255481/R
Tests: 25 Reactions: 31 x 2
REF: GEN-005-50 RDM Code: 1730063/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-005-25	GEN-005-50	
Oligonucleotides Mix	Mix PAI-1 5G 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Oligonucleotides Mix	Mix PAI-1 4G 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 755 µl	2 x 755 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1 HOMO 5G	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control 2 HET 4G/5G	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control 3 HOMO 4G	1 x 35 µl	2 x 35 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-005-25 / COD. GEN-005-50

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 (GEN-005-25), Recombinant DNA for at least 6 analytical sessions (GEN-005-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; specific oligonucleotides; 1 SYBR-GREEN/FAM fluorescence channel
RUNNING TIME	150 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (2 min); 1 cycle at 94 °C (5 min); 30 cycles at 95 °C (50 sec) + 60 °C (40 sec) + 72 °C (50 sec) + 1 dissociation cycle from 70 °C to 90°C with 0,2 °C increase.
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; 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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BioMol LABORATORIES

FIBRINOGEN -455 G>A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-006-25 RDM Code: 2255483/R
Tests: 25 Reactions: 31
REF: GEN-006-50 RDM Code: 1735836/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 the -455 G>A polymorphism of the FGB gene (fibrinogen) by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Fibrinogen is a 340 kDa acute phase dimeric glycoprotein synthesized by the liver. It consists of three polypeptides Aα, Bβ and γ encoded by the alpha (FGA), beta (FGB) and gamma (FGG) genes, respectively. Fibrinogen is an important component of the coagulation cascade and an important determinant of blood viscosity and platelet aggregation. Modulates endothelial function and promotes proliferation and migration of smooth muscle cells. Smoking increases the concentration of fibrinogen in the blood and is a significant risk factor for stroke. Recently, obesity has been associated with an elevated plasma fibrinogen level.

CLINICAL SIGNIFICANCE

It is known that elevated plasma fibrinogen levels can be influenced by environmental and genetic factors. It has been reported that some of the 10 or more genetic polymorphisms of the fibrinogen gene that have been studied to date may be involved in the increase in plasma fibrinogen level. Polymorphisms of the β-fibrinogen (FGB) gene including the -455 G/A polymorphism of the FGB gene have been shown to be closely related to increased plasma fibrinogen levels. Several studies have suggested that the FGB -455 G/A polymorphism is associated with elevated plasma fibrinogen concentration which has been shown to have a positive association with the risk of cardiovascular disease (CVD) such as ischemic heart disease, myocardial infarction, ischemic stroke, as well as chronic kidney disease

§ ACS Omega. 2024 Sep 11;9(38):39836-39845. doi: 10.1021/acsomega.4c05204. eCollection 2024 Sep 24. The Impact of Cardiovascular Disease Gene Polymorphism and Interaction with Homocysteine on Deep Vein Thrombosis.
§ Eur J Clin Invest. 2022 Apr;52(4):e13718. doi: 10.1111/eci.13718. Epub 2021 Nov 21. Fibrinogen β chain and FXIII polymorphisms affect fibrin clot properties in acute pulmonary embolism.
§ Mol Biol Rep. 2021 May;48(5):4397-4404. doi: 10.1007/s11033-021-06455-1. Epub 2021 Jun 1. An association between fibrinogen gene polymorphisms and diabetic peripheral neuropathy in young patients with type 1 diabetes
§ Gynecol Endocrinol. 2017; 33 (sup1):32-35. doi: 10.1080/09513590.2017.1404237. Genetic and hemostasiological predictors of IVF pregnancy.
§ Antihypertensive pharmacogenetic effect of fibrinogen-beta variant -455G>A on cardiovascular disease, end-stage renal disease, and mortality: the GenHAT study. Pharmacogenet Genomics. 2009 Jun; 19 (6):415-21.
§ Analysis of the effect of multiple genetic variants of cardiovascular disease risk on insulin concentration variability in healthy adults of the STANISLAS cohort. The role of FGB-455 G/A polymorphism. Atherosclerosis. 2007 Apr; 191 (2):369-76.

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BioMol LABORATORIES

FIBRINOGEN -455 G>A POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-006-25 RDM Code: 2255483/R
Tests: 25 Reactions: 31
REF: GEN-006-50 RDM Code: 1735836/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-006-25	GEN-006-50	
Mix oligonucleotides and probes	Mix -455 G>A FGB 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-006-25 / COD. GEN-006-50

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 (GEN-006-25) Recombinant DNA for at least 6 analytical sessions (GEN-006-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

GPIIIa T1565C POLYMORPHISM (ITGB3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-007-25 RDM Code: 2254597/R
Tests: 25 Reactions: 31
REF: GEN-007-50 RDM Code: 1734432/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 the T1565C GPIIIa (PIA1/A2) polymorphism by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Integrin receptors are heterodimeric cell adhesion proteins that consist of an α and a β subunit. Integrin β3 is essentially expressed on endothelial cells, platelets, osteoclasts and hematopoietic cells and corresponds to the group of integrins that bind to proteins containing the arginine-glycine-aspartic acid (RGD) motif. Glycoprotein IIIa (GPIIIa), also referred to as the beta subunit of the platelet membrane protein GP IIb/IIIa receptor complex, is encoded by the ITGB3 gene and is a surface protein found in various tissues. Exons and introns of the entire ITGB3 gene have been shown to contain many polymorphic regions, one of which has been associated with multiple pathologies.

CLINICAL SIGNIFICANCE

This polymorphism (T1565C, dbSNP ID: rs5918) corresponds to a substitution of the amino acid residue (leucine/proline) in position 33 (PIA1/A2) of the polypeptide chain. This SNP has been reported to be a risk factor for many types of diseases, such as myocardial infarction, ischemic heart disease, type 2 diabetes, asthma, many cancers including non-Hodgkin's lymphoma, colon cancer, ovarian cancer and cancer. renal. It has also been documented that platelets bearing the β3 subunit of the αIIbβ3 integrin with a proline at position 33 are characterized by an increased risk of platelet aggregation and immunogenic properties.

§ Platelet Glycoprotein Receptor Ia-C807T and IIIa-PIA1/PIA2 Genetic Polymorphisms Are Associated With Enhanced Platelet Function in Women With Recurrent Miscarriages Cureus 2023 Oct 27;15(10):e47832. doi: 10.7759/cureus.47832. eCollection 2023 Oct.
§ Thromb J. 2023 Jul 28;21(1):81. doi: 10.1186/s12959-023-00525-z.High prevalence of thrombophilic risk factors in patients with central retinal artery occlusion
§ Cureus. 2023 Oct 27;15(10):e47832. doi: 10.7759/cureus.47832. eCollection 2023 Oct. Platelet Glycoprotein Receptor Ia-C807T and IIIa-PIA1/PIA2 Genetic Polymorphisms Are Associated With Enhanced Platelet Function in Women With Recurrent Miscarriages
§ Genetic variants associated with colorectal brain metastases susceptibility and survival. Pharmacogenomics J. 2017 Jan; 17 (1):29-35. Epub 2015 Dec 22.
§ Common rs5918 (PIA1/A2) polymorphism in the ITGB3 gene and risk of coronary artery disease. Arch Med Sci Atheroscler Dis. 2016 Apr 27; 1 (1):e9-e15. eCollection 2016.
§ Integrin beta-3 genetic variants and risk of venous thromboembolism in colorectal cancer patient. Thromb Res. 2015 Nov; 136 (5):865-9. Epub 2015 Aug 28.

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BioMol LABORATORIES

GPIIIa T1565C POLYMORPHISM (ITGB3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-007-25 RDM Code: 2254597/R
Tests: 25 Reactions: 31
REF: GEN-007-50 RDM Code: 1734432/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-007-25	GEN-007-50	
Mix oligonucleotides and probes	Mix T1565C GPIIIa 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-007-25 / COD. GEN-007-50

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 (GEN-007-25) Recombinant DNA for at least 6 analytical sessions (GEN-007-50).
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

APO-E (CYS112ARG) T3932C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-008-25 RDM Code: 2255489/R
Tests: 25 Reactions: 31
REF: GEN-008-50 RDM Code: 1735881/R
Tests: 50 Reactions: 62
CND Code: W0106010499
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

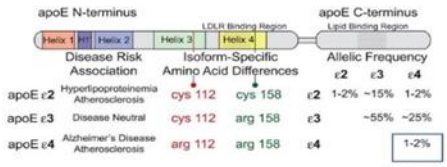
The kit consists of reagents for Real-Time PCR amplification
**reagents for the extraction of genomic DNA are not supplied in the kit*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS.** Detection of T3932C polymorphism (also called C112R, Cys-Arg) of the APO-E gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE e Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The genetic origin of the three variants of the human apolipoprotein E (apoE) protein, known as E2, E3, and E4, was understood in 1981. The underlying genetic variants of these protein isoforms, known as ε2, ε3, and ε4, are allelic forms of the APOE gene, resulting from different haplotypes at the APOE locus (19q13.31). APOE is polymorphic with three main alleles (e2, e3 and e4): APOE-ε2 (cys112, cys158), APOE-ε3 (cys112, arg158) and APOE-ε4 (arg112, arg158). Although these allelic forms differ from each other by only one or two amino acids at positions 112 and 158, these differences alter the structure and function of APOE.



§ Meta-analysis: BMC Neurosci. 2024 Jun 25;25(1):28. Diabetes mellitus and risk of incident dementia in APOE ε4 carriers: an updated meta-analysis
§ Meta-analysis: Behav Brain Res. 2024 Aug 5:471:115123. Cognitive deficits in human ApoE4 knock-in mice: A systematic review and meta-analysis
§ Meta-analysis: J Alzheimers Dis. 2023;93(3):1095-1109. Meta-Analysis of Variations in Association between APOE ε4 and Alzheimer's Disease and Related Dementias Across Hispanic Regions of Origin
§ The APOE E4 Allele Confers Increased Risk of Ischemic Stroke Among Greek Carriers. Adv Clin Exp Med. 2016 May-Jun; 25 (3):471-8.
§ Plasma levels of apolipoprotein E, APOE genotype and risk of dementia and ischemic heart disease: A review Atherosclerosis. 2016 Dec; 255: 145-155.
§ Genetics of healthy aging and longevity. Hum Genet. 2013 Dec; 132 12):1323-38.
§ APOE epsilon 4 allele predicts faster cognitive decline in mild Alzheimer disease. Neurology 70: 1842–1849. Cosentino S, Scarmeas N, Helzner E, Glymour MM, Brandt J, et al. (2008).

CLINICAL SIGNIFICANCE

The combination of the various polymorphisms is responsible for some risk conditions:

- ε2 (rs7412-T, rs429358-T) has an allele frequency of about 7%. This apolipoprotein variant binds poorly to cell surface receptors while E3 and E4 bind well. Individuals with an e2/e2 combination may have an increased risk of early vascular disease. The e2 allele has also been implicated in Parkinson's disease.
- ε3 (rs7412-C, rs429358-T) has an allele frequency of approximately 79%. It is considered the "neutral" Apo E genotype.
- ε4 (rs7412-C, rs429358-C) has an allele frequency of approximately 14%. ε4 has been implicated in atherosclerosis, Alzheimer's disease, decreased cognition, decreased hippocampal volume, time to disease progression in multiple sclerosis, poor outcome after traumatic brain injury, cerebrovascular disease ischemia, sleep apnea, telomere shortening, and impaired neurite outgrowth.

There are two forms of Alzheimer's disease (AD): the rare, early-onset (familial) and the common, late-onset (sporadic) forms. Late-onset AD accounts for approximately 95% of AD cases and is not caused by mutations in single genes. However, the epsilon-4 variant of the apolipoprotein E gene (APOE) has been shown to have deleterious effects on both the lifetime risk and age of onset of the disease.

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BioMol LABORATORIES

APO-E (CYS112ARG) T3932C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-008-25 RDM Code: 2255489/R
Tests: 25 Reactions: 31
REF: GEN-008-50 RDM Code: 1735881/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-008-25	GEN-008-50	
Mix oligonucleotides and probes	Mix T3932C APO-E 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-008-25 / COD. GEN-008-50

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 (GEN-008-25) Recombinant DNA for at least 6 analytical sessions (GEN-008-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

APO-E (ARG158CYS) C4070T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-009-25 RDM Code: 2255495/R
Tests: 25 Reactions: 31
REF: GEN-009-50 RDM Code: 1735882/R
Tests: 50 Reactions: 62
CND Code: W0106010499
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

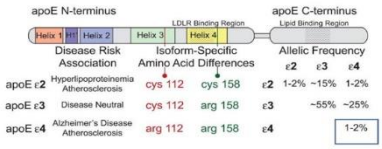
The kit consists of reagents for Real-Time PCR amplification
**reagents for the extraction of genomic DNA are not supplied in the kit*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR -GENETIC VARIANTS.** Detection of C4070T polymorphism (called R158C, ARG158CYS) of the APO-E gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus DX, Agilent AriaDx, Hyris bCUBE e Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The genetic origin of the three variants of the human apolipoprotein E (apoE) protein, known as E2, E3, and E4, was understood in 1981. The underlying genetic variants of these protein isoforms, known as ε2, ε3, and ε4, are allelic forms of the APOE gene, resulting from different haplotypes at the APOE locus (19q13.31). In particular, APOE is polymorphic with three main alleles (e2, e3 and e4): APOE-ε2 (cys112, cys158), APOE-ε3 (cys112, arg158) and APOE-ε4 (arg112, arg158). Although these allelic forms differ from each other by only one or two amino acids at positions 112 and 158, these differences alter the structure and function of APOE.



§ Meta-analysis: BMC Neurosci. 2024 Jun 25;25(1):28. Diabetes mellitus and risk of incident dementia in APOE ε4 carriers: an updated meta-analysis
§ Meta-analysis: Behav Brain Res. 2024 Aug 5:471:115123. Cognitive deficits in human ApoE4 knock-in mice: A systematic review and meta-analysis
§ Meta-analysis: J Alzheimers Dis. 2023;93(3):1095-1109. Meta-Analysis of Variations in Association between APOE ε4 and Alzheimer's Disease and Related Dementias Across Hispanic Regions of Origin
§ The APOE E4 Allele Confers Increased Risk of Ischemic Stroke Among Greek Carriers. Adv Clin Exp Med. 2016 May-Jun; 25 (3):471-8.
§ Plasma levels of apolipoprotein E, APOE genotype and risk of dementia and ischemic heart disease: A review Atherosclerosis. 2016 Dec; 255: 145-155.
§ Genetics of healthy aging and longevity. Hum Genet. 2013 Dec; 132 12):1323-38.
§ APOE epsilon 4 allele predicts faster cognitive decline in mild Alzheimer disease. Neurology 70: 1842–1849. Cosentino S, Scarmeas N, Helzner E, Glymour MM, Brandt J, et al. (2008).

CLINICAL SIGNIFICANCE

The combination of the various polymorphisms is responsible for some risk conditions:
- ε2 (rs7412-T, rs429358-T) has an allele frequency of about 7%. This apolipoprotein variant binds poorly to cell surface receptors while E3 and E4 bind well. Individuals with an e2/e2 combination may have an increased risk of early vascular disease. The e2 allele has also been implicated in Parkinson's disease.
- ε3 (rs7412-C, rs429358-T) has an allele frequency of approximately 79%. It is considered the "neutral" Apo E genotype.
- ε4 (rs7412-C, rs429358-C) has an allele frequency of approximately 14%. ε4 has been implicated in atherosclerosis, Alzheimer's disease, decreased cognition, decreased hippocampal volume, time to disease progression in multiple sclerosis, poor outcome after traumatic brain injury, cerebrovascular disease ischemia, sleep apnea, telomere shortening, and impaired neurite outgrowth.

There are two forms of Alzheimer's disease (AD): the rare, early-onset (familial) and the common, late-onset (sporadic) forms. Late-onset AD accounts for approximately 95% of AD cases and is not caused by mutations in single genes. However, the epsilon-4 variant of the apolipoprotein E gene (APOE) has been shown to have deleterious effects on both the lifetime risk and age of onset of the disease.

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BioMol LABORATORIES

APO-E (ARG158CYS) C4070T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-009-25 RDM Code: 2255495/R
Tests: 25 Reactions: 31
REF: GEN-009-50 RDM Code: 1735882/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-009-25	GEN-009-50	
Mix oligonucleotides and probes	Mix C4070T APO-E 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-009-25 / COD. GEN-009-50

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 (GEN-009-25) Recombinant DNA for at least 6 analytical sessions (GEN-009-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris bCUBE, Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

ANGIOTENSINOGEN (M235T) T9543C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-010-25 RDM Code: 1737722/R
Tests: 25 Reactions: 31
REF: GEN-010-50 RDM Code: 2255499/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 the T9543C polymorphism of the angiotensinogen gene, AGT, by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

The renin-angiotensin-aldosterone system (SRAA) is a hormonal mechanism that regulates blood pressure, circulating plasma volume, arterial muscle tone through various mechanisms and aldosterone secretion; it also plays an important role in the etiology of hypertension.

There are numerous components of this system: renin, prorenin, angiotensin converting enzyme (ACE), angiotensinogen (AGT), angiotensin I and angiotensin II; the latter represents the final effector of the renin-angiotensin system and exerts its effects on the cardiovascular system through binding with specific receptors. The first step in the enzymatic cascade leading to the production of angiotensin II is the conversion of angiotensinogen to angiotensin I by the proteolytic enzyme renin. The second step in the process involves the conversion of angiotensin I to angiotensin II, via a reaction catalysed by ACE. Angiotensin II is the main active peptide of the RAAS which functions through at least four types of receptors. The AGTR1 receptor mediates cardiovascular effects, including vasoconstriction, aldosterone synthesis, vasopressin secretion, vascular smooth muscle cell proliferation, renal blood flow, regulation of renin activity, renal sodium absorption, modulation of sympathetic nervous system activity, and cardiac function.

§ Associations between AGT M235T Polymorphism and Cancer: An Updated Meta-Analysis. J Renin Angiotensin Aldosterone Syst. 2022 Mar 4:2022:7862709 doi: 10.1155/2022/7862709

§ AGT M235T polymorphism and heart failure in a cohort of Tunisian population: diagnostic and prognostic value. Int J Clin Exp Med. 2015 Sep 15;8(9):16346-51.

§ Renin-angiotensin-aldosterone system gene polymorphisms and coronary artery disease: detection of gene-gene and gene-environment interactions. Cell Physiol Biochem. 2012;29(3-4):443-52.

§ Genetic variation in renin predicts the effects of thiazide diuretics. Eur J Clin Invest. 2011 Aug;41(8):828-35.

CLINICAL SIGNIFICANCE

The renin-angiotensin system (SRAA) also exerts local effects on cell proliferation, apoptosis, inflammation and angiogenesis in various tissues. Furthermore, there are data in the literature correlating SRAA with tumor tumorigenesis and angiogenesis. There are genetic polymorphisms in the various components of the RAS that may have clinical relevance. For the AGT gene, located on the chromosome and encoding the angiotensinogen protein, a single nucleotide polymorphism has been described, causing the substitution of methionine to threonine at amino acid residue 235 (M235T). This polymorphism (AGT T9543C) has been associated with hypertension in Caucasian populations and several studies have linked the 235TT genotype with a higher risk of breast cancer. Each of the SRAA-related polymorphisms, alone or in combination, may be related to increased or decreased activity of the SRAA system and thus to the physiological processes controlled by that system. Out come after traumatic brain injury, cerebrovascular disease ischemia, sleep apnea, telomere shortening, and impaired neurite outgrowth.

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BioMol LABORATORIES

ANGIOTENSINOGEN (M235T) T9543C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-010-25 RDM Code: 1737722/R
Tests: 25 Reactions: 31
REF: GEN-010-50 RDM Code: 2255499/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-010-25	GEN-010-50	
Mix oligonucleotides and probes	Mix T9543C AGT 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-010-25 / COD. GEN-010-50

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 (GEN-010-25) Recombinant DNA for at least 6 analytical sessions (GEN-010-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

AGTR1 A1166C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-011-25 RDM Code: 1737734/R
Tests: 25 Reactions: 31
REF: GEN-011-50 RDM Code: 2256357/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 A1166C polymorphism of the gene coding for the type I angiotensin 2 receptor, AGTR1, by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

There are numerous components of this system: renin, prorenin, angiotensin converting enzyme (ACE), angiotensinogen (AGT), angiotensin I and angiotensin II; the latter represents the final effector of the renin-angiotensin system and exerts its effects on the cardiovascular system through binding with specific receptors. The first step in the enzymatic cascade leading to the production of angiotensin II is the conversion of angiotensinogen to angiotensin I by the proteolytic enzyme renin. The second step in the process involves the conversion of angiotensin I to angiotensin II, via a reaction catalysed by ACE. Angiotensin II is the main active peptide of the RAAS which functions through at least four types of receptors. The AGTR1 receptor mediates cardiovascular effects, including vasoconstriction, aldosterone synthesis, vasopressin secretion, vascular smooth muscle cell proliferation, renal blood flow, regulation of renin activity, renal sodium absorption, modulation of sympathetic nervous system activity, and cardiac function.

There are genetic polymorphisms in the various components of the RAS that may have clinical relevance. A single nucleotide polymorphism has been described for the AGTR1 gene, causing the A1166C substitution in the 3'-untranscribed region.

The presence of the C allele correlates with a greater risk of developing arterial hypertension, being subject to cerebral stroke especially in smokers and a greater risk of recurrence of acute myocardial infarction.

CLINICAL SIGNIFICANCE

The renin-angiotensin-aldosterone system (SRAA) is a hormonal mechanism that regulates blood pressure, circulating plasma volume, arterial muscle tone through various mechanisms and aldosterone secretion; it also plays an important role in the etiology of hypertension.

The renin-angiotensin system (SRAA) also exerts local effects on cell proliferation, apoptosis, inflammation and angiogenesis in various tissues. Furthermore, there are data in the literature correlating SRAA with tumor tumorigenesis and angiogenesis.

Each of the SRAA-related polymorphisms, alone or in combination, may be related to increased or decreased activity of the SRAA system and thus to the physiological processes controlled by that system.

§ Meta-Analysis PLoS One. 2024 Jan 2;19(1):e0295626. doi: 10.1371/journal.pone.0295626. eCollection 2024. Impact of the gene polymorphisms in the renin-angiotensin system on cardiomyopathy risk: A meta-analysis
§ PLoS One. 2024 Apr 18;19(4):e0300273. doi: 10.1371/journal.pone.0300273. eCollection 2024. Effect of AGTR1 A1166C genetic polymorphism on coronary artery lesions and mortality in patients with acute myocardial infarction
§ J Renin Angiotensin Aldosterone Syst. 2023 Nov 16:2023:9002021. doi: 10.1155/2023/9002021. eCollection 2023. Genetic Variants Associated with High Susceptibility of Premature Ischemic Stroke
§ Front Biosci (Landmark Ed). 2023 Jul 24;28(7):146. doi: 10.31083/j.fbl2807146.Association between AGTR1 (c.1166 A>C) Polymorphisms and Kidney Injury in Hypertension
§ Association of AGTR1 A1166C and CYP2C9*3 Gene Polymorphisms with the Antihypertensive Effect of Valsartan. Int J Hypertens 2022 Mar 19:2022:7677252. doi: 10.1155/2022/7677252
§ Medicine (Baltimore). 2018 Oct;97(41):e07689. doi: 10.1097/MD.0000000000007689. Association between AGTR1 A1166C polymorphism and the susceptibility to diabetic nephropathy: Evidence from a meta-analysis
§ AGT M235T polymorphism and heart failure in a cohort of Tunisian population: diagnostic and prognostic value. Int J Clin Exp Med. 2015 Sep 15;8(9):16346-51.
§ Renin-angiotensin-aldosterone system gene polymorphisms and coronary artery disease: detection of gene-gene and gene-environment interactions. Cell Physiol Biochem. 2012;29(3-4):443-52.
§ Genetic variation in renin predicts the effects of thiazide diuretics. Eur J Clin Invest. 2011 Aug;41(8):828-35.

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BioMol LABORATORIES

AGTR1 A1166C POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-011-25 RDM Code: 1737734/R
Tests: 25 Reactions: 31
REF: GEN-011-50 RDM Code: 2256357/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-011-25	GEN-011-50	
Mix oligonucleotides and probes	Mix A1166C AGTR1 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase	Mix Real-Time PCR 5X	1 x 155 µl	2 x 155 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-011-25 / COD. GEN-011-50

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 (GEN-011-25) Recombinant DNA for at least 6 analytical sessions (GEN-011-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

FXIII G103T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-012-25 RDM Code: 1737859/R
Tests: 25 Reactions: 31
REF: GEN-012-50 RDM Code: 2164384/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 the G103T polymorphism of the gene coding for FXIII factor, by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Several genetic alterations, in particular those affecting physiological anticoagulants (antithrombin III, proteins C and S) and the procoagulant systems (factor V Leiden, prothrombin, fibrinogen), have been identified as risk factors for venous thromboembolism. Coagulation factor XIII (FXIII) is a transglutaminase that plays an important role in the final stage of blood coagulation, where it catalyzes the formation of covalent bonds between fibrin monomers to produce clot stabilization and resistance to fibrinolysis. Hereditary FXIII deficiency causes severe bleeding and a high risk of miscarriage in women with the homozygous mutation.Although several polymorphisms have been identified in the gene encoding the FXIII A subunit (Val34Leu, Pro564Leu, Val650Ile and Glu651Gln), the Val34Leu polymorphism is the most important functional polymorphism capable of influencing FXIII activation. This polymorphism is a G>T substitution at position 103 in exon 2, three amino acids away from the thrombin cleavage site that occurs in Arg37-Gly38. The release of the activating peptide is accelerated in this genetic condition. The less frequent allele (Leu34) has been described as a protective factor against myocardial infarction and venous thrombosis.

CLINICAL SIGNIFICANCE

Venous thromboembolism (VTE), usually involving deep vein thrombosis, pulmonary embolism, or both, is a complex, multifactorial disorder in which a number of conditions interact and contribute to increased individual risk culminating in the development of venous occlusives. Thrombophilia is commonly defined as a propensity to develop venous thromboembolism based on a hypercoagulable condition attributable to inherited or acquired disorders involving blood clotting or fibrinolysis.

§ J Clin Med. 2024 Nov 15;13(22):6871. doi: 10.3390/jcm13226871. Recurrent Early Pregnancy Loss and Congenital Thrombophilia: A Prospective Study
§ Thrombophilic gene polymorphisms and recurrent pregnancy loss: a systematic review and meta-analysis. J Assist Reprod Genet .2023 Jul;40(7):1533-1558. doi: 10.1007/s10815-023-02823-
§ J Clin Med. 2022 Jun 15;11(12):3454. doi: 10.3390/jcm11123454. Coagulation Factor XIII Val34Leu Polymorphism in the Prediction of Premature Cardiovascular Events-The Results of Two Meta-Analyses
§ Int J Mol Sci. 2021 Feb 1;22(3):1459. doi: 10.3390/ijms22031459. Factor XIII-A in Diseases: Role Beyond Blood Coagulation
§ Effect of factor XIII levels and polymorphisms on the risk of myocardial infarction in young patient. Balogh L, Mol Cell Biochem. 2018 Feb 26.
§ Association of the F13A1 Val34Leu polymorphism and recurrent pregnancy loss: A meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2017 Aug; 215:234-240. doi: 10.1016/j.ejogrb.2017.06.032. Epub 2017 Jun 23.
§ Association of the F13A1 Val34Leu polymorphism and recurrent pregnancy loss: A meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2017 Aug; 215:234-240
§ Genetic association between FXIII and β-fibrinogen genes and women with recurrent spontaneous abortion: a meta- analysis. J Assist Reprod Genet. 2015 May;32(5):817-25. doi: 10.1007/s10815-015-0471-9. Epub 2015 Apr 11.
§ Blood coagulation factor XIII-A subunit Val34Leu polymorphisms and intracerebral hemorrhage risk: A meta-analysis of case-control studies. Br J Neurosurg. 2015;29(5):672-7.
§ Risk for early pregnancy loss by factor XIII Val34Leu: the impact of fibrinogen concentration. J Clin Lab Anal. 2013 Nov;27(6):444-9. doi: 10.1002/jcla.21626.

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BioMol LABORATORIES

FXIII G103T POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-012-25 RDM Code: 1737859/R
Tests: 25 Reactions: 31
REF: GEN-012-50 RDM Code: 2164384/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-012-25	GEN-012-50	
Mix oligonucleotides and probes	Mix Val34Leu FXIII 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-012-25 / COD. GEN-012-50

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 (GEN-012-25) Recombinant DNA for at least 6 analytical sessions (GEN-012-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

CBS 844ins68 POLYMORPHISM (CYSTATHIONINE β- SYNTHETASE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-014-25 Code RDM: 2256364/R
Tests: 25 Reactions: 31
REF: GEN-014-50 Code RDM: 1793904/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 844ins68 polymorphism of the cystathionine β-synthase (CBS) gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Numerous studies have demonstrated that hyperhomocysteinemia (HHcy) is an independent risk factor for cardiovascular and cerebrovascular diseases and that an increase in hypertension and plasma homocysteine (Hcy) has a synergistic effect in causing these diseases.Homocysteine is an important intermediate product in the metabolism of methionine and cysteine. The enzymes 5,10-methylenetetrahydrofolate reductase (MTHFR) and cystathionine β-synthetase (CBS) are key enzymes in homocysteine metabolic pathways. The catalytic activity of the MTHFR enzyme creates an irreversible reduction of 5,10-methylenetetrahydrofolate (THF) which is converted to 5-methyl-THF during this process. 5-methyl-THF is the most abundant circulating form of folic acid, serving as a methyl donor for the remethylation of homocysteine to methionine, a reaction (catalyzed by methionine synthase) for which vitamin B12 is required. The cystathionine β - synthetase (CBS) gene is located on chromosome 21q22.3 and codes for an enzyme that participates in the folate pathway and catalyzes the transsulfuration of homocysteine and serine to cystathionine as a precursor of cysteine.

CLINICAL SIGNIFICANCE

The CBS gene has many mutations and polymorphisms.
The 844ins68 polymorphism at position 844 in the CBS gene generates an alternative splice site that disrupts the protein, resulting in decreased functional activity of CBS. The deficiency of this enzyme causes an increase in homocysteine in the blood and homocystinuria.
Furthermore, the T833C mutation generating a restriction site of BsrI (CBS I278T) has been shown to segregate in cis with the 844ins68 polymorphism in exon 8.
Significant interactions were observed between the polymorphisms of MTHFR C677T, MTHFR A1298C and the CBS 844ins68/T833C haplotype for Hcy levels. In fact, heterozygotes show higher homocysteine values.
Interactions between the various polymorphisms may therefore influence serum Hcy levels, where multiple heterozygosity could be a risk factor for vaso-occlusive episodes.
The 844ins68 polymorphism has also been associated with other diseases, including neural tube defects and cancer.

§ Folate gene polymorphisms CBS 844ins68 and RFC1 A80G and risk of Down syndrome offspring in young Iranian women: A cross-sectional study. Int J Reprod Biomed. 2024 Mar 25;22(2):127-138. doi: 10.18502/ijrm.v22i2.15709

§ MTR, MTRR and CBS Gene Polymorphisms in Recurrent Miscarriages: A Case Control Study from North India. J Hum Reprod Sci 2022 Apr-Jun;15(2):191-196. doi: 10.4103/jhrs.jhrs_186_21.

§ Interactions among methylenetetrahydrofolate reductase (MTHFR) and cystathionine β-synthase (CBS) polymorphisms - a cross-sectional study: multiple heterozygosis as a risk factor for higher homocysteine levels and vaso-occlusive episodes. Genet Mol Res. 2017 Feb 23;16(1). doi: 10.4238/gmr16019374.

§ Association between 11 genetic polymorphisms in folate-metabolising genes and head and neck cancer risk. Eur J Cancer. 2012 Jul;48(10):1525-31. doi: 10.1016/j.ejca.2011.09.025. Epub 2011 Nov 1.

§ The 844ins68 polymorphism of the cystathionine beta-synthase gene is associated with schizophrenia. Psychiatry Res. 2009 Dec 30;170(2-3):168-71. doi: 10.1016/j.psychres.2008.07.007. Epub 2009 Nov 10.

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BioMol LABORATORIES

CBS 844ins68 POLYMORPHISM (CYSTATHIONINE β- SYNTHETASE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-014-25 Code RDM: 2256364/R
Tests: 25 Reactions: 31
REF: GEN-014-50 Code RDM: 1793904/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-014-25	GEN-014-50	
Mix oligonucleotides	Mix CBS 844ins68 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1 HOMOZYGOUS D/D	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2 HETEROZYGOUS I/D	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3 HOMOZYGOUS I/I	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-014-25 / COD. GEN-014-50

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 (GEN-014-25) Recombinant DNA for at least 6 analytical sessions (GEN-014-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Hyris Bcube, Hyris bCUBE3 con Hyris bAPP
TECHNOLOGY	Real-time PCR; specific oligonucleotides; 1 SYBR-GREEN/FAM fluorescence channel
RUNNING TIME	150 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (2 min); 1 cycle at 94 °C (5 min); 30 cycles at 95 °C (50 sec) + 60 °C (40 sec) + 72 °C (50 sec) + 1 dissociation cycle from 70°C to 90°C with 0,2 °C increments.
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; 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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BioMol LABORATORIES

FV H1299R POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-015-25 Code RDM: 1744019/R
Tests: 25 Reactions: 31 x 2
REF: GEN-015-50 Code RDM: 2256370/R
Tests: 50 Reactions: 62 x 2
Code CND: W0106010499
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 A4070G polymorphism of the FV (H1299R) gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Venous thromboembolism has a strong genetic basis, with approximately 50-60% of the variance in incidence attributable to genetic effects. Some genetic susceptibility variants that contribute to risk have been identified in candidate genes, such as factor V Leiden and prothrombin.
Factor V 1691 G→A (FV Leiden, FVL) is the most common genetic risk factor for hereditary thrombophilia resulting from a G→A nucleotide residue substitution at position 1691, causing the Arg→Glu substitution of amino acid 506 (R506Q). In addition to the FVL mutation, a substitution of a nucleotide residue A to G at residue 4070 of exon 13 of the factor V gene results in the H-R 1299 substitution of the protein and has been described as an R2 polymorphism. The R2 variation has been shown to affect plasma FV concentration and its association causes mild resistance to activated protein C. The polymorphism has been associated with an increased risk of thrombosis alone or in association in heterozygosity with the FV G1691A mutation.

CLINICAL SIGNIFICANCE

Venous thromboembolism (VTE), usually involving deep vein thrombosis, pulmonary embolism, or both, is a complex, multifactorial disorder in which a number of conditions interact and contribute to an individual's risk, culminating in the development of venous occlusives. Thrombophilia is commonly defined as a propensity to develop venous thromboembolism based on a hypercoagulable condition attributable to inherited or acquired disorders involving blood coagulation or fibrinolysis.

Among the acquired risk factors, some can cause an increase in hypercoagulability, for example cancer, surgery, trauma or fractures, immobilization, pregnancy and the postpartum period, long-distance travel, hospitalization, catheterization and acute infection and others may be considered as predisposing conditions, such as age, sex, race/ethnicity, body mass index and obesity, use of oral contraceptive or hormone therapy , corticosteroids or statins, diet, physical activity, sedentary time and air pollution.

§ A Systematic Review and Meta-Analysis of the Association between the FV H1299R Variant and the Risk of Recurrent Pregnancy Loss. Biology (Basel)2022 Nov 3;11(11):1608. doi: 10.3390/biology11111608

§ Genotyping analysis of the factor V Nara mutation, Hong Kong mutation, and 16 single-nucleotide polymorphisms, including the R2 haplotype, and the involvement of factor V activity in patients with recurrent miscarriage. Blood Coagul Fibrinolysis. 2017 Jun; 28(4):323-328.

§ Genetic modulation of the FV (Leiden)/normal FV ratio and risk of venous thrombosis in factor V Leiden heterozygotes. J Thromb Haemost. 2012 Jan;10(1):73-80.

§ Impaired APC cofactor activity of factor V plays a major role in the APC resistance associated with the factor V Leiden (R506Q) and R2 (H1299R) mutations. Blood. 2004 Jun 1;103(11):4173-9.

§ Multicentrum Study: Blood. 1999 Nov 1;94(9):3062-6. Coinheritance of the HR2 haplotype in the factor V gene confers an increased risk of venous thromboembolism to carriers of factor V R506Q (factor V Leiden)

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BioMol LABORATORIES

FV H1299R POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-015-25 Codice RDM: 1744019/R
Test: 25 Reazioni: 31 x 2
REF: GEN-015-50 Codice RDM: 2256370/R
Test: 50 Reazioni: 62 x 2
Codice CND: W0106010499
Produttore: 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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-015-25	GEN-015-50	
Oligonucleotides Mix	Mix A FV H1299R 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Oligonucleotides Mix	Mix B FV H1299R 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 775 µl	2 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 35 µl	2 x 35 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-015-25 / COD. GEN-015-50

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 (GEN-015-25) Recombinant DNA for at least 6 analytical sessions (GEN-015-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; specific oligonucleotides; 1 SYBR-GREEN/FAM fluorescence channel
RUNNING TIME	150 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (2 min); 1 cycle at 94 °C (5 min); 30 cycles at 95 °C (50 sec) + 60 °C (40 sec) + 72 °C (50 sec) + 1 dissociation cycle from 70°C to 90°C with 0,2 °C increments.
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; 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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BioMol LABORATORIES

APO B-100 G10580A (R3500Q) MUTATION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-016-25 RDM Code: 2256375/R
Tests: 25 Reactions: 31
REF: GEN-016-50 RDM Code: 1791315/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 G10580A (R3500Q/R3527Q) polymorphism of the APO-B 100 gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

One of the forms of familial hypercholesterolemia is familial apolipoprotein B-100 deficiency (FDB-Familial defective apolipoprotein B100), an autosomal dominant hereditary disease caused by mutations in the apo B gene. The gene contains 29 exons and 28 introns with a total length of 43 kb and is located on the short arm of chromosome 2. Apo B is a large amphipathic glycoprotein with two isoforms: apo B-100, which is synthesized in hepatocytes, and apo B-48, which is synthesized in the cells of the small intestine. Apolipoprotein B-100 (Apo B) is a protein involved in lipid metabolism and is the main constituent protein of very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL). The Apo B-100-cholesterol complex is recognized by LDL membrane receptors and then reabsorbed into cells. Four mutations in the APO B gene, R3480P, R3500Q (new nomenclature R3527Q), R3500W and R3531C are responsible for FDB by reducing the binding of LDL particles to the LDL receptor. The R3500Q mutation (rs5742904) was the first described and is the most widespread. The prevalence of FDB has been estimated to be approximately 1/500 in North America, while in Europe it appears to be highest in northwestern Switzerland (1/114), eastern France, and southern Germany and lower in Italy and Spain. The Apo B-100 protein with the mutation remains free in the blood, causing hypercholesterolemia and increased risk of the formation of obstructive plaques, constituting an important risk factor for the development of early atherosclerosis and coronary artery deficiencies (coronary artery disease, CAD)

CLINICAL SIGNIFICANCE

Familial hypercholesterolemia is a genetic pathology characterized by high concentrations of cholesterol in the plasma, transported by low-density lipoproteins (LDL). Under normal conditions, LDL particles are removed from the plasma approximately 2.5 days after their production through their binding to the LDL receptor, LDLR.
In Familial Hypercholesterolemia there is a persistence of LDL cholesterol in the blood and its deposition in the walls of the arteries (mainly coronary arteries, aorta and heart valves), in the tendons and in the skin. The main consequence of this pathology is premature atherosclerosis, responsible for myocardial infarction and angina pectoris which appear at variable ages in relation to the type of genetic defect.

§ Metabolites. 2024 Feb 12;14(2):123. doi: 10.3390/metabo14020123. ApoB100 and Atherosclerosis: What's New in the 21st Century?
§ Int J Mol Sci. 2023 Apr 21;24(8):7635. doi: 10.3390/ijms24087635. Identification and Functional Analysis of APOB Variants in a Cohort of Hypercholesterolemic Patients
§ J Intern Med. 2023 Feb;293(2):144-165. doi: 10.1111/joim.13577. Epub 2022 Oct 17. Genetic and molecular architecture of familial hypercholesterolemia
§ Familial defective apolipoprotein B-100: A review. J Clin Lipidol. 2016 Nov - Dec; 10 (6):1297-1302. doi: 10.1016/j.jacl.2016.09.009. Epub 2016 Sep 22.
§ Decreased bone mineral density in subjects carrying familial defective apolipoprotein B-100. J Clin Endocrinol Metab. 2013 Dec; 98 (12):E1999-2005. doi: 10.1210/jc.2013-2471. Epub 2013 Oct 8.
§ Genetic cardiovascular risk factors and age-related macular degeneration. Acta Ophthalmol. 2011 Jun; 89 (4):335-8. doi: 10.1111/j.1755-3768.2009. 01697.x Epub 2009 Oct 23.

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BioMol LABORATORIES

APO B-100 G10580A (R3500Q) MUTATION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-016-25 RDM Code: 2256375/R
Tests: 25 Reactions: 31
REF: GEN-016-50 RDM Code: 1791315/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-016-25	GEN-016-50	
Mix oligonucleotides and probes	Mix G10580A APO-B 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-016-25 / COD. GEN-016-50

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 (GEN-016-25) Recombinant DNA for at least 6 analytical sessions (GEN-016-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

HFE C282Y MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-017-25 RDM Code: 2256871/R
Tests: 25 Reactions: 31
REF: GEN-017-50 RDM Code: 2142453/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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 C282Y mutation (G>A; TGC>TAC; Cys>Tyr) of the HFE gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Type 1 hemochromatosis: it is an autosomal recessive disease with incomplete penetrance that causes an excessive accumulation of iron in the tissues, responsible for chronic liver disease, fibrosis, cirrhosis and an increase in cardiovascular phenomena such as coronary heart disease (CHD). The most common form is caused by a homozygous C282Y (G>A, rs1800562) mutation in exon 4 of the HFE gene. In exon 2 of the HFE gene, however, there is a further variant, H63D (C>G, rs1799945) widely studied together with the C282Y variant in cases of iron overload, as metagenetic analyzes have shown that this allele is heterozygous with the C282Y allele might in some populations increase the risk of coronary heart disease. Adjacent to the H63 residue, the S65C variant (rs1800730) was also identified, which in the form of the C282Y/S65C genotype can produce a mild HH phenotype.
Type 2 hemochromatosis: rarer than the previous one, it is distinguished in two forms, both transmitted in an autosomal recessive way: type 2a due to mutations in the hemojuvelin gene and type 2b caused by mutations in the hepcidin gene (HAMP).
Type 3 hemochromatosis: determined by mutations in the transferrin receptor gene (TFR2).
Type 4 hemochromatosis: due to mutations in the ferroportin gene (SLC40A1 or FPN1), transmitted in an autosomal dominant manner.

CLINICAL SIGNIFICANCE

Hemochromatosis is a set of hereditary diseases characterized by the development of a progressive accumulation of iron in the body. Five genetically distinct forms of hemochromatosis are recognized, with varying frequency and severity.

§ *Muhammad JS, Islam N, Mehboobali N, Iqbal K, Azam I, Iqbal MP. Lack of association of HFE gene polymorphism with high body iron status in Pakistani patients with type 2 diabetes mellitus. J Pak Med Assoc. 2021 Feb; 71(2(B)):608-613. doi: 10.47391/JPMA.563.*
§ *Ogouma-Aworet L, Rabes JP, de Mazancourt P. A Simple RFLP-Based Method for HFE Gene Multiplex Amplification and Determination of Hereditary Hemochromatosis-Causing Mutation C282Y and H63D Variant with Highly Sensitive Determination of Contamination. Biomed Res Int. 2020 Dec 28; 2020:9396318. doi: 10.1155/2020/9396318. eCollection 2020.PMID: 33457423*
§ *Lian J, Xu L, Huang Y, Le Y, Jiang D, Yang X, Xu W, Huang X, Dong C, Ye M, Zhou J, Duan S. Meta-analyses of HFE variants in coronary heart disease. Gene.2013 Sep 15; 527(1):167-73. doi: 10.1016/j.gene.2013.06.034.*
§ *Hanson E. H., Imperatore G., Burke W. HFE Gene and Hereditary Hemochromatosis: A HuGE Review. American Journal of Epidemiology.2001; 154(3):193–206. doi: 10.1093/aje/154.3.193.*
§ *Feder J. N., Gnirke A., Thomas W., et al. A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. Nature genetics. 1996; 13 (4):399–408.*

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BioMol LABORATORIES

HFE C282Y MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-017-25 RDM Code: 2256871/R
Tests: 25 Reactions: 31
REF: GEN-017-50 RDM Code: 2142453/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-017-25	GEN-017-50	
Mix oligonucleotides and probes	Mix HFE C282Y 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22µl	2 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22µl	2 x 22µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-017-25 / COD. GEN-017-50

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 (GEN-017-25) Recombinant DNA for at least 6 analytical sessions (GEN-017-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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ED.1 REV.0 of 01/10/2024

BioMol LABORATORIES

HFE H63D MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-018-25 RDM Code: 257789/R
Tests: 25 Reactions: 31
REF: GEN-018-50 RDM Code: 2142452/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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 PCR QUALITATIVE-GENETIC VARIANTS.** Detection of H63D mutation (C>G; CAT>GAT, His>Asp) of the HFE gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Type 1 hemochromatosis: it is an autosomal recessive disease with incomplete penetrance that causes an excessive accumulation of iron in the tissues, responsible for chronic liver disease, fibrosis, cirrhosis and an increase in cardiovascular phenomena such as coronary heart disease (CHD). The most common form is caused by a homozygous C282Y (G>A, rs1800562) mutation in exon 4 of the HFE gene. In exon 2 of the HFE gene, however, there is a further variant, H63D (C>G, rs1799945) widely studied together with the C282Y variant in cases of iron overload, as metagenetic analyzes have shown that this allele is heterozygous with the C282Y allele might in some populations increase the risk of coronary heart disease. Adjacent to the H63 residue, the S65C variant (rs1800730) was also identified, which in the form of the C282Y/S65C genotype can produce a mild HH phenotype.
Type 2 hemochromatosis: rarer than the previous one, it is distinguished in two forms, both transmitted in an autosomal recessive way: type 2a due to mutations in the hemojuvelin gene and type 2b caused by mutations in the hepcidin gene (HAMP).
Type 3 hemochromatosis: determined by mutations in the transferrin receptor gene (TFR2).
Type 4 hemochromatosis: due to mutations in the ferroportin gene (SLC40A1 or FPN1), transmitted in an autosomal dominant manner.

CLINICAL SIGNIFICANCE

Hemochromatosis is a set of hereditary diseases characterized by the development of a progressive accumulation of iron in the body. Five genetically distinct forms of hemochromatosis are recognized, with varying frequency and severity.

§ *Case Reports Cureus. 2024 Dec 24;16(12):e76335. doi: 10.7759/cureus.76335. eCollection 2024 Dec. Iron Overload in Histidine-to-Aspartic Acid Substitution at 63 (H63D) Gene Heterozygous Hereditary Hemochromatosis With Erythrocytosis: A Case Report.*
§ *Muhammad JS, Islam N, Mehboobali N, Iqbal K, Azam I, Iqbal MP. Lack of association of HFE gene polymorphism with high body iron status in Pakistani patients with type 2 diabetes mellitus. J Pak Med Assoc. 2021 Feb; 71(2(B)):608-613. doi: 10.47391/JPMA.563.*
§ *Ogouma-Aworet L, Rabes JP, de Mazancourt P. A Simple RFLP-Based Method for HFE Gene Multiplex Amplification and Determination of Hereditary Hemochromatosis-Causing Mutation C282Y and H63D Variant with Highly Sensitive Determination of Contamination. Biomed Res Int. 2020 Dec 28; 2020:9396318. doi: 10.1155/2020/9396318. eCollection 2020.PMID: 33457423*
§ *Lian J, Xu L, Huang Y, Le Y, Jiang D, Yang X, Xu W, Huang X, Dong C, Ye M, Zhou J, Duan S. Meta-analyses of HFE variants in coronary heart disease. Gene.2013 Sep 15; 527(1):167-73. doi: 10.1016/j.gene.2013.06.034.*
§ *Hanson E. H., Imperatore G., Burke W. HFE Gene and Hereditary Hemochromatosis: A HuGE Review. American Journal of Epidemiology.2001; 154(3):193–206. doi: 10.1093/aje/154.3.193.*
§ *Feder J. N., Gnirke A., Thomas W., et al. A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. Nature genetics. 1996; 13 (4):399–408.*

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BioMol LABORATORIES

HFE H63D MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-018-25 RDM Code: 257789/R
Tests: 25 Reactions: 31
REF: GEN-018-50 RDM Code: 2142452/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-018-25	GEN-018-50	
Mix oligonucleotides and probes	Mix HFE H63D 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22µl	2 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22µl	2 x 22µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-018-25 / COD. GEN-018-50

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 (GEN-018-25) Recombinant DNA for at least 6 analytical sessions (GEN-018-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

HFE S65C MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-019-25 RDM Code: 2257822/R
Tests: 25 Reactions: 31
REF: GEN-019-50 RDM Code: 2142454/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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 PCR QUALITATIVE-GENETIC VARIANTS.** Detection of S65C mutation (c.193 A>T; AGT>TGT; Ser65Cys) of the HFE gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Type 1 hemochromatosis: it is an autosomal recessive disease with incomplete penetrance that causes an excessive accumulation of iron in the tissues, responsible for chronic liver disease, fibrosis, cirrhosis and an increase in cardiovascular phenomena such as coronary heart disease (CHD). The most common form is caused by a homozygous C282Y (G>A, rs1800562) mutation in exon 4 of the HFE gene. In exon 2 of the HFE gene, however, there is a further variant, H63D (C>G, rs1799945) widely studied together with the C282Y variant in cases of iron overload, as metagenetic analyzes have shown that this allele is heterozygous with the C282Y allele might in some populations increase the risk of coronary heart disease. Adjacent to the H63 residue, the S65C variant (rs1800730) was also identified, which in the form of the C282Y/S65C genotype can produce a mild HH phenotype.
Type 2 hemochromatosis: rarer than the previous one, it is distinguished in two forms, both transmitted in an autosomal recessive way: type 2a due to mutations in the hemojuvelin gene and type 2b caused by mutations in the hepcidin gene (HAMP).
Type 3 hemochromatosis: determined by mutations in the transferrin receptor gene (TFR2);
Type 4 hemochromatosis: due to mutations in the ferroportin gene (SLC40A1 or FPN1), transmitted in an autosomal dominant manner.

CLINICAL SIGNIFICANCE

Hemochromatosis is a set of hereditary diseases characterized by the development of a progressive accumulation of iron in the body. Five genetically distinct forms of hemochromatosis are recognized, with varying frequency and severity.

§ *Case Reports Cureus. 2024 Dec 24;16(12):e76335. doi: 10.7759/cureus.76335. eCollection 2024 Dec. Iron Overload in Histidine-to-Aspartic Acid Substitution at 63 (H63D) Gene Heterozygous Hereditary Hemochromatosis With Erythrocytosis: A Case Report.*

§ *Muhammad JS, Islam N, Mehboobali N, Iqbal K, Azam I, Iqbal MP. Lack of association of HFE gene polymorphism with high body iron status in Pakistani patients with type 2 diabetes mellitus. J Pak Med Assoc. 2021 Feb; 71(2(B)):608-613. doi: 10.47391/JPMA.563.*

§ *Ogouma-Aworet L, Rabes JP, de Mazancourt P. A Simple RFLP-Based Method for HFE Gene Multiplex Amplification and Determination of Hereditary Hemochromatosis-Causing Mutation C282Y and H63D Variant with Highly Sensitive Determination of Contamination. Biomed Res Int. 2020 Dec 28; 2020:9396318. doi: 10.1155/2020/9396318. eCollection 2020.PMID: 33457423*

§ *Lian J, Xu L, Huang Y, Le Y, Jiang D, Yang X, Xu W, Huang X, Dong C, Ye M, Zhou J, Duan S. Meta-analyses of HFE variants in coronary heart disease. Gene.2013 Sep 15; 527(1):167-73. doi: 10.1016/j.gene.2013.06.034.*

§ *Hanson E. H., Imperatore G., Burke W. HFE Gene and Hereditary Hemochromatosis: A HuGE Review. American Journal of Epidemiology.2001; 154(3):193–206. doi: 10.1093/aje/154.3.193.*

§ *Feder J. N., Gnirke A., Thomas W., et al. A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. Nature genetics. 1996; 13 (4):399–408.*

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BioMol LABORATORIES

HFE S65C MUTATION (HEMOCHROMATOSIS)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-019-25 RDM Code: 2257822/R
Tests: 25 Reactions: 31
REF: GEN-019-50 RDM Code: 2142454/R
Tests: 50 Reactions: 62
CND Code: W0106010105
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-019-25	GEN-019-50	
Mix oligonucleotides and probes	Mix HFE S65C 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-019-25 / COD. GEN-019-50

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 (GEN-019-25) Recombinant DNA for at least 6 analytical sessions (GEN-019-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

POLYMORPHISM T307A (A919G) (FSH Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-020-25
RDM Code: 1730069/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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 T307A (A919G) polymorphism of the FSHR gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

The physiological action of the hormone FSH depends on its receptor activation (FSHR). The FSH receptor is expressed in ovarian granulosa cells and on Sertoli cells and is encoded by the FSHR gene located on chromosome 2p21-p16. Inactivating mutations of the FSHR gene have been described, but also multiple gene polymorphisms (about 900). The most common polymorphisms are rs6165 and rs6166, which correspond to FSHR substitutions Thr307Ala and Asn680Ser respectively. Both polymorphisms are present in the same exon 10 and have been found to be in «linkage disequilibrium». The two isoforms are considered variants of the FSH glycosylation/phosphorylation sites; Asn680, in fact, represents a consensus sequence for glycosylation while Thr307 represents a potential phosphorylation site. Variants of post-translational modification sites can influence the transduction of the ligand-dependent signal. In assisted reproductive technology programmes, women's ovulatory response to stimulation with exogenous follicular hormone (FSH) shows an inter-individual variability. The ovarian response to intense gonadotropin stimulation is difficult to predict, but it is known that a deficient ovarian response results in insufficient stimulation and cycle cancellation and vice versa, a hyper-response can potentially induce a serious and dangerous complication such as ovarian hyperstimulation syndrome (OHSS). The rs6165 and rs6166 polymorphisms have been extensively studied and it has been shown that the FSHR genotype related to these SNPs is predictive of ovarian responsiveness to treatment with FSH. The analysis of the FSH receptor genotype allows, therefore, to modulate individually the administration of FSH and thus increase the effectiveness and safety of the therapy. In addition, many scientific papers have recently been published on the correlation between FSH receptor polymorphisms (FSHR) and the risks of a non-physiological spermatogenesis correlated to a functional deficit in the process of spermatogenesis and therefore to a possible concause in the phenomena of oligospermia or azoospermia.

CLINICAL SIGNIFICANCE

The follicle-stimulating hormone (FSH) performs its ovarian function through important effects on granulosa cell proliferation, egg cell maturation and estrogen synthesis. Multiple studies have shown that a decrease in FSH concentration followed by a high estrogen concentration plays an important role in the selection of the dominant follicle. In humans, on the other hand, FSH is important for the regulation of metabolic functions of Sertoli cells, an essential stage for maintaining a normal spermatogenesis from a qualitative and quantitative point of view.

§ Multicenter Study Reprod Sci. 2024 Nov;31(11):3560-3568. The Additive Effect of Combinations of FSH Receptor Gene Variants in Ovarian Response to Stimulation
§ J Clin Med. 2024 Apr 13;13(8):2261. doi: 10.3390/jcm13082261. Application of Biomarkers in Obese Infertile Women: A Genetic Tool for a Personalized Treatment
§ J Reprod Infertil. 2023 Oct-Dec;24(4):240-247. The Effect of FSHR (G2039A) Polymorphism on Müllerian Duct Development and Hormonal Profile of Women with Primary Amenorrhea
§ J Ovarian Res. 2023 Sep 1;16(1):183. doi: 10.1186/s13048-023-01238-7. Polymorphisms in FSHR modulating susceptibility to polycystic ovary syndrome: an updated meta-analysis
§ Multicenter Study Genes (Basel). 2023 Jun 15;14(6):1269. doi: 10.3390/genes14061269. Genetic Variants of Gonadotropins and Their Receptors Could Influence Controlled Ovarian Stimulation: IVF Data from a Prospective Multicenter Study
§ Int J Mol Sci. 2023 Jan 5;24(2):1080. doi: 10.3390/ijms24021080. The Polymorphism Asn680Ser on the FSH Receptor and Abnormal Ovarian Response in Patients with Normal Values of AMH and AFC
§ Front Endocrinol (Lausanne). 2022 Feb 1:12:797365. doi: 10.3389/fendo.2021.797365. eCollection 2021. Effect of Genetic Variants of Gonadotropins and Their Receptors on Ovarian Stimulation Outcomes: A Delphi Consensus
§ The susceptibility of FSHB -211G > T and FSHR G-29A, 919A > G, 2039A > G polymorphisms to men infertility: an association study and meta-analysis. BMC Med Genet. 2017 Aug 1; 18(1):81.
§ FSH receptor gene p. Thr307Ala and p. Asn680Ser polymorphisms are associated with the risk of polycystic ovary syndrome. J Assist Reprod Genet. 2017 Aug; 34(8):1087-1093. Epub 2017 May 25.
§ Follicle-Stimulating Hormone Receptor (FSHR): A Promising Tool in Oncology? Mol Diagn Ther. 2016 Dec; 20(6):523-530. Review.

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BioMol LABORATORIES

POLYMORPHISM T307A (A919G) (FSH Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-020-25
RDM Code: 1730069/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		GEN-020-25	
Mix oligonucleotides and probes	Mix T307A FSHR 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-020-25

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
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

POLYMORPHISM N680S (A2039G) FSHR (FSH Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-021-25
RDM Code: 1730074/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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 N680S (A2039G) polymorphism of the FSHR gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

In assisted reproductive technology programs, the ovulatory response of women to exogenous follicular hormone (FSH) stimulation exhibits interindividual variability. It is difficult to predict the ovarian response to intense gonadotropin stimulation, but it is known that a deficient ovarian response results in under stimulation and cycle cancellation and conversely, an overresponse can potentially lead to a serious and life-threatening complication such as ovarian hyperstimulation (OHSS). The analysis of the genotype of the FSH receptor therefore allows to individually modulate the administration of FSH and therefore to increase the efficacy and safety of the therapy. Several studies support a role for the FSHR rs6166 (c.2039A>G, p. Asn680Ser) variant as a prognostic indicator of ovarian response to FSH stimulation. The Ser/Ser variant was associated with higher basal levels of FSH, a higher total dose of gonadotropins required during ovarian stimulation, lower peak estradiol levels and fewer retrieved oocytes. Collectively these studies suggest that the Ser/Ser variant is associated with a reduced sensitivity of the FSHR to exogenous FSH. A randomized controlled trial (RCT) demonstrated that this reduced sensitivity of the FSHR may be overcome by increasing the FSH dose. Furthermore, many scientific works have recently been published on the correlation between FSH receptor polymorphisms (FSHR) and the risks of non-physiological spermatogenesis, correlating them with a functional deficit in the spermatogenesis process and therefore with a possible contributing cause in the phenomena of oligospermia or azoospermia.

CLINICAL SIGNIFICANCE

Follicle Stimulating Hormone (FSH) performs its ovarian function through important effects on granulosa cell proliferation, oocyte maturation and estrogen synthesis. Multiple studies have shown that a decrease in FSH concentration followed by a high concentration of estrogen plays an important role in the selection of the dominant follicle. In humans, on the other hand, FSH is important for the regulation of the metabolic functions of Sertoli cells, an essential stage for the maintenance of normal spermatogenesis from a qualitative and quantitative point of view.The physiological action of the FSH hormone depends on the activation of its receptor (FSHR). The FSH receptor is expressed in ovarian granulosa cells and Sertoli cells and is encoded by the FSHR gene located on chromosome 2p21-p16. Inactivating mutations of the FSHR gene have been described, but also multiple gene polymorphisms (about 900). The most common are the rs6165 and rs6166 polymorphisms, which correspond to the FSHR substitutions Thr307Ala and Asn680Ser respectively. Both polymorphisms are present in the same exon 10 and were found to be in «linkage disequilibrium». The two isoforms are considered variants of the glycosylation/phosphorylation sites of the FSH receptor; Indeed, Asn680 represents a consensus sequence for glycosylation while Thr307 represents a potential site of phosphorylation. Variants of post-translational modification sites can affect ligand-dependent signal transduction.

§ J Clin Med. 2024 Apr 13;13(8):2261. doi: 10.3390/jcm13082261. Application of Biomarkers in Obese Infertile Women: A Genetic Tool for a Personalized Treatment
§ J Reprod Infertil. 2023 Oct-Dec;24(4):240-247. The Effect of FSHR (G2039A) Polymorphism on Müllerian Duct Development and Hormonal Profile of Women with Primary Amenorrhea
§ J Ovarian Res. 2023 Sep 1;16(1):183. doi: 10.1186/s13048-023-01238-7. Polymorphisms in FSHR modulating susceptibility to polycystic ovary syndrome: an updated meta-analysis
§ Multicenter Study Genes (Basel). 2023 Jun 15;14(6):1269. doi: 10.3390/genes14061269. Genetic Variants of Gonadotropins and Their Receptors Could Influence Controlled Ovarian Stimulation: IVF Data from a Prospective Multicenter Study
§ Int J Mol Sci. 2023 Jan 5;24(2):1080. doi: 10.3390/ijms24021080. The Polymorphism Asn680Ser on the FSH Receptor and Abnormal Ovarian Response in Patients with Normal Values of AMH and AFC
§ Front Endocrinol (Lausanne). 2022 Feb 1:12:797365. doi: 10.3389/fendo.2021.797365. eCollection 2021. Effect of Genetic Variants of Gonadotropins and Their Receptors on Ovarian Stimulation Outcomes: A Delphi Consensus
§ The susceptibility of FSHB -211G > T and FSHR G-29A, 919A > G, 2039A > G polymorphisms to men infertility: an association study and meta-analysis. BMC Med Genet. 2017 Aug 1; 18(1):81.
§ FSH receptor gene p. Thr307Ala and p. Asn680Ser polymorphisms are associated with the risk of polycystic ovary syndrome. J Assist Reprod Genet. 2017 Aug; 34(8):1087-1093. Epub 2017 May 25.
§ Follicle-Stimulating Hormone Receptor (FSHR): A Promising Tool in Oncology? Mol Diagn Ther. 2016 Dec; 20(6):523-530. Review.

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BioMol LABORATORIES

POLYMORPHISM N680S (A2039G) FSHR (FSH Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-021-25
RDM Code: 1730074/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		GEN-021-25	
Mix oligonucleotides and probes	Mix N680S FSHR 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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. GEN-021-25

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
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

POLYMORPHISM *39 A/G (A1730G) ESR2 GENE (Estrogen Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-022-25
RDM Code: 1730075/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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 A1730G (*39 A/G) polymorphism of the ESR2 gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instruments Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Estrogen receptors (ERs) are members of the large superfamily of ligand-activated nuclear receptors. To date, two receptor isoforms have been identified: ER-α (ESR1 gene) and ER-β (ESR2 gene). Both receptors belong to the nuclear receptor superfamily,but are synthesized by different genes and have unique structures and functions. The two isoforms consist of six domains and show high sequence homology (96%) in the DNA binding region, while they have distinct structures in the site of interaction with ligands (53% homology). The ESR1 gene is located on chromosome 6 and encodes the ER-α protein, abundantly expressed in the liver, adipose tissue, breast and cardiovascular system. Activated ER-α receptor has been shown to regulate the hepatic expression of many genes involved in lipoprotein metabolism, resulting in increased serum HDL cholesterol (HDL) and triglyceride concentrations while decreasing serum low-density lipoprotein and cholesterol lipoprotein (LDL). The ESR2 gene encodes the ER-β protein and is located on chromosome 14q23.1. ER-β is expressed in many tissues including the uterus, tissue monocytes and macrophages, colonic and lung epithelial cells, and in the prostatic epithelium and in the malignant counterparts of these tissues. Furthermore, ER-β is expressed throughout the brain at different concentrations in relation to neuronal areas.

CLINICAL SIGNIFICANCE

For the ESR1 and ESR2 genes there are multiple SNPs whose genotypic combinations explain the variability of the receptors in terms of quality and quantity. For the ESR2 gene, the most studied polymorphism is located in the 3'UTR region of the gene, at the level of nucleotide 1730 (1730 A→G) (rs4986938), and is recognized by the restriction enzyme AluI. This polymorphism is also known as *39 A→G. The *39GG genotype is associated with a reduced response to estrogen.The presence of these polymorphic variants represents a susceptibility factor for multiple conditions such as the risk of developing cancer (breast, colorectal, prostate cancer), neurodegenerative diseases (e.g. Parkinson's, Alzheimer's) and the couple's fertility status. Positive interactions were noted between ESR2 rs4986938; ESR1 rs2234693 and triple negative breast cancer (TNBC).

§ Diagnostics (Basel). 2024 Aug 28;14(17):1889. Association of Polymorphisms in FSHR, ESR1, and BMP15 with Primary Ovarian Insufficiency and Meta-Analysis
§ Meta-Analysis Cancer Genomics Proteomics. 2024 Sep-Oct;21(5):421-438. Pharmacogenetics of Toxicities Related to Endocrine Treatment in Breast Cancer: A Systematic Review and Meta-analysis
§ In Vivo. 2024 Sep-Oct;38(5):2134-2143. Analysis of Single Nucleotide Polymorphisms (SNPs) rs2234693 and rs9340799 of the ESR1 Gene and the Risk of Breast Cancer
§ Urol J. 2024 Jun 12. Association of Polymorphisms in Estrogen Receptors with non-obstructive Azoospermia and Severe Secretory Oligozoospermia: Meta-Analysis
§ Gene. 2023 Jan 30:851:146969. Unique ESR1 and ESR2 estrogen receptor gene variants associated with altered risk of triple-negative breast cancer: A case-control study
§ ESR1 PvuII polymorphism: from risk factor to prognostic and predictive factor of the success of primary systemic therapy in advanced breast cancer. BMC Cancer volume 21, Article number: 1348 (2021)
§ BMC Cardiovasc Disord. 2021 Jun 4;21(1):275. The association between estrogen receptor 2 gene polymorphism and complexity of coronary artery disease: an analysis in elective percutaneous coronary intervention patients
§ Medicine (Baltimore). 2021 Feb 19;100(7):e24398. The role of estrogen receptor-beta gene +1730G/A polymorphisms in recurrent pregnancy loss: A protocol for systematic review and meta-analysis
§ Differential association of ESR1 and ESR2 gene variants with the risk of breast cancer and associated features: A case-control study. Gene. 2018 Apr 20; 651:194-199. Epub 2018 Feb 4.
§ Polymorphisms in the estrogen receptor alpha gene (ESR1), daily cycling estrogen and mammographic density phenotypes.BMC Cancer. 2016 Oct 7; 16(1):776.
§ A Study on the Role of Estrogen Receptor Gene Polymorphisms in Female Infertility. Genet Test Mol Biomarkers. 2016 Nov; 20 (11):692-695. Epub 2016 Aug 30.

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BioMol LABORATORIES

POLYMORPHISM *39 A/G (A1730G) ESR2 GENE (Estrogen Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-022-25
RDM Code: 1730075/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		GEN-022-25	
Mix oligonucleotides and probes	Mix *39 A/G ESR2 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-022-25	
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
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

POLYMORPHISM -397 T>C ESR1 OF THE ESR1 GENE (Estrogen Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-023-25 RDM Code: 1734263/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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 -397 T/C polymorphism of the ESR1 (rs2234693) gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instruments Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Estrogen receptors (ERs) are members of the large superfamily of ligand-activated nuclear receptors. To date, two receptor isoforms have been identified: ER-α (ESR1 gene) and ER-β (ESR2 gene). Both receptors belong to the nuclear receptor superfamily but are synthesized by different genes and have unique structures and functions. The two isoforms consist of six domains and show high sequence homology (96%) in the DNA binding region, while they have distinct structures in the site of interaction with ligands (53% homology). The ESR1 gene is located on chromosome 6 and encodes the ER-α protein, abundantly expressed in the liver, adipose tissue, breast and cardiovascular system. Activated ER-α receptor has been shown to regulate the hepatic expression of many genes involved in lipoprotein metabolism, resulting in increased serum HDL cholesterol (HDL) and triglyceride concentrations while decreasing serum low-density lipoprotein and cholesterol lipoprotein (LDL). The ESR2 gene encodes the ER-β protein and is located on chromosome 14q23.1. ER-β is expressed in many tissues including the uterus, tissue monocytes and macrophages, colonic and lung epithelial cells, and in the prostatic epithelium and in the malignant counterparts of these tissues. Furthermore, ER-β is expressed throughout the brain at different concentrations in relation to neuronal areas.

CLINICAL SIGNIFICANCE

For the ESR1 and ESR2 genes there are multiple SNPs whose genotypic combinations explain the variability of the receptors in terms of quality and quantity. For the ESR1 gene (6q25) the most studied polymorphism is the T/C-397 polymorphism (rs2234693) localized in intron 1 of the gene. Such polymorphism is also called PvuII polymorphism, classified as Pp, depending on the presence or absence of the restriction site. The T nucleotide is also termed the p allele, while the C nucleotide is termed the P allele. The PP genotype (CC) is associated with receptor dysfunction with impaired response to estrogen.

§ Diagnostics (Basel). 2024 Aug 28;14(17):1889. Association of Polymorphisms in FSHR, ESR1, and BMP15 with Primary Ovarian Insufficiency and Meta-Analysis
§ Meta-Analysis Cancer Genomics Proteomics. 2024 Sep-Oct;21(5):421-438. Pharmacogenetics of Toxicities Related to Endocrine Treatment in Breast Cancer: A Systematic Review and Meta-analysis
§ In Vivo. 2024 Sep-Oct;38(5):2134-2143. Analysis of Single Nucleotide Polymorphisms (SNPs) rs2234693 and rs9340799 of the ESR1 Gene and the Risk of Breast Cancer
§ Urol J. 2024 Jun 12. Association of Polymorphisms in Estrogen Receptors with non-obstructive Azoospermia and Severe Secretory Oligozoospermia: Meta-Analysis
§ Gene. 2023 Jan 30:851:146969. Unique ESR1 and ESR2 estrogen receptor gene variants associated with altered risk of triple-negative breast cancer: A case-control study
§ ESR1 PvuII polymorphism: from risk factor to prognostic and predictive factor of the success of primary systemic therapy in advanced breast cancer. BMC Cancer volume 21, Article number: 1348 (2021)
§ BMC Cardiovasc Disord. 2021 Jun 4;21(1):275. The association between estrogen receptor 2 gene polymorphism and complexity of coronary artery disease: an analysis in elective percutaneous coronary intervention patients
§ Medicine (Baltimore). 2021 Feb 19;100(7):e24398. The role of estrogen receptor-beta gene +1730G/A polymorphisms in recurrent pregnancy loss: A protocol for systematic review and meta-analysis
§ Differential association of ESR1 and ESR2 gene variants with the risk of breast cancer and associated features: A case-control study. Gene. 2018 Apr 20; 651:194-199. Epub 2018 Feb 4.
§ Polymorphisms in the estrogen receptor alpha gene (ESR1), daily cycling estrogen and mammographic density phenotypes.BMC Cancer. 2016 Oct 7; 16(1):776.
§ A Study on the Role of Estrogen Receptor Gene Polymorphisms in Female Infertility. Genet Test Mol Biomarkers. 2016 Nov; 20 (11):692-695. Epub 2016 Aug 30.

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BioMol LABORATORIES

POLYMORPHISM -397 T>C ESR1 OF THE ESR1 GENE (Estrogen Receptor)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-023-25 RDM Code: 1734263/R
Tests: 25 Reactions: 31
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		GEN-023-25	
Mix oligonucleotides and probes	Mix -397 T/C ESR1 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 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. GEN-023-25	
STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissues, cells
CONTROLS	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

LCT GENE POLYMORPHISMS
LACTOSE INTOLERANCE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-024-25 RDM Code: 2256381/R
Tests: 25 Reactions: 31 x 2
REF: GEN-024-50 RDM Code: 2145488/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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 -13910 C>T and -22018 G>A polymorphisms of the gene encoding the enzyme lactose-phenytoin hydrolase (LPH) by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Lactose is the main sugar in milk, and lactose intolerance (LI) is very common. Symptoms of LI include diarrhea, abdominal pain, and flatulence after drinking or eating milk or products containing milk. These symptoms are caused by low levels of intestinal lactase due to mucosal injury or, more often, due to reduced genetic expression of the enzyme lactose-phenytoin hydrolase (LPH).

§ Nutrients. 2024 Sep 5;16(17):3002. doi: 10.3390/nu16173002. Bone Mineral Density and the Risk of Type-2 Diabetes in Postmenopausal Women: rs4988235 Polymorphism Associated with Lactose Intolerance Effects

§ Int J Mol Sci. 2023 Jun 15;24(12):10191. doi: 10.3390/ijms241210191. A Comprehensive Look at the -13910 C>T LCT Gene Polymorphism as a Molecular Marker for Vitamin D and Calcium Levels in Young Adults in Central and Eastern Europe: A Preliminary Study

§ United European Gastroenterol J. 2019 Mar;7(2):210-216. doi: 10.1177/2050640618814136. Epub 2018 Nov 15. 13910C>T and 22018G>A LCT gene polymorphisms in diagnosing hypolactasia in children

§ Association of lactase 13910 C/T polymorphism with bone mineral density and fracture risk: a meta-analysis.J Genet. 2017. Dec;96(6):993-1003. doi: 10.1007/s12041-017-0866-8.

§ BMJ Open. 2011 Jul 29; 1 (1):e000125. doi: 10.1136/bmjopen-2011-000125.

CLINICAL SIGNIFICANCE

Lactose intolerance (LI) is inherited as an autosomal recessive trait that causes reduction in the enzymatic activity of lactose-phenytoin hydrolase (LPH) in intestinal cells, causing a decrease in the ability to convert lactose into the absorbable sugars glucose and galactose. Decline in LPH enzyme activity is known to occur at age 12, however a portion of individuals retain neonatal LPH activity by exhibiting lifelong lactose tolerance (LT). Lactase persistence varies among different human populations, from 95% in Northern Europeans and North Americans to about 50% or less in South American and African countries, such as Cameroon, Mali, and South Africa, to about 0%. in some Asian countries, including China. The literature reports that in addition to biochemical blood analyses, genetic markers can be useful for the diagnosis of LI. To date, two main markers have been identified: single nucleotide polymorphisms (SNPs) C>T-13910 (rs4988235) and G>A-22018 (rs182549), located upstream of the lactase gene (LCT). In heterozygous -13910 C/T individuals, the 50% reduction in lactase activity level is normally sufficient to ensure digestion of lactose. Individuals with the 13910T/T genotype are perfectly tolerant to lactose while if the -13910 mutation is present in the homozygous state (C/C) there is a total deficiency of the lactase enzyme in adults. 100% of individuals with primary lactose intolerance (IPL) have the -13910 C/C genotype. Approximately 90% of these also have the -22018 G/G genotype while the remaining 10% have the -22018 G/A or A/A genotype, generally with milder symptoms.
Recent is the relationship between lactase activity and vitamin D and calcium levels.

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BioMol LABORATORIES

LCT GENE POLYMORPHISMS
LACTOSE INTOLERANCE

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-024-25 RDM Code: 2256381/R
Tests: 25 Reactions: 31 x 2
REF: GEN-024-50 RDM Code: 2145488/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-024-25	GEN-024-50	
Mix oligonucleotides and probes	Mix LCT -13910 C>T 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix LCT -22018 G>A 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 775 µl	2 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA Control 1	**Control 1** CC/GG	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA Control 2	**Control 2** CT/GA	1 x 35 µl	2 x 35 µl	-20°C
Genomic DNA or recombinant DNA Control 3	**Control 3** TT/AA	1 x 35 µl	2 x 35 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-024-25 / COD. GEN-024-50

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 (GEN-024-25) Recombinant DNA for at least 6 analytical sessions (GEN-024-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
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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BioMol LABORATORIES

MTRR A66G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-027-25 RDM Code: 2257737/R
Tests: 25 Reactions: 31
REF: GEN-027-50 RDM Code: 2159830/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 A66G polymorphism of the MTRR gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Although there is a correlation between HHcy and MetS, the mechanisms are still unclear and that is why many researchers have proposed several theories including promotion of endothelial dysfunction, induction of insulin resistance, and DNA methylation status. Consequently, both DNA methylation and DNA synthesis can be altered by interaction with homocysteine, vitamin B12, and folate.
The MTRR A66G polymorphism appears to be associated with an increased risk of MetS only when combined with the MTHFR 677TT genotype. In fact, the combined TT/GG, TT/AG and TT/AA genotypes confer a greater risk of MetS compared to the MTHFR C677T mutant genotypes alone.
Although no association was found between MetS and the MTRR A66G polymorphism alone, the MTRR 66GG genotype was associated with high fasting blood glucose values and high triglyceride levels although these results need to be confirmed with further studies given the relatively frequent low of the MTRR 66GG genotype in many populations.

§ Association of MTR A2756G and MTRR A66G Polymorphisms with Male Infertility: An Updated Meta-Analysis. Am J Mens Health 2023 May-Jun;17(3):15579883231176657.
§ Du B, Tian H, Tian D, Zhang C, Wang W, Wang L, et al. Genetic polymorphisms of key enzymes in folate metabolism affect the efficacy of folate therapy in patients with hyperhomocysteinaemia. Br J Nutr. 2018; 119(8): 887-895
§ Kurzawski M, Wajda A, Malinowski D, Kazienko A, Kurzawa R, Drozdzik M. Association study of folate-related enzymes (MTHFR, MTR, MTRR) genetic variants with non-obstructive male infertility in a Polish population. Genet Mol Biol. 2015; 38(1): 42-47
§ Yang B, Fan S, Zhi X, Wang D, Li Y, Wang Y, et al. Associations of MTHFR C677T and MTRR A66G gene polymorphisms with metabolic syndrome: a case-control study in Northern China. Int J Mol Sci. 2014; 15(12): 21687-21702
§ Jiang, S.; Zhao, R.; Pan, M.; Venners, S.A.; Zhong, C.; Hsu, Y.H. Associations of MTHFR and MTRR Polymorphisms with serum lipid levels in Chinese hypertensive patients. Clin. Appl. Thromb. most. 2014, 4, 200–210.
§ Jacques, P.F.; Boston, A.G.; Selhub, J.; Rich, S.; Elison, R.C.; Eckfeldt, J.H.; Gravel, R.A.; Rozen, R.; National Heart, Lung; Blood Institute; et al. Effects of polymorphisms of methionine synthase and methionine synthase reductase on total plasma homocysteine in the NHLBI Family Heart Study. Atherosclerosis 2003, 166, 49–55 elevated levels of triglycerides even if these results need to be confirmed with further studies given the relatively low frequency of the MTRR 66GG genotype in many populations.

CLINICAL SIGNIFICANCE

Methionine synthase reductase (MTRR) plays a key role in folate metabolism, in interconnection with the enzyme 5,10-methylenetetrahydrofolate reductase (MTHFR). MTHFR catalyzes the regulation of cellular methylation through the conversion of 5, 10-methylene tetrahydrofolate (THF) to 5-methyl-THF, the major circulating form of folate metabolism. MTRR, on the other hand, is required for the reductive methylation of vitamin B12, also known as cobalamin, an activated cofactor for methionine synthase (MTR), which catalyzes the methylation of homocysteine to methionine.
The methionine synthase reductase (MTRR) gene is located on chromosome 5 and plays a critical role in DNA synthesis.
The A66G polymorphism has been described for the MTRR gene, resulting in a substitution of the amino acid methionine to isoleucine at codon 22 (M22I).
This MTRR 66A>G polymorphism would also appear to be involved in the conversion of homocysteine into methionine, which negatively influences enzymatic activity and is therefore considered a genetic risk factor for hyperhomocysteinemia (HHcy). MTRR A66G can also induce DNA hypomethylation by regulating homocysteine levels. Homocysteine plays a role in the development of metabolic syndrome (MetS). MetS is caused by the interaction of multiple genetic and environmental factors.

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BioMol LABORATORIES

MTRR A66G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-027-25 RDM Code: 2257737/R
Tests: 25 Reactions: 31
REF: GEN-027-50 RDM Code: 2159830/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-027-25	GEN-027-50	
Mix oligonucleotides and probes	Mix A66G MTRR 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-027-25 / COD. GEN-027-50

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 (GEN-027-25) Recombinant DNA for at least 6 analytical sessions (GEN-027-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

(ACE I/D) INS/DEL POLYMORPHISM (Angiotensin-converting enzyme)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-035-25 RDM Code: 2159760/R
Tests: 25 Reactions: 31
REF: GEN-035-50 RDM Code: 2165040/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 the nucleotide polymorphism insertion (allele I) or deletion (allele D) in intron 16 of the gene encoding the human angiotensin converting enzyme (ACE) by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

The renin-angiotensin-aldosterone system (SRAA) is a hormonal system that regulates blood pressure, circulating plasma volume, arterial muscle tone through different mechanisms and the secretion of aldosterone; it also plays an important role in the etiology of hypertension. There are numerous components of this system: renin, prorenin, angiotensin converting enzyme (ACE), angiotensinogen (AGT), angiotensin I and angiotensin II; the latter represents the final effector of the renin-angiotensin system and exerts its effects on the cardiovascular system through binding to specific receptors. The first stage of the enzymatic cascade that leads to the production of angiotensin II consists in the conversion of angiotensinogen to angiotensin I, by the proteolytic enzyme renin. The second stage of the process involves the conversion of angiotensin I to angiotensin II, through a reaction catalyzed by ACE. Angiotensin II is the main active peptide of SRAA that functions through at least four types of receptors. The AGTR1 receptor mediates cardiovascular effects, including vasoconstriction, aldosterone synthesis, vasopressin secretion, vascular smooth muscle cell proliferation, renal blood flow, regulation of renin activity, renal sodium absorption, the modulation of the activity of the sympathetic nervous system, and cardiac function.

§ J Clin Med Res. 2024 Aug;16(7-8):355-362 Renin-Angiotensin System Genes Polymorphisms in Patients With COVID-19 and Its Relation to Severe Cases of SARS-CoV-2 Infection
§ Pediatr Res. 2024 Jan 4. doi: 10.1038/s41390-023-02982-8. Online ahead of print. Association of ACE1 I/D polymorphism and susceptibility to COVID-19 in Egyptian children and adolescents
§ Association of angiotensin-converting enzyme gene **I/D** polymorphism with chronic obstructive pulmonary disease: a meta-analysis. J Renin Angiotensin Aldosterone Syst. 2018 Apr-Jun;19(2):1470320318770546.
§ Genetic polymorphism of angiotensin-converting enzyme and hypertrophic cardiomyopathy risk: A systematic review and meta-analysis. Medicine (Baltimore). 2017 Dec;96(48):e8639.
§ Ace Gene Plays A Key Role In Reducing Blood Pressure In Hypertensive Elderlies After Resistance Training Resistance Exercise And **Ace** Polymorphism. J Strength Cond Res. 2017 Dec 1.
§ Association of insertion-deletions polymorphisms with colorectal cancer risk and clinical features. World J Gastroenterol. 2017 Oct 7;23(37):6854–6867.

CLINICAL SIGNIFICANCE

The renin-angiotensin system (SRAA) also exerts local effects on cell proliferation, apoptosis, inflammation and angiogenesis in different tissues. Furthermore, there are data in the literature correlating SRAA with tumor tumorigenesis and tumor angiogenesis. There are genetic polymorphisms in the various components of the SRAA that may have clinical relevance. The insertion/deletion (I/D) of the ACE gene is directly associated with the circulatory level of the enzyme itself. The nature of the ACE1 rs1799752 gene polymorphism is in the insertion (insertion, I) or loss (deletion, D) of the Alu repeat in 289 nucleotide pairs in the 16th intron.
Deletion of the Alu repeat is accompanied by a significant increase in the expression of the ACE1 gene and a rise of ACE1 levels. The increase in ACE1 levels occurs even in case of heterozygous status (I/D). The highest level is observed in patients with homozygous genotype D/D rs1799752, which is twice higher than in patients with genotype I/I. The relation between the D/D genotype and a wide range of CVDs, including coronary heart disease (CHD), heart attack, left ventricular hypertrophy, hypertension, kidney disease, and neurodegenerative diseases has been detected.
Furthermore, in a recent meta-analysis a significant association between I/D polymorphisms and recurrent miscarriages was reported. Women with the “DD” or “ID” ACE genotypes are at higher risk of experiencing recurrent pregnancy loss.

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BioMol LABORATORIES

(ACE I/D) INS/DEL POLYMORPHISM (Angiotensin-converting enzyme)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-035-25 RDM Code: 2159760/R
Tests: 25 Reactions: 31
REF: GEN-035-50 RDM Code: 2165040/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-035-25	GEN-035-50	
Mix oligonucleotides and probes	Mix PCR ACE I/D 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1 HOMO DD	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2 HET ID	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3 HOMO II	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-035-25 / COD. GEN-035-50

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 (GEN-035-25) Recombinant DNA for at least 6 analytical sessions (GEN-035-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 45 cycles at 95 °C (15 sec) + 60 °C at (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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BioMol LABORATORIES

MTR A2756G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-036-25 RDM Code: 2248813/R
Tests: 25 Reactions: 31
REF: GEN-036-50 RDM Code: 2248811/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 A2756G polymorphism of the MTR gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

The MTR gene is mapped to chromosome 1q43 and the extensively studied A2756G (rs1805087) polymorphism leads to a change of the amino acid aspartate to the amino acid glycine at codon 919 (D919G), with consequent reduction of the enzymatic activity. It has been reported that this polymorphism can increase homocysteine levels by suppressing methionine metabolism and consequently can lead to DNA hypomethylation and promote tumourigenesis. Numerous studies have shown that the MTR A2756G polymorphism is linked to various types of cancer, such as prostate cancer, retinoblastoma, acute lymphoblastic leukemia (ALL), and some cases of autism. In fact, the heterozygous AG and homozygous GG genotypes are associated with an increased risk of these pathologies.

CLINICAL SIGNIFICANCE

Methionine synthase (MTR) plays a crucial role in the folate metabolic network. It is a vitamin B12-dependent enzyme that remethylates homocysteine to methionine with simultaneous conversion of 5-methyl-tetrahydrofolate (5-methyl-THF) to tetrahydrofolate (THF). THF is essential for the synthesis of nucleotides while methionine is essential for the synthesis of S adenosil methionine (SAM). MTR helps maintain adequate intracellular folate levels and normal concentrations of homocysteine and methionine, which are used for proper DNA methylation or other methylation processes. However, some other studies have revealed a modest inverse association between the GG genotype (A2756G MTR) and HCY levels indicating increased enzymatic activity of the variant genotype.

§ *Li-Min Ma, Hai-Ping Yang, Xue-Wen Yang and Lin-Hai Ruan. Methionine synthase A2756G polymorphism influences pediatric acute lymphoblastic leukemia risk: a meta-analysis. Bioscience Reports (2019) 39 BSR20181770 https://doi.org/10.1042/BSR20181770*

§ *Xiaosong Zhang, Jilei Tang, Nan Shen, Kewei Ren, Single-nucleotide polymorphism (rs1805087) in the methioninesynthase (METH) gene increases the risk of prostate cancer. AGING 2018, Vol. 10, No. 10*

§ *Du B, Tian H, Tian D, Zhang C, Wang W, Wang L, et al. Genetic polymorphisms of key enzymes in folate metabolism affect the efficacy of folate therapy in patients with hyperhomocysteinaemia. Br J Nutr. 2018; 119(8): 887-895*

§ *Rosa Haghiri, Farhad Mashayekhi, Elham Bidabadi, and Zivar Salehi. Analysis of methionine synthase (rs1805087) gene polymorphism in autism patients in Northern Iran Acta Neurobiol Exp 2016, 76: 318–323*

§ *Kurzawski M, Wajda A, Malinowski D, Kazienko A, Kurzawa R, Drozdzik M. Association study of folate-related enzymes (MTHFR, MTR, MTRR) genetic variants with non-obstructive male infertility in a Polish population. Genet Mol Biol. 2015; 38(1): 42-47*

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BioMol LABORATORIES

MTR A2756G POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-036-25 RDM Code: 2248813/R
Tests: 25 Reactions: 31
REF: GEN-036-50 RDM Code: 2248811/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-036-25	GEN-036-50	
Mix oligonucleotides and probes	Mix A2756G MTR 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-036-25 / COD. GEN-036-50

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 (GEN-036-25), Recombinant DNA for at least 6 analytical sessions (GEN-036-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

FV Y1702C (A5279G) POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-037-25 RDM Code: 2248815/R
Tests: 25 Reactions: 31
REF: GEN-037-50 RDM Code: 2248816/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 Y1702C (A5279G) polymorphism of the FV gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Venous thromboembolism (VTE), usually involving deep vein thrombosis, pulmonary embolism, or both, is a complex, multifactorial disorder in which several conditions interact and contribute to increased individual risk culminating in the development of venous occlusives. Thrombophilia is commonly defined as a propensity to develop venous thromboembolism based on a hypercoagulable condition attributable to inherited or acquired disorders involving blood clotting or fibrinolysis.
Among acquired risk factors, some may lead to increased hypercoagulability, for example, cancer, surgery, injury or fracture, immobilization, pregnancy and the postpartum period, long-distance travel, hospitalization, catheterization and acute infection and others may be considered as predisposing conditions, such as age, gender, race/ethnicity, body mass index and obesity, use of oral contraceptive or hormone therapy , corticosteroids or statins, diet, physical activity, sedentary weather and air pollution.

CLINICAL SIGNIFICANCE

Furthermore, venous thromboembolism has a strong genetic basis, with approximately 50-60% of the variance in incidence attributable to genetic effects. Some genetic susceptibility variants that contribute to risk have been identified in candidate genes, such as factor V Leiden and prothrombin.
A missense mutation in factor V resulting from a nucleotide residue substitution A →G at position 5279 in exon 15 has recently been identified, causing the Tyr→Cys substitution of amino acid 1702 (Y1702C) in the A3 domain of FV. This mutation appears to cause a deficiency in this factor, increasing the resistance of factor V to the anticoagulant action of activated protein C.

§ Genotyping analysis of the factor V Nara mutation, Hong Kong mutation, and 16 single-nucleotide polymorphisms, including the R2 haplotype, and the involvement of factor V activity in patients with recurrent miscarriage. Blood Coagul Fibrinolysis. 2017 Jun; 28(4):323-328.

§ Genetic modulation of the FV (Leiden)/normal FV ratio and risk of venous thrombosis in factor V Leiden heterozygotes. J Thromb Haemost. 2012 Jan; 10(1):73-80.

§ Impaired APC cofactor activity of factor V plays a major role in the APC resistance associated with the factor V Leiden (R506Q) and R2 (H1299R) mutations. Blood. 2004 Jun 1; 103(11):4173-9.

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BioMol LABORATORIES

FV Y1702C (A5279G) POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-037-25 RDM Code: 2248815/R
Tests: 25 Reactions: 31
REF: GEN-037-50 RDM Code: 2248816/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-037-25	GEN-037-50	
Mix oligonucleotides and probes	Mix FV Y1702C (A5279G) 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-037-25 / COD. GEN-037-50

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 (GEN-037-25), Recombinant DNA for at least 6 analytical sessions (GEN-037-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

FVII R353Q POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-038-25 RDM Code: 2254578/R
Tests: 25 Reactions: 31
REF: GEN-038-50 RDM Code: 2254587/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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 R353Q (G>A) polymorphism of the FVII gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

Myocardial infarction (MI) occurs due to blockages in the coronary arteries that decrease blood flow to the myocardium, causing the rapid death of myocytes. Coagulation factor VII (FVII), the initiator of the extrinsic coagulation pathway, has been linked to the risk of myocardial infarction. In fact, activated FVII binds to a tissue factor thus activating extrinsic coagulation, which promotes fibrin conversion and thrombosis and leads to the formation of a blood clot in the vessels.
This process also accelerates in the presence of unstable atherosclerotic plaques. Therefore, FVII levels are considered predictive of MI and are influenced by multiple factors such as genetic architecture.

CLINICAL SIGNIFICANCE

The R353Q polymorphism was identified in exon 8 of the FVII gene which could increase or decrease the level of gene expression.
Since guanine is replaced with adenine at codon 353 of the FVII gene, the R353Q polymorphism is related to the missense substitution of the amino acid arginine (R) with glutamine (Q).
Patients with the RR genotype have a higher concentration of FVII than those with the RQ genotype, who, in turn, have a higher concentration of FVII than those with the QQ genotype.

§ Association Between R353Q (rs6046) Polymorphism in Factor VII with Coronary Heart Disease. Int Heart J. 2020 Jul 30; 61(4):641-650.

§ Polymorphism of R353Q (rs6046) in factor VII and the risk of myocardial infarction: A systematic review and meta-analysis. Medicine (Baltimore) 2018 Sep; 97 (39):e12566.

§ Association between polymorphisms in the coagulation factor VII gene and coronary heart disease risk in different ethnicities: a meta-analysis. BMC Med Genet. 2011 Aug 12; 12: 107

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BioMol LABORATORIES

FVII R353Q POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-038-25 RDM Code: 2254578/R
Tests: 25 Reactions: 31
REF: GEN-038-50 RDM Code: 2254587/R
Tests: 50 Reactions: 62
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-038-25	GEN-038-50	
Mix oligonucleotides and probes	Mix FVII R353Q (G>A) 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	2 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-038-25 / COD. GEN-038-50

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
CONTROL	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

CBS A114V AND I278T POLYMORPHISMS (CYSTATHIONINE-β SYNTHASE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-040-25 RDM Code: 2254596/R
Tests: 25 Reactions: 31 x 2
REF: GEN-040-50 RDM Code: 2254595/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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 A114V and I278T polymorphisms of the cystathionine β-synthase (CBS) gene by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus DX and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Numerous studies have demonstrated that hyperhomocysteinemia (HHcy) is an independent risk factor for cardiovascular and cerebrovascular diseases and that an increase in hypertension and plasma homocysteine (Hcy) has a synergistic effect in causing these diseases. Homocysteine is an important intermediate product in the metabolism of methionine and cysteine. 5,10-methylenetetrahydrofolate reductase (MTHFR) and cystathionine β-synthase (CBS) are key enzymes in homocysteine metabolic pathways. The catalytic activity of the MTHFR enzyme creates an irreversible reduction of 5,10-methylenetetrahydrofolate (THF) which is converted to 5-methyl-THF during this process. 5-methyl-THF is the most abundant circulating form of folic acid, serving as a methyl donor for the remethylation of homocysteine to methionine, a reaction (catalyzed by methionine synthase) for which vitamin B12 is required.

§ Interactions among methylenetetrahydrofolate reductase (MTHFR) and cystathionine β-synthase (CBS) polymorphisms - a cross-sectional study: multiple heterozygosis as a risk factor for higher homocysteine levels and vaso-occlusive episodes. Genet Mol Res. 2017 Feb 23; 16 (1). doi: 10.4238/gmr16019374.
§ Association between 11 genetic polymorphisms in folate-metabolising genes and head and neck cancer risk. Eur J Cancer. 2012 Jul; 48 (10):1525-31. doi: 10.1016/j.ejca.2011.09.025. Epub 2011 Nov 1.
§ The 844ins68 polymorphism of the cystathionine beta-synthase gene is associated with schizophrenia. Psychiatry Res. 2009 Dec 30; 170 (2-3):168-71. doi: 10.1016/j.psychres. 2008.07.007. Epub 2009 Nov 10.

CLINICAL SIGNIFICANCE

The cystathionine β-synthase (CBS) gene is located on chromosome 21q22.3 and encodes an enzyme that participates in the folate pathway and catalyzes the transsulfuration of homocysteine and serine to cystathionine as a cysteine precursor. The CBS gene has a large number of mutations and polymorphisms. The 844ins68 polymorphism at position 844 in the CBS gene generates an alternative splice site that disrupts the protein, resulting in decreased functional activity of CBS. The deficiency of this enzyme causes an increase in homocysteine in the blood and homocystinuria.
The A114V (c.341C>T) and I278T (c.833T>C) mutations are carried by three and seven independent alleles, respectively.
Furthermore, the T833C mutation generating a restriction site of BsrI (CBS I278T) has been shown to segregate in cis with the 844ins68 polymorphism in exon 8.
Significant interactions were observed between the polymorphisms of MTHFR C677T, MTHFR A1298C and the CBS 844ins68/T833C haplotype for Hcy levels. In fact, heterozygotes show higher homocysteine values. Interactions between the various polymorphisms may therefore influence serum Hcy levels, where multiple heterozygosity could be a risk factor for vaso-occlusive episodes.
The 844ins68 polymorphism has also been associated with other diseases, including neural tube defects and cancer.

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BioMol LABORATORIES

CBS A114V AND I278T POLYMORPHISMS (CYSTATHIONINE-β SYNTHASE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GEN-040-25 RDM Code: 2254596/R
Tests: 25 Reactions: 31 x 2
REF: GEN-040-50 RDM Code: 2254595/R
Tests: 50 Reactions: 62 x 2
CND Code: W0106010499
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-040-25	GEN-040-50	
Mix oligonucleotides and probes	Mix PCR CBS I278T 10X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix oligonucleotides and probes	Mix PCR CBS A114V 10X	1 x 77,5 µl	2 x 77,5 µl	
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 775 µl	2 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-040-25 / COD. GEN-040-50

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 (GEN-040-25), Recombinant DNA for at least 6 analytical sessions (GEN-040-50)
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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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BioMol LABORATORIES

REPRODUCTION

Y CHROMOSOME MICRODELETIONS (AZFa, AZFb, AZFbc, AZFc)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GR-011-25-AG
RDM Code: 1694068/R
Tests: 25
Reactions: 31 x 2
CND Code: W01060299
Manufacturer: BioMol Laboratories s.r.l.

CONTENT OF THE KIT

The kit consists of PCR amplification reagents and detection kit
**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 **PCR END-POINT**. Determination of the presence/absence of Y chromosome microdeletions (AZFa, AZFb, AZFbc, AZFc) and detection on agarose gel. Kit optimized for any CE-IVD validated thermal cycler.

The product GR-011-25-AG allows the determination of the presence/absence of Y chromosome microdeletions (AZFa, AZFb, AZFbc, AZFc) to perform a basic marker analysis.

SCIENTIFIC BACKGROUND

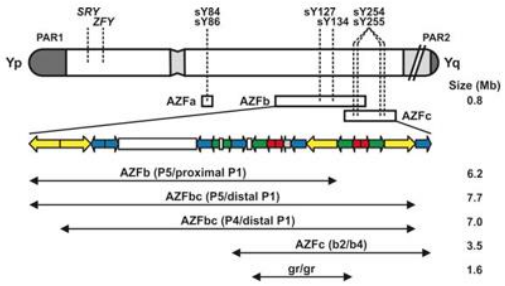
Male infertility can be attributed to several factors such as cryptorchidism, varicocele, endocrinological disorders, obstruction/absence of seminal ducts, infections, alcohol consumption or chemotherapy. However, genetic alterations have also emerged as a major cause of male infertility. Genetic defects commonly seen in infertile males include karyotypic abnormalities, gene copy number variations, single gene mutations/polymorphisms, and deletions on the long arm of the Y chromosome. Y chromosomal microdeletions are the second most frequent genetic cause of male infertility. Microdeletions occur in approximately one in 4,000 men in the general population, but their frequency is significantly increased among infertile men. Molecular diagnosis of Y chromosomal microdeletions is a genetic test that is part of routine diagnostics in the study of azoospermic and severe oligozoospermic men.

The following recurrent Y chromosome microdeletions are clinically relevant and have been found in men with severe oligo- or azoospermia: AZFa, AZFb (P5/proximal P1),AZFbc (P5/distal P1 or P4/distal P1), AZFc (b2/ b4). The most frequent type of microdeletion is that of the AZFc region (~80%) followed by the microdeletions AZFa (0.5-4%, AZFb (1-5%) and AZFbc (1-3%).

CLINICAL SIGNIFICANCE

Y chromosome microdeletions are the second most frequent cause of failure of spermatogenesis in infertile men. The incidence of these microdeletions in infertile subjects reported in the literature is about 2-10%. However, it is higher in azoospermic men than in oligozoospermic men.

It is clinically appropriate to consider Y deletions as a cause of oligo/azoospermia rather than a cause of "infertility", fertility being possible even with a low sperm count.



§ EAA/EMQN best practice guidelines for molecular diagnosis of Y-chromosomal microdeletions: State of the art 2023. Andrology. August 2023 DOI: 10.1111/andr.13514.Review
§ Genetics of the human Y chromosome and its association with male infertility. Reprod Biol Endocrinol. 2018 Feb 17; 16(1):14.
§ EAA/EMQN best practice guidelines for molecular diagnosis of Y-chromosomal microdeletions: state-of-the-art 2013. Andrology. 2014 Jan; 2(1):5-19. Review.
§ EAA/EMQN best practice guidelines for molecular diagnosis of y-chromosomal microdeletions. State of the art 2004. Int J Androl 27, 240–249.

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BioMol LABORATORIES

Y CHROMOSOME MICRODELETIONS (AZFa, AZFb, AZFbc, AZFc)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: GR-011-25-AG
RDM Code: 1694068/R
Tests: 25
Reactions: 31 x 2
CND Code: W01060299
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of PCR amplification reagents and detection kit
**the reagents for the extraction of genomic DNA are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		GR-011-25-AG	-20°C
Oligonucleotides mix	Mix Multiplex A 2X	1 x 387,5 µl	-20°C
Oligonucleotides mix	Mix Multiplex B 2X	1 x 387,5 µl	-20°C
Amplifying enzyme	Taq polymerase (5U/µl)	1 x 31 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Positive control XX	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Positive control XY	1 x 22 µl	-20°C
Detection kit	Ready to use 3% Nusieve agarose gel, TBE buffer, molecular weight markers		RT

TECHNICAL CHARACTERISTICS

COD. GR-011-25-AG

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA from whole blood, tissue, cells
POSITIVE CONTROLS	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Thermal cycler for end-point PCR, heated cap
TECHNOLOGY	PCR (polymerization chain reaction)
RUNNING ON AGAROSE GEL	Electrophoretic running equipment
THERMAL CYCLING PROFILE	1 cycle at 95 °C (15 min); 35 cycles at 95 °C (30 sec) +57 °C at (90 sec) + 72°C at (60 sec); 1 cycle 72°C (10 min)
ANALYTICAL SPECIFICITY	Absence of non-specific primer pairings; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 2,5 ng of genomic DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

HLA

HLA-G 14 bp INS/Del POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: HLA-001-25 RDM Code: 2256387/R
Tests: 25 Reactions: 31
REF: HLA-001-50 RDM Code: 1694059/R
Tests: 50 Reactions: 62
CND Code: W106010499
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.** Detection of Ins/Del 14 bp polymorphism of the HLA-G gene (rs371194629) by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Human leukocyte antigen G (HLA-G) is a member of the HLA class I family. The HLA-G gene is located in chromosomal region 6p21.3 and its exon/intron structure resemble that of other classical class I genes (HLA-A, HLA-B or HLA-C), composed of seven introns and eight exons that encode the heavy chain of the molecule. Under physiological conditions HLA-G is highly expressed in fetal cells at the maternal-fetal interface, thymus, pancreas, cornea, nail matrix and erythroblasts during hematopoiesis. The membrane-bound or soluble HLA-G protein strongly binds its receptors on immune cells, inhibits the functions of these effectors, and causes immune inhibition.

§ Am J Reprod Immunol. 2023 Dec;90(6): e13792. doi: 10.1111/aji.13792. Association of human leukocyte antigen-G and -F with recurrent miscarriage and implantation failure: A systematic review
§ Pharmaceutics. 2022 Dec 7;14(12):2737. doi: 10.3390/pharmaceutics14122737. Association of HLA-G 3'UTR Polymorphisms with Response to First-Line FOLFIRI Treatment in Metastatic Colorectal Cancer
§ Immunol Lett. 2022 Aug: 248:78-89. doi: 10.1016/j.imlet.2022.06.010. Epub 2022 Jun 22. 3'UTR-HLA-G polymorphisms and circulating sHLA-G are associated with breast cancer: Evidence from a meta-analysis
§ Pediatr Diabetes. 2018 Dec;19(8):1357-1361. doi: 10.1111/pedi.12768. Epub 2018 Sep 25. Association between 14 bp insertion/deletion HLA-G functional polymorphism and insulin resistance in a cohort of Italian children with obesity§ The HLA-G 14-bp polymorphism and recurrent implantation failure: a meta-analysis. J Assist Reprod Genet. 2017 Nov;34(11):1559-1565.
§ HLA-G 3' untranslated region polymorphic sites associated with increased HLA-G production are more frequent in patients exhibiting differentiated thyroid tumours. Clin Endocrinol (Oxf). 2017 Apr;86(4):597-605.
§ Recent Advances in Our Understanding of HLA-G Biology: Lessons from a Wide Spectrum of Human Diseases. J Immunol Res. 2016; 2016:4326495. doi: 10.1155/2016/4326495. Epub 2016 Aug 29. Review
§ The impact of HLA-G 3' UTR variants and sHLA-G on risk and clinical correlates of schizophrenia. Hum Immunol 2016 Dec;77(12):1166-1171.
§ Hum Immunol. 2014 Aug;75(8):827-32. doi: 10.1016/j.humimm.2014.06.004. Epub 2014 Jun 19. Association between human leukocyte antigen-G 14-bp insertion/deletion polymorphism and cancer risk: a meta-analysis and systematic review.

CLINICAL SIGNIFICANCE

HLA-G protein can be expressed de novo at high levels in several pathological conditions, including solid and hematologic tumors and during microbial or viral infections, leading to impaired immune response against tumor cells or pathogens, respectively. On the other hand, loss of HLA-G-mediated control of immune responses can lead to the onset of autoimmune/inflammatory diseases, caused by uncontrolled activation of immune effector cells. HLA-G also has an important role in human pregnancy as the different isoforms of HLA-G are expressed by trophoblast cells at the maternal-fetal interface. HLA-G expressed and released by trophoblast cells can interact with cellular receptors expressed by immune (T cells, NK cells, macrophages and dendritic cells) and non-immune cells (endothelial cells) present in the decidua, activating inhibitory or activating signals. It has been demonstrated that low levels of expression of this soluble protein do not seem to trigger the process of immunological tolerance necessary for the survival of the embryo. The most polymorphic regions of the gene are in the 5'UTR and 3'UTR regulatory regions which may contribute to the regulation of HLA-G expression. The 14-bp insertion/deletion polymorphism (rs371194629) in the 3'UTR region of exon 8 correlated with mRNA stability and the amount of HLA-G protein produced. The allele with a 14bp insertion was associated with lower HLA-G expression levels than the allele with the 14bp deletion and an increased risk of recurrent implantation failure (RIF)in Caucasians.

Recently a meta-analysis demonstrated the association of both HLA-G 14-bp Ins/Del and HLA-G +3142 C/G polymorphisms with breast cancer susceptibility, high circulating sHLA-G in patients with breast versus healthy controls and that the Del and C alleles were significant risk factors for breast cancer.

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BioMol LABORATORIES

HLA-G 14 bp INS/DEL POLYMORPHISM

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: HLA-001-25 RDM Code: 2256387/R
Tests: 25 Reactions: 31
REF: HLA-001-50 RDM Code: 1694059/R
Tests: 50 Reactions: 62
CND Code: W106010499
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.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		HLA-001-25	HLA-001-50	
Mix oligonucleotides and probes	Mix Ins/Del 14 bp HLA-G 10 X	1 x 77,5 µl	2 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 5X	1 x 155 µl	2 x 155 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control Del/Del	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control Ins/Del	1 x 22 µl	2 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control Ins/Ins	1 x 22 µl	2 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. HLA-001-25 / COD. HLA-001-50

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 (HLA-001-25) Recombinant DNA for at least 6 analytical sessions (HLA-001-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 fluorescence channels HEX/JOE and FAM
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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BioMol LABORATORIES

INFECTIOUS DISEASES

SARS-CoV-2 RT-PCR KIT VIRAL 3

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-002-100
RDM Code: 2012127/R
Tests: 100 Reactions: 110
CND Code: W0105040599
Produttore: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and amplification in Real-Time PCR
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

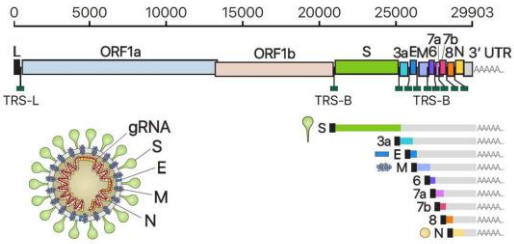
Molecular method "NAT" (Nucleic Acid Testing): Qualitative analysis of of SARS-CoV-2 (N-nucleocapsid, ORF1ab-polyprotein, E-envelope genes) viral genome and human RNase P gene by RT-PCR technique (Reverse transcriptase -polymerase chain reaction) and subsequent detection in PCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx. The INFET-002 kit provides reagents optimized for qualitative analysis of viral genome even in case of infections caused by the SARS-CoV-2 variants B.1.1.7 (United Kingdom), B.1.351 (South Africa), P1 (Brazil) and Delta (India).

SCIENTIFIC BACKGROUND

Coronaviruses (CoV) are important pathogens capable of infecting the respiratory, gastrointestinal, hepatic and central nervous systems of humans, livestock, birds, bats, mice and many other wildlife.
SARS-CoV-2 (CoV19) is the seventh member of the family of coronaviruses that infect humans, after MERS-nCoV and SARS-nCoV. It has a diameter of 60–140 nm and a single-stranded RNA genome of 29891 bp. Genome sequence alignment revealed 79.5% sequence identity between SARS-CoV-2 and SARS-CoV and remarkable identity (93.1%) with the RaTG12 virus sequence isolated from a bat (Rhinolophus affinis) from Yunnan province in China. These data, therefore, suggest that the SARS-CoV-2 virus could come from a virus endemic to this bat species.

CLINICAL SIGNIFICANCE

Viral infection is cytopathic for human airway epithelial cells and also for alveolar cells. However, similarly to what has been observed in response to SARS-CoV, immune-mediated injury may play a critical role in the pathogenesis of COVID-19 infection, particularly among individuals with comorbidities. Indeed, cytokine storm is thought to be a key factor underlying both ARDS and extra-pulmonary organ failure.



§ CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel CDC, Revision 2 3/15/2020
§ https://www.who.int/emergencies/diseases/novel coronavirus-2019/technical guidance/laboratory-guidance
§ Development of a Laboratory-safe and Low-cost Detection Protocol for SARS-CoV-2 of the Coronavirus Disease 2019 (COVID-19). Exp Neurobiol 2020 Apr 30;29(2):107-119. doi: 10.5607/en20009.
§ Novel 2019 Coronavirus: Genome Structure, Clinical Trials, and Outstanding Questions. Exp Biol Med (Maywood) 2020 Apr 19;1535370220920540. doi: 10.1177/1535370220920540.
§ The Architecture of SARS-CoV-2 Transcriptome. Cell 2020 May 14;181(4):914-921.e10. doi: 10.1016/j.cell.2020.04.011. Epub 2020 Apr 23.
§ Comparative Performance of SARS-CoV-2 Detection Assays Using Seven Different Primer-Probe Sets and One Assay Kit. J Clin Microbiol 2020 May 26;58(6):e00557-20. doi: 10.1128/JCM.00557-20.
§ Gruppo di Lavoro ISS Test Diagnostici COVID-19 e Gruppo di Lavoro ISS Dispositivi Medici COVID-19. Dispositivi diagnostici in vitro per COVID-19. Parte 1: normativa e tipologie. Versione del 18 maggio 2020. Roma: Istituto Superiore di Sanità; 2020. (Rapporto ISS COVID-19 n. 28/2020)
§ Gruppo di Lavoro ISS Test Diagnostici COVID-19 e Gruppo di Lavoro ISS Dispositivi Medici COVID-19. Dispositivi diagnostici in vitro per COVID-19. Parte 2: evoluzione del mercato e informazioni per gli stakeholder. Versione del 23 maggio 2020. Roma: Istituto Superiore di Sanità; 2020. (Rapporto ISS COVID-19 n. 46/2020).

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EN ISO 9001 CERTIFICATE
EN ISO 13485 CERTIFICATE

BioMol LABORATORIES

SARS-CoV-2 RT-PCR KIT VIRAL 3

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-002-100
RDM Code: 2012127/R
Tests: 100 Reactions: 110
CND Code: W0105040599
Produttore: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
Mix RT-PCR	Mix RT-PCR 4X	1 x 560 µl	-20° C
Mix probes and oligonucleotides Mix for N, ORF1a, E envelope and RNaseP genes	Mix CoV19 Viral 3	1 x 560 µl	-20° C
Recombinant RNA Positive Control (200 copies/µl)	Control +	1 x 40 µl	-20° C
Buffer Negative Control	Control -	1 x 80 µl	-20° C

TECHNICAL CHARACTERISTICS

COD. INFET-002- 100

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA of cells contained in buffer rhino-oropharyngeal, in biological fluids, saliva and tissue
POSITIVE CONTROL	Recombinant RNA
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx e Agilent AriaDx
TECHNOLOGY	RT-PCR (Reverse transcriptase-polymerase chain reaction) and subsequent detection with qPCR-Real-time
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 25 °C (2 min); 1 cycle at 50 °C (15 min); 1 cycle at 95 °C (2 min); 45 cycles at 95 °C (3 sec) + 60 °C (30 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	100 copies of viral genome
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100% /98%

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BioMol LABORATORIES

Subgenomic N(sgN) SARS-CoV-2 ONE-STEP RT-PCR KIT

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-004-100
RDM Code: 2218988/R
Tests: 100 Reactions: 110
CND Code: W0105040599
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and amplification in Real-Time PCR
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

"NAT" (Nucleic Acid Testing) molecular method: qualitative determination of the viral genome of SARS-CoV-2 (ORF1ab-polyprotein gene, E-envelope gene and subgenomic-N transcript) and human RNase P gene by RT-PCR (Reverse transcriptase -polymerase chain reaction) technique and subsequent detection by PCR-Real-time. sgN mRNA expression, in particular, reflects a stage of viral replication and discriminates between an active phase of replication and a medium-long term carrier state, in which there is accumulation of viral genomic material without being more infectious. The INFET-004 kit detects the presence of known SARS-CoV-2 variants. The kit is optimized for Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

SARS-CoV-2 is an enveloped virus with a single-stranded RNA genome of ~30 kb belonging to the betacoronavirus genus. It is known that coronaviruses produce subgenomic RNA fragments (sgRNAs) and that these fragments can be considered markers of viral replication. In fact, subgenomic RNAs are particularly abundant during early infection (up to 70 times more abundant than virus genomic RNA at the peak of RNA transcription). The expression of sgN mRNA, in particular, reflects a stage of viral replication and allows to discriminate between an active phase of replication and a medium-long term carrier state, in which there is accumulation of viral genomic material without being more infectious.

§ Loss of Detection of sgN Precedes Viral Abridged Replication in COVID-19-Affected Patients-A Target for SARS-CoV-2 Propagation Ferrucci V, de Antonellis P, Quarantelli F, Asadzadeh F, Bibbò F, Siciliano R, Sorice C, Pisano I, Izzo B, Di Domenico C, Boccia A, Vargas M, Pierri B, Viscardi M, Brandi S, Fusco G, Cerino P, De Pietro L, Furfaro C, Napolitano LA, Paolella G, Festa L, Marzinotto S, Conte MC, Gentile I, Servillo G, Curcio F, de Cristofaro T, Broccolo F, Capoluongo E, Zollo M. Int J Mol Sci. 2022 Feb 9;23(4):1941. doi: 10.3390/ijms23041941.

§ Viral Culture Confirmed SARS-CoV-2 Subgenomic RNA Value as a Good Surrogate Marker of Infectivity. Santos Bravo M, Berengua C, Marín P, Esteban M, Rodriguez C, Del Cuerpo M, Miró E, Cuesta G, Mosquera M, Sánchez-Palomino S, Vila J, Rabella N, Marcos MÁ. J Clin Microbiol. 2022 Jan 19;60(1):e0160921. doi: 10.1128/JCM.01609-21. Epub 2021 Oct 20. PMID: 34669457

§ Diagnostic usefulness of subgenomic RNA detection of viable SARS-CoV-2 in patients with COVID-19. Kim JY, Bae JY, Bae S, Cha HH, Kwon JS, Suh MH, Lee HJ, Jung J, Kim MJ, Cui C, Park H, Lee J, Park MS, Kim SH. Clin Microbiol Infect. 2022 Jan;28(1):101-106. doi: 10.1016/j.cmi.2021.08.009. Epub 2021 Aug 13. PMID: 34400343.

§ SARS-CoV-2 Subgenomic RNA Kinetics in Longitudinal Clinical Samples. Verma R, Kim E, Martínez-Colón GJ, Jagannathan P, Rustagi A, Parsonnet J, Bonilla H, Khosla C, Holubar M, Subramanian A, Singh U, Maldonado Y, Blish CA, Andrews JR. Open Forum Infect Dis. 2021 Jun 11;8(7):ofab310. doi: 10.1093/ofid/ofab310. eCollection 2021 Jul. PMID: 34295944

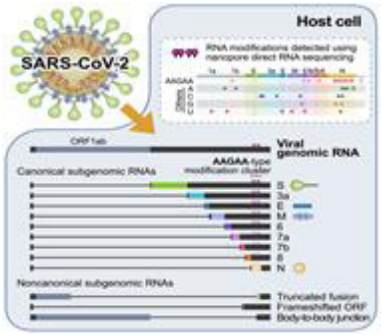
§ SARS-CoV-2 Subgenomic N (sgN) Transcripts in Oro-Nasopharyngeal Swabs Correlate with the Highest Viral Load, as Evaluated by Five Different Molecular Methods. Zollo M, Ferrucci V, Izzo B, Quarantelli F, Domenico CD, Comegna M, Paolillo C, Amato F, Siciliano R, Castaldo G, Capoluongo E. Diagnostics (Basel). 2021 Feb 12;11(2):288.

§ The Architecture of SARS-CoV-2 Transcriptome Kim D, Lee JY, Yang JS, Kim JW, Kim VN, Chang H. Cell. 2020 May 14;181(4):914-921.e10.

§ Test on stool samples improves the diagnosis of hospitalized patients: Detection of SARS-CoV-2 genomic and subgenomic RNA.
Moreira LVL, de Souza Luna LK, Barbosa GR, Perosa AH, Chaves APC, Conte DD, Carvalho JMA, Bellei N. J Infect. 2020 Dec 1:S0163-4453(20)30753-2. doi: 10.1016/j.jinf.2020.11.034.

CLINICAL SIGNIFICANCE

The search for the SARS-Cov-2 viral genome can be carried out on a naso-oropharyngeal swab using the NAT (Nucleic Acid Testing) molecular method in order to identify the subjects in which the infection is present. This approach, in fact, allows to identify the presence of viral genes in the naso-oropharyngeal swab in a highly specific and sensitive way. However, commonly used tests do not provide information on the presence of an active viral load or not. In fact, it is known that the viral load reaches an early peak in SARS-CoV-2 infections and then gradually declines, with small amounts of viral RNA that can remain in the nasopharyngeal tract for weeks or sometimes months.



Cell 2020 May 14;181(4):914-921.e10.

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Subgenomic N (sgN) SARS-CoV-2 ONE-STEP RT-PCR KIT

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-004-100
RDM Code: 2218988/R
Tests: 100 Reactions: 110
CND Code: W0105040599
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
Mix RT-PCR	Mix RT-PCR 4X	1 x 560 µl	-20° C
Mix probes and oligonucleotides Mix for subN, ORF1a, E envelope and RNaseP genes	Mix sgN SARS-CoV-2	1 x 560 µl	-20° C
Recombinant RNA Positive Control (200 copies/µl)	Control +	1 x 40 µl	-20° C
Buffer Negative Control	Control -	1 x 80 µl	-20° C

TECHNICAL CHARACTERISTICS

COD. INFET-004- 100

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA of cells contained in nasopharyngeal and/or oropharyngeal swab
POSITIVE CONTROL	Recombinant RNA
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx e Agilent AriaDx
TECHNOLOGY	RT-PCR (Reverse transcriptase-polymerase chain reaction) and subsequent detection with qPCR-Real-time
RUNNING TIME	75 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (15 min); 1 cycle at 95 °C (2 min); 44 cycles at 95 °C (5 sec) + 60 °C (45 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	30 copies of viral genome
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100% /98%

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BioMol LABORATORIES

S.T.D.

SEXUALLY TRANSMITTED DISEASES (STDs)
Qualitative determination

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-006-25
RDM Code: 2256478/R
Tests: 25 Reactions: 31 X 2
CND Code: W0105040599
Produttore: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for Real-Time PCR amplification
**reagents for the extraction of microbial DNA are not supplied in the kit*

PRODUCT CHARACTERISTICS

Molecular method "NAT" (Nucleic Acid Testing): Qualitative determination of the genome of sexually transmitted microbiological species *Mycoplasma hominis*, *Ureaplasma parvum* and *urealyticum*, *Gardnerella vaginalis*, *Neisseria gonorrhoea*, *Trichomonas vaginalis* and *Mycoplasma genitalium* by PCR (polymerase chain reaction) technique and subsequent detection in PCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Sexually transmitted diseases (STDs) are a leading cause of infertility, long-term disability, ectopic pregnancy, and premature birth. They increase the risk of developing genital cancers and represent a serious medical, social and economic problem for thousands of adults and children around the world.

To date, it has been shown that more than 30 pathogens such as bacteria, viruses, and parasites are transmitted via sexual contact. *Gardnerella vaginalis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, *Trichomonas vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Ureaplasma parvum*, are the main pathogens responsible for sexually transmitted diseases.

§ The diagnostics landscape for sexually transmitted infections ISBN 978-92-4-007712-6 (electronic version); ISBN 978-92-4-007713-3 (print version) World Health Organization 2023
§ PLoS One. 2023 Mar 6;18(3):e0282439. doi: 10.1371/journal.pone.0282439. eCollection 2023. Simultaneous real-time PCR detection of nine prevalent sexually transmitted infections using a predesigned double-quenched TaqMan probe panel
§ Molecular Detection of Sexually Transmitted Infections in Women with and without Human Papillomaviruses Infection Who Referred to Tehran West Hospitals in Iran. Reports of Biochemistry & Molecular Biology Vol.10, No.3, Oct 2021.
§ Design and Evaluation of a Novel Multiplex Real-Time PCR Melting Curve Assay for the Simultaneous Detection of Nine Sexually Transmitted Disease Pathogens in Genitourinary Secretions. Front. Cell. Infect. Microbiol., 12 November 2019 Sec. Clinical Microbiology Volume 9 - 2019
§ Journal of Medical Microbiology (2014), 63, 162–175. Identification, quantification and subtyping ofGardnerella vaginalis in noncultured clinical vaginalsamples by quantitative PCR
§ PCR for Diagnosis of Male Trichomonas vaginalis Infection with Chronic Prostatitis and Urethritis. Korean J Parasitol Vol. 50, No. 2: 157-159, June 2012.
§ A comparative study of three different PCR assays for detection of Mycoplasma genitalium in urogenital specimens from men and women. Journal of Medical Microbiology (2008), 57, 304–309.
§ Specific and Sensitive Detection of Neisseria gonorrhoeae in Clinical Specimens by Real-Time PCR. JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2005, p. 5653–5659 Vol. 43, No. 11 doi: 10.1128/JCM.43.11.5653–5659.2005.
§ Sequence of cDNA coding for a 65 kDa adhesive protein for the specific detection of Trichomonas vaginalis by PCR. FEMS Microbiology Lcrters 12Y (IYYS) 21-26.
§ Detection of Mycoplasma genitalium by PCR Amplification of the 16S rRNA Gene. JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2003, p. 261–266. DOI: 10.1128/JCM.41.1.261–266.2003
§ Species Identification and Subtyping of Ureaplasma parvum and Ureaplasma urealyticum Using PCR-Based Assays. JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2000, p. 1175–1179.

CLINICAL SIGNIFICANCE

Gardnerella vaginalis is a predominant anaerobic bacterium responsible for bacterial vaginosis (BV) in women. Gonorrhea, caused by the bacterium *Neisseria gonorrhoeae*, is the second most common STD after *Chlamydia trachomatis* infection. Infections can lead to long-term consequences, such as pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancy, neonatal conjunctivitis, and infertility. *Neisseria gonorrhoeae* infection has also been reported to increase the risk of human immunodeficiency virus (HIV) infection. *Mycoplasma genitalium* accounts for approximately 15-20% of cases of nongonococcal urethritis and 40% of cases of persistent or recurrent urethritis. Trichomoniasis, an infection caused by the protozoan *Trichomonas vaginalis*, can be associated with urethritis and prostatitis. *Mycoplasma hominis* is commonly implicated in the genesis of bacterial vaginosis and pelvic inflammatory disease. *Ureaplasma* is a bacterium of the mycoplasma family, responsible for the onset of infections especially at the genital level. There are two species of *Ureaplasma*: *urealyticum* and *parvum*.

The product INFET-006 allows the qualitative determination of the genome of sexually transmitted microbiological species *Mycoplasma hominis*, *Ureaplasma parvum* and *urealyticum*, *Gardnerella vaginalis*, *Neisseria gonorrhoea*, *Trichomonas vaginalis* and *Mycoplasma genitalium* by PCR (polymerase chain reaction) technique and subsequent detection in Real-time PCR.

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BioMol LABORATORIES

SEXUALLY TRANSMITTED DISEASES (STDs)
Qualitative determination

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: INFET-006-25
RDM Code: 2256478/R
Tests: 25 Reactions: 31 X 2
CND Code: W0105040599
Produttore: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for Real-Time PCR amplification
**reagents for the extraction of microbial DNA are not supplied in the kit*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		INFET-006-25	
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 5X	1 x 310 µl	-20° C
Mix oligonucleotides and probes Mycoplasma hominis, Ureaplasma parvum and urealyticum, Gardnerella vaginalis	Mix MST-1 10 X	1 x 77,5 µl	-20° C
Mix oligonucleotides and probes Neisseria gonorrhoea, Trichomonas vaginalis, Mycoplasma genitalium	Mix MST-2 10X	1 x 77,5 µl	-20° C
Deionized H_20	Deionized H_20	1 x 1 ml	-20° C
Genomic DNA or recombinant DNA	Control +	1 x 40 µl	-20° C
Genomic DNA or recombinant DNA	Control -	1 x 40 µl	-20° C

TECHNICAL CHARACTERISTICS

COD. INFET-006- 25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Microbial DNA in vaginal swab and biological fluids
POSITIVE CONTROLS	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; Oligonucleotides and specific probes
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 40 cycles at 95 °C (15 sec) + 57 °C (25 sec) + 72 °C (40 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,016 ng of host-cell genomic DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100% /98%

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BioMol LABORATORIES

ONCOHEMATOLOGY

MGMT gene promoter methylation (O^6-methylguanine DNA methyltransferase)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-001-25
CND Code: W01060299
RDM Code: 2256631/R
Tests: 25 Reactions: 31 x 2
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

*The kit consists of reagents for modification with sodium bisulfite and for amplification in MSP-PCR *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-SOMATIC MUTATIONS.** Determination of the methylation status of the MGMT (O6-methylguanine DNA methyltransferase) gene promoter by MSP (methylation-specific PCR) technique and subsequent detection by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

DNA O^6-methylguanine methyltransferase (MGMT) is a DNA repair enzyme encoded by the MGMT gene present at the 10q26 locus. The MGMT enzyme removes the alkyl groups from the O^6 position of guanine acting itself as an acceptor and this reaction leads to an irreversible inactivation of the enzyme. MGMT transcription is regulated by epigenetic mechanisms. Indeed, methylation of CpG dinucleotides in the promoter region of MGMT causes gene silencing, loss of MGMT expression and inability to remove alkyl groups from methylated guanine with consequent alteration of the normal DNA structure.

§ Cancer Sci. 2024 Oct;115(10):3394-3402. doi: 10.1111/cas.16297. Epub 2024 Jul 30. MGMT protein expression is a reliable predictive biomarker for temozolomide-containing chemotherapy in osteosarcoma

§ Cochrane Database Syst Rev. 2021 Mar 12;3(3):CD013316. doi: 10.1002/14651858.CD013316.pub2.

§ Prognostic value of test(s) for O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation for predicting overall survival in people with glioblastoma treated with temozolomide

§ Genome-wide methylation profiling of glioblastoma cell-derived extracellular vesicle DNA allows tumor classification. Neuro Oncol 2021 Jul 1; 23 (7):1087-1099. doi: 10.1093/neuonc/noab012

§ MGMT methylation may benefit overall survival in patients with moderately vascularized glioblastomas. Eur Radiol 2021 Mar; 31(3):1738-1747. doi: 10.1007/s00330-020-07297-4. Epub 2020 Oct 1.

§ The significance of MGMT methylation in Glioblastoma Multiforme prognosis. J Pak Med Assoc 2018 Jul; 68(7):1137-1139.

§ Role of MGMT as biomarker in colorectal cancer. World J Clin Cases 2014 Dec 16; 2(12): 835–839.

§ Characterizing DNA methylation alterations from The Cancer Genome Atlas. J Clin Invest 2014 Jan 2; 124(1): 17–23.

§ Detection of aberrant promoter hypermethylation of tumor suppressor genes in serum DNA from non-small cell lung cancer patients. Cancer Res 1999 59: 67-70.

§ Methylation-specific PCR: a novel PCR assay for methylation status of CpG islands. Proc Natl Acad Sci U S A 1996 Sep 3; 93(18): 9821–9826.

CLINICAL SIGNIFICANCE

MGMT protects normal cells from carcinogens, but the activity of MGMT also protects cancer cells from the lethal effects of chemotherapy with alkylating agents such as dacarbazine (DTIC) or temozolomide (TMZ), which are widely used for the treatment of melanoma and glioblastoma. In fact, MGMT removes the methyl groups from the O^6 position of the guanines, thus making TMZ ineffective.

In glioblastomas, MGMT promoter methylation is predictive of the therapeutic benefit of the alkylating agent temozolomide, as shown in several phase III clinical trials, and MGMT gene methylation status has become the first predictive biomarker in neuro-oncology.

MGMT gene promoter methylation also plays an important role in colorectal carcinogenesis, occurring in approximately 30%-40% of metastatic colorectal cancer. Its prognostic role is not yet defined, but the loss of MGMT expression, which is secondary to gene promoter methylation, results in an interestingly high response to alkylating agents.

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BioMol LABORATORIES

MGMT gene promoter methylation (O^6-methylguanine DNA methyltransferase)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-001-25
CND Code: W01060299
RDM Code: 2256631/R
Tests: 25 Reactions: 31 x 2
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

*The kit consists of reagents for modification with sodium bisulfite and for amplification in MSP-PCR *reagents for the extraction of genomic DNA are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-001-25	
Conversion reagent	Conversion reagent	3 tubes	RT
Dilution buffer	Buffer A	900 µl	RT
Buffer	Buffer B	200 µl	RT
Binding Buffer	Buffer C	15 ml	RT
Wash buffer	Buffer D	3 ml	RT
Desulphonation Buffer	Buffer E	5 ml	RT
Elution Buffer	Buffer F	750 µl	RT
Columns	Columns	25	RT
Collection tubes	Collection tubes	25	RT
Mix oligonucleotides	Mix A methylated 10X	1 x 77,5 µl	-20°C
Mix oligonucleotides	Mix B unmethylated 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real time PCR 2X	1 x 775 µl	-20°C
Deionized H_20	Deionized H_20	1 x 1 ml	-20°C
Genomic or recombinant DNA methylated and unmethylated	Control +	100 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. ONC-001-25

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 4 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides; 1 SYBR-GREEN/FAM fluorescence channel
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
RUNNING TIME	150 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (15 min); 45 cycles 95 °C (40 sec) +60 °C (40 sec) + 72 °C (40 sec); 1 dissociation cycle at 70 °C with an increase of 0,2 °C
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 2.5 ng of sodium bisulfite modified DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

BCR-ABL1 t (9;22) ONE-STEP RT-PCR QUALITATIVE DETECTION (p210, p190, p230)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-010-25
CND Code: W01060208-T(9;22)
RDM Code: 2079229/R
Tests: 25
Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS**.
Qualitative detection of the t(9;22) BCR-ABL1 translocation by RT-PCR technique (Reverse transcriptase-polymerase chain reaction) and subsequent detection in Real-time-PCR.
The device has been developed in accordance with Europe Against Cancer (EAC) guidelines and optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

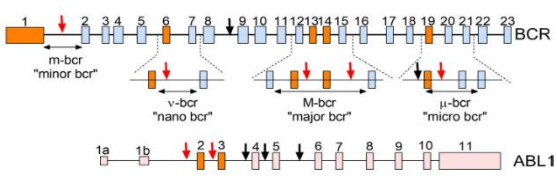
SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell. According to the 2016 World Health Organization criteria, the MPN classification includes seven subcategories: chronic myeloid leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), eosinophilic leukemia chronic - not otherwise specified and MPN, unclassifiable (MPN-U).
The Philadelphia chromosome (Ph) derived from the translocation between chromosomes 9 and 22 with subsequent BCR-ABL1 fusion, is present in about 95% of cases of chronic myeloid leukemia (CML), in 25-30% of cases of acute lymphoblastic leukemia (ALL) of adults and in 2-4% of ALL of children.

§ Am J Hematol. 2024 Aug 2.doi: 10.1002/ajh.27443. Online ahead of print. Chronic myeloid leukemia: 2025 update on diagnosis, therapy, and monitoring
§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9; 129(6):667-679. Review.
§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19; 127(20): 2391-405.
§ Leukemia. 2015 May;29(5):999-1003. doi: 10.1038/leu.2015.29. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia
§ Guidelines for the measurement of BCR-ABL1 transcripts in chronic myeloid leukaemia. Br J Haematol. 2011 Apr; 153(2):179-90.
§ J Clin Oncol. 2009 Dec 10;27(35):6041-51. doi: 10.1200/JCO.2009.25.0779. Epub 2009 Nov 2. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet
§ Leukemia. 2009 Nov;23(11):1957-63. doi: 10.1038/leu.2009.168. Epub 2009 Aug 27. Harmonization of molecular monitoring of CML therapy in Europe
§ European LeukemiaNet (2009). Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. Journal of Clinical Oncology, 27, 6041–6051.
§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan; 22(1):14-22. Review.
§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

CLINICAL SIGNIFICANCE

The BCR-ABL1 rearrangement results in the generation of fusion proteins with constitutive tyrosine kinase activity. Based on the specific breakpoints of the rearrangement, different isoforms of the BCR-ABL1 fusion protein are generated, which correlate with different leukemic phenotypes.
Three breakpoint regions in the BCR gene have been described: major (M-BCR), minor (m-BCR), and micro (µBCR). More than 95% of Ph+ CML patients have the rearrangement in the M-BCR region (p210 BCR-ABL1), with the e13a2 and e14a2 transcripts most represented. The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript mostly represented. A third BCR-ABL1 protein, p230BCR-ABL1, can also be observed.
The ONC-010 medical device allows the qualitative detection of the t(9; 22) BCR-ABL1 translocation and the M-bcr (e14a2, e13a2, e13a3 and 14a3), m-bcr (e1a3 and e1a2), and µ-bcr (e18a2, e18a3, e19a2 and e19a3) transcripts by RT-PCR (Reverse transcriptase-polymerase chain reaction) technique and subsequent detection in Real-time PCR.



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BioMol LABORATORIES

BCR-ABL1 t (9; 22) ONE-STEP RT-PCR QUALITATIVE DETECTION (p210, p190, p230)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-010-25
CND Code: W01060208
RDM Code: 2079229/R
Tests: 25
Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-010-25	
Mix oligonucleotides and probes	Mix PCR p210 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR p190 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR p230 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix buffer and RT enzyme and Taq-polymerase	Mix RT-PCR 4X	1 X 465 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	- 20 °C
Recombinant RNA	**Positive control** p190/p210/p230-abl	1 X 90 µl	- 20 °C
Recombinant RNA	**Negative control** housekeeping	1 X 90 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-010-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions (ONC-010-25); positive control for p190/p210/p230 and abl; negative control for abl.
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes for the translocation and for the abl gene; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris b-CUBE and Hyris b-CUBE3 with Hyris bAPP.
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles 95 °C (5 sec) + 60 °C (45 sec).
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 10,8 COPIES; ≥ 0,0032%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

JAK2 (Janus kinase 2) V617F GENE MUTATION
Qualitative detection

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-011-25 RDM Code: 1699886/R
Tests: 25 Reactions: 31
REF: ONC-011-50 RDM Code: 2256590/R
Tests: 50 Reactions: 62
CND Code: W01060299
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-SOMATIC MUTATIONS.**
Qualitative detection of the V617F mutation of the JAK2 gene (Janus kinase 2) by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell.
The JAK (Janus Kinases) family of enzymes includes JAK1, JAK2, JAK3, and TYK2. These molecules bind to the cytosolic domains of cytokine receptors and are essential for the message transduction of cytokines and growth factors.
Polycythemia vera (PV), idiopathic myelofibrosis (PMF), and essential thrombocythemia (ET) show shared phenotypic features (MPN BCR/ABL neg) that result from direct or indirect constitutive activation of the related tyrosine kinase JAK2 to the hematopoietic growth factor receptors for erythropoietin (EPOR) and thrombopoietin (MPL) and to the G-CSF (granulocyte colony-stimulating factor) receptor.

§ Cancers (Basel). 2024 Apr 26;16(9):1679. doi: 10.3390/cancers16091679.Advances in Molecular Understanding of Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis: Towards Precision Medicine
§ Front. Pharmacol., 22 July 2024 Sec. Pharmacogenetics and Pharmacogenomics Volume 15 - 2024
§ Myelofibrosis Blood, 20 APRIL 2023 | VOLUME 141, NUMBER 16 1
§ Diagnostics (Basel). 2023 Jan 3;13(1):163. doi: 10.3390/diagnostics13010163. Molecular Genetics of Thrombotic Myeloproliferative Neoplasms: Implications in Precision Oncology
§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9;129(6):667-679. Review.
§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-405. Epub 2016 Apr 11.
§ Mutations in MPNs: prognostic implications, window to biology, and impact on treatment decision. Hematology Am Soc Hematol Educ Program.2016 Dec 2;2016(1):552-560.
§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan;22(1):14-22. Epub 2007 Sep 20. Review.

CLINICAL SIGNIFICANCE

Direct activation of JAK2 is caused by a point mutation (V617F in JAK2 exon 14 or, less commonly, by insertions or deletions in exon 12 of the JAK2 gene).
Indirect activation, on the other hand, is caused by point mutations in the thrombopoietin receptor, MPL, or by mutations in the CALR chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly.
The JAK2 V617F mutation results from a guanine-to-thymine substitution at nucleotide 1849 of exon 14 of the JAK2 gene, resulting in a single amino acid valine/phenylalanine substitution at codon 617. The mutation results in ligand-independent JAK2 kinase activity. This mutation can be found in approximately 70% of Philadelphia chromosome-negative MPNs (Ph-MPDs): it is present in 65-95% of PV patients, 23-57% of ET patients, and 35-50 % of patients affected by PMF.
20-30% of patients with polycythemia vera become homozygous for the mutation through a loss-of-heterozygosity mechanism.

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BioMol LABORATORIES

JAK2 (Janus kinase 2) V617F MUTATION
Qualitative detection

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-011-25 RDM Code: 1699886/R
Tests: 25 Reactions: 31
REF: ONC-011-50 RDM Code: 2256590/R
Tests: 50 Reactions: 62
CND Code: W01060299
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		ONC-011-25	ONC-011-50	
Mix oligonucleotides and probes	Mix V617F JAK2 10X	1 x 77,5 µl	2 x 77,5 µl	- 20 °C
Mix buffer and Taq-polymerase	Mix Real-Time PCR 5X	1 x 155 µl	2 x 155 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	- 20 °C
Genomic DNA or recombinant DNA Control 1	Control 1 MUT 40-70% V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA Control 2	Control 2 MUT 100% V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA Control 3	Control 3 WT 100% V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-011-25 / COD. ONC-011-50

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 (ONC-011-25) Recombinant DNA for at least 6 analytical sessions (ONC-011-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris b-CUBE and Hyris b-CUBE3 con Hyris bAPP
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles at 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of genomic DNA; ≥ 2% JAK2 (MUT) versus JAK2 (WT).
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

JAK2 (Janus kinase 2) - V617F MUTATION
Quantitative detection

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-012-25 RDM Code: 2256685/R
Tests: 25 Reactions: 38
REF: ONC-012-50 RDM Code: 1775837/R
Tests: 50 Reactions: 76
CND Code: W01060299
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 QUANTITATIVE PCR-SOMATIC MUTATIONS.** Relative quantitative detection of the V617F mutation of the JAK2 (Janus kinase 2) gene by Real-Time PCR technique. Optimized Kit for Biorad CFX96, Biorad Opus Dx and Agilent AriaDx Real-Time PCR.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell.
The JAK (Janus Kinases) family of enzymes includes JAK1, JAK2, JAK3, and TYK2. These molecules bind to the cytosolic domains of cytokine receptors and are essential for the message transduction of cytokines and growth factors.
Polycythemia vera (PV), idiopathic myelofibrosis (PMF), and essential thrombocythemia (ET) show shared phenotypic features (MPN BCR/ABL neg) that result from direct or indirect constitutive activation of the related tyrosine kinase JAK2 to the hematopoietic growth factor receptors for erythropoietin (EPOR) and thrombopoietin (MPL) and to the G-CSF (Granulocyte Colony-Stimulating Factor) receptor.

CLINICAL SIGNIFICANCE

Direct activation of JAK2 is caused by a point mutation (V617F in JAK2 exon 14 or, less commonly, by insertions or deletions in exon 12 of the JAK2 gene). Indirect activation, on the other hand, is caused by point mutations in the thrombopoietin receptor, MPL, or by mutations in the CALR chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly. The JAK2 V617F mutation results from a guanine-to-thymine substitution at nucleotide 1849 of exon 14 of the JAK2 gene, resulting in a single amino acid valine/phenylalanine substitution at codon 617. The mutation results in ligand-independent JAK2 kinase activity. This mutation can be found in approximately 70% of Philadelphia chromosome-negative MPNs (Ph-MPDs): it is present in 65-95% of PV patients, 23-57% of ET patients, and 35-50 % of patients affected by PMF. The new molecular knowledge in the field of chromosome-Philadelphia negative MPNs has allowed to identify in the V617F mutation of the JAK2 gene a sure diagnostic criterion to be included in the laboratory routine in case of suspected MPN (as suggested by the diagnostic criteria of the WHO (World Health Organization; Tefferi et al., Leukemia 2008).

§ Cancers (Basel). 2024 Apr 26;16(9):1679. Advances in Molecular Understanding of Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis: Towards Precision Medicine
§ Front. Pharmacol., 22 July 2024 Sec. Pharmacogenetics and Pharmacogenomics Volume 15 - 2024
§ Ir J Med Sci. 2024 Aug 14. Association between JAK2V617F variable allele frequency and risk of thrombotic events in patients with myeloproliferative neoplasms
§ Myelofibrosis Blood, 20 APRIL 2023 | VOLUME 141, NUMBER 16 1
§ Diagnostics (Basel). 2023 Jan 3;13(1):163. doi: 10.3390/diagnostics13010163. Molecular Genetics of Thrombotic Myeloproliferative Neoplasms: Implications in Precision Oncology
§ Ann Hematol. 2019 May;98(5):1111-1118. International external quality assurance of JAK2 V617F quantification
§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9;129(6):667-679. Review.
§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-405. Epub 2016 Apr 11.
§ Mutations in MPNs: prognostic implications, window to biology, and impact on treatment decision. Hematology Am Soc Hematol Educ Program.2016 Dec 2;2016(1):552-560.
§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan;22(1):14-22. Epub 2007 Sep 20. Review.

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BioMol LABORATORIES

JAK2 (Janus kinase 2) - V617F MUTATION
Quantitative detection

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-012-25 RDM Code: 2256685/R
Tests: 25 Reactions: 45
REF: ONC-012-50 RDM Code: 1775837/R
Tests: 50 Reactions: 70
CND Code: W01060299
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		ONC-012-25	ONC-012-50	
Mix oligonucleotides and probes	Mix V617F JAK2 10X	1 x 95 µl	2 x 95 µl	- 20 °C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 5X	1 x 190 µl	2 x 190 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	- 20 °C
Genomic DNA or recombinant DNA-standard	CAL 1 (Standard 1) (600000 copies) V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA-standard	CAL 2 (Standard 2) (60000 copies) V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA-standard	CAL 3 (Standard 3) (6000 copies) V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA-standard	CAL 4 (Standard 4) (600 copies) V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA Control 1	**Control 1** Range 40-70% **MUT** V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA Control 2	**Control 2 MUT** 100% V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA Control 3	**Control 3 WT** 100% V617F JAK2	1 x 22 µl	2 x 22 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-012-25 / COD. ONC-012-50

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 (ONC-012-25) Recombinant DNA for at least 6 analytical sessions (ONC-012-50)
STANDARD CURVE	Recombinant DNA, 4 points at known concentration from 300 to 300000 copies for each allele. Analysis result as allelic burden (% MUT/WT+ MUT).
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	110 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles at 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of genomic DNA; ≥ 2% JAK2 (MUT) versus JAK2 (WT); ≥ 10 copies.
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

MPL W515L/K MUTATION (MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-013-25 RDM Code: 1772905/R
Tests: 25 Reactions: 31 x 2
REF: ONC-013-50 RDM Code: 2256722/R
Tests: 50 Reactions: 62 x 2
CND Code: W01060299
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-SOMATIC MUTATIONS.**
Detection of the W515L/K mutation of the MPL gene (MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE) by Real-Time PCR technique. Kit optimized for Real Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematological malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic and/or mast cell. The JAK (Janus Kinases) family of enzymes includes JAK1, JAK2, JAK3, and TYK2. These molecules bind to the cytosolic domains of cytokine receptors and are essential for the transduction of cytokine and growth factor messages. Polycythemia vera (PV), idiopathic myelofibrosis (PMF) and essential thrombocythemia (ET) show shared phenotypic features (MPN BCR/ABL neg) that are the consequence of direct or indirect constitutive activation of JAK2, the tyrosine kinase related to hematopoietic growth factor receptors for erythropoietin (EPOR) and thrombopoietin (MPL) and to the G-CSF receptor (Granulocyte Colony-Stimulating Factor).

CLINICAL SIGNIFICANCE

Direct activation of JAK2 is caused by a point mutation (V617F in exon 14 JAK2 or, less commonly, by insertions or deletions in exon 12 of the JAK2 gene). Indirect activation, on the other hand, is caused by point mutations in the thrombopoietin receptor, MPL or by mutations in the CALR chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly. The JAK2 V617F mutation is the result of the substitution of a guanine in thymine at nucleotide 1849 of exon 14 of the JAK2 gene, which causes a single valine/phenylalanine amino acid substitution at codon 617. The mutation causes ligand-independent JAK2 kinase activity. This mutation can be found in about 70% of Philadelphia chromosome-negative MPNs (Ph-MPDs): it is present in 65-95% of PV patients, 23-57% of ET patients and 35-50% of PMF patients. The new molecular knowledge in the field of chromosome-negative Philadelphia MPNs has made it possible to identify the V617F mutation of the JAK2 gene as a safe diagnostic criterion to be included in the laboratory routine in case of suspected MPN (as suggested by the diagnostic criteria of the WHO (World Health Organization; Tefferi et al. Leukemia 2008).

§ *The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and indepth discussion. Blood Cancer J.2018 Feb 9; 8 (2):15. Doi: 10.1038/s41408-018-0054-y. Review*

§ *Essential thrombocythemia: a review of the clinical features, diagnostic challenges, and treatment modalities in the era of molecular discovery. Leuk Lymphoma. 2017 Dec; 58 (12):2786-2798.doi: 10.1080/10428194.2017.1312371. Epub 2017 May 15.*

§ *Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9; 129 (6):667-679. Review.*

§ *Mutations in MPNs: prognostic implications, window to biology, and impact on treatment decision. Hematology Am Soc Hematol Educ Program.2016 Dec 2; 2016 (1):552-560.*

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BioMol LABORATORIES

MPL W515L/K MUTATION (MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-013-25 RDM Code: 1772905/R
Tests: 25 Reactions: 31 x 2
REF: ONC-013-50 RDM Code: 2256722/R
Tests: 50 Reactions: 62 x 2
CND Code: W01060299
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		ONC-013-25	ONC-013-50	
Mix oligonucleotides and probes	Mix W515L MPL 10 X	1 x 77,5 µl	2 x 77,5 µl	- 20 °C
Mix oligonucleotides and probes	Mix W515K MPL 10 X	1 x 77,5 µl	2 x 77,5 µl	- 20 °C
Mix buffer and Taq-polymerase	Mix Real-Time PCR 2X	1 x 775 µl	2 x 775 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	1 x 1 ml	- 20 °C
Genomic DNA or recombinant DNA Negative control	Negative control W515W MPL	1 x 40 µl	2 x 40 µl	- 20 °C
Genomic DNA or recombinant DNA Positive control	Positive control W515L MPL W515K MPL	1 x 40 µl	2 x 40 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-013-25 / COD. ONC-013-50

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 (ONC-013-25) Recombinant DNA for at least 6 analytical sessions (ONC-013-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles at 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of genomic DNA, ≥ 2%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

CALR EXON 9 MUTATION
Type I (DEL 52bp) And Type II (INS 5bp)
(chaperone calreticulin)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-014-25 RDM Code: 1761183/R
Tests: 25 Reactions: 31 x 2
REF: ONC-014-50 RDM Code: 2256763/R
Tests: 50 Reactions: 62 x 2
CND Code: W01060299
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-SOMATIC MUTATIONS.**
Qualitative detection of the INS 5bp/DEL 52bp mutation of exon 9 of the CALR gene (chaperone calreticulin) by Real-Time PCR technique. The kit is optimized for Real-Time PCR instruments Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematological malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic and/or mast cell. According to the 2016 World Health Organization criteria, the classification of MPNs includes seven subcategories: chronic myeloid leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic eosinophilic leukemia - not otherwise specified, and MPN, unclassifiable (MPN-U). Polycythemia vera (PV), idiopathic myelofibrosis (PMF) and essential thrombocythemia (ET) show shared phenotypic features (MPN BCR/ABL neg) that are the consequence of direct or indirect constitutive activation of JAK2, the tyrosine kinase related to hematopoietic growth factor receptors for erythropoietin (EPOR) and thrombopoietin (MPL) and to the G-CSF receptor (Granulocyte Colony-Stimulating Factor). Direct activation of JAK2 is caused by a point mutation (V617F in exon 14 JAK2) or, less commonly, by insertions or deletions in exon 12 of the JAK2 gene. Indirect activation of JAK2 is caused by point mutations in the thrombopoietin receptor, MPL or by mutations in the CAL chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly. CALR is a multi-functional protein (Ca^{2}+-binding protein) with chaperone activity, mainly located in the endoplasmic reticulum (ER).

CLINICAL SIGNIFICANCE

Somatic mutations of CALR are often represented by deletions/insertions in exon 9 and generate a "frameshift" mutation on the reading frame resulting in a new amino acid sequence at the carboxy-terminal domain of the protein. The mutated protein also loses the KDEL signal, which is necessary for the protein to localize in the endoplasmic reticulum. The two most frequent mutations correspond to a deletion of 52 bp (p.L367fs*46), also called type 1, and an insertion of 5 bp (p.K385fs*47), also called type 2. CALR mutations usually occur in the heterozygous state although few cases of homozygous mutations have been observed, more often for type 2 mutations.

§ Cancers (Basel). 2024 Apr 26;16(9):1679. doi: 10.3390/cancers16091679. Advances in Molecular Understanding of Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis: Towards Precision Medicine
§ Front. Cell Dev. Biol., 26 March 2024 Sec. Cancer Cell Biology Volume 12 – 2024
§ Essential thrombocythemia: a review of the clinical features, diagnostic challenges, and treatment modalities in the era of molecular discovery. Leuk Lymphoma. 2017 Dec; 58 (12):2786-2798. doi: 10.1080/10428194.2017.1312371. Epub 2017 May 15. Review
§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9; 129 (6):667-679. Review.
§ Mutations in MPNs: prognostic implications, window to biology, and impact on treatment decision. Hematology Am Soc Hematol Educ Program.2016 Dec 2; 2016 (1):552-560.
§ The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. Blood Cancer J. 2018 Feb 9; 8 (2):15. doi: 10.1038/s41408-018-0054-y. Review.

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BioMol LABORATORIES

CALR EXON 9 MUTATION
Type I (DEL 52bp) And Type II (INS 5bp)
(chaperone calreticulin)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-014-25 RDM Code: 1761183/R
Tests: 25 Reactions: 31 x 2
REF: ONC-014-50 RDM Code: 2256763/R
Tests: 50 Reactions: 62 x 2
CND Code: W01060299
Manufacturer: BioMol Laboratories srl

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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME		STORAGE
		ONC-014-25	ONC-014-50	
Mix oligonucleotides and probes	Mix Ins 5bp CALR 10X	1 x 77,5 µl	2 x 77,5 µl	- 20 °C
Mix oligonucleotides and probes	Mix Del 52bp CALR 10X	1 x 77,5 µl	2 x 77,5 µl	- 20 °C
Mix buffer and Taq-polymerase	Mix Real-Time PCR 5X	1 x 310 µl	2 x 310 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	2 x 1 ml	- 20 °C
Genomic DNA or recombinant DNA Positive control	Positive control Ins 5bp CALR Del 52bp CALR	1 x 30 µl	2 x 30 µl	- 20 °C
Genomic DNA or recombinant DNA Negative Control	Negative control Housekeeping	1 x 30 µl	2 x 30 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-014-25 / COD. ONC-014-50

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 (ONC-014-25) Recombinant DNA for at least 6 analytical sessions (ONC-014-50)
NEGATIVE CONTROLS	Recombinant DNA for at least 3 analytical sessions (ONC-014-25) Recombinant DNA for at least 6 analytical sessions (ONC-014-50)
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles at 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of genomic DNA, ≥ 1%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

BCR-ABL1 t (9; 22) ONE-STEP RT-PCR QUANTITATIVE DETECTION p210 (M-BCR)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-015-25
CND Code: W01060208– T(9;22)
RDM Code: 2259479/R
Tests: 25
Reactions: 50
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and PCR amplification.
**the reagents for total RNA extraction are not supplied in the kit*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUANTITATIVE PCR-SOMATIC MUTATIONS.**
Quantitative detection of the t(9;22) BCR-ABL1 breakpoint M-bcr translocation (p210, b3a2 and b2a2 transcripts) by RT-PCR (Reverse transcriptase-polymerase chain reaction) technique and subsequent detection in PCR-Real-time with **standard curve calibrated on ERM-AD623** curve (plasmid reference material produced and certified in accordance with European Reference Materials guidelines) and BCR-ABL1 M-bcr reference RNA.
The device was developed in accordance with **the Europe Against Cancer (EAC) guidelines** and optimized for Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx Real-Time PCR instruments.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell. According to the 2016 World Health Organization criteria, the MPN classification includes seven subcategories: chronic myeloid leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), eosinophilic leukemia chronic - not otherwise specified and MPN, unclassifiable (MPN-U).

The Philadelphia chromosome (Ph) derived from the translocation between chromosomes 9 and 22 with subsequent BCR-ABL1 fusion, is present in about 95% of cases of chronic myeloid leukemia (CML), in 25-30% of cases of acute lymphoblastic leukemia (ALL) of adults and in 2-4% of ALL of children.

§ Am J Hematol. 2024 Aug 2.doi: 10.1002/ajh.27443. Online ahead of print. Chronic myeloid leukemia: 2025 update on diagnosis, therapy, and monitoring

§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19; 127(20): 2391-405. Epub 2016 Apr 11.

§ Leukemia. 2015 May;29(5):999-1003. doi: 10.1038/leu.2015.29. Epub 2015 Feb 5. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia

§ Guidelines for the measurement of BCR-ABL1 transcripts in chronic myeloid leukaemia. Br J Haematol. 2011 Apr; 153(2):179-90. doi: 10.1111/j.1365-2141.2011.08603.x. Epub 2011 Mar 8.

§ J Clin Oncol. 2009 Dec 10;27(35):6041-51. doi: 10.1200/JCO.2009.25.0779. Epub 2009 Nov 2. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet

§ Leukemia. 2009 Nov;23(11):1957-63. doi: 10.1038/leu.2009.168. Epub 2009 Aug 27. Harmonization of molecular monitoring of CML therapy in Europe

§ European LeukemiaNet (2009). Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. Journal of Clinical Oncology, 27, 6041–6051.

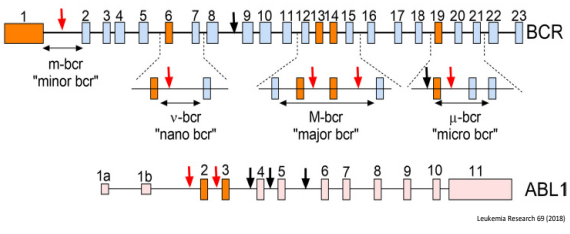
§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan; 22(1):14-22. Epub 2007 Sep 20. Review.

§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

CLINICAL SIGNIFICANCE

The BCR-ABL1 rearrangement results in the generation of fusion proteins with constitutive tyrosine kinase activity. Based on the specific breakpoints of the rearrangement, different isoforms of the BCR-ABL1 fusion protein are generated, which correlate with different leukemic phenotypes. Three breakpoint regions in the BCR gene have been described: major (M-BCR), minor (m-BCR), and micro (µ-BCR). More than 95% of Ph+ CML patients have the rearrangement in the M-BCR region (p210 BCR-ABL1), with the e13a2 and e14a2 transcripts most represented. The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript mostly represented. The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript mostly represented.

The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript most represented. Furthermore, a third BCR-ABL1 protein, p230BCR-ABL1, can be observed.



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BioMol LABORATORIES

BCR-ABL1 t (9; 22) ONE-STEP RT-PCR QUANTITATIVE DETECTION p210 (M-BCR)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-015-25
CND Code: W01060208– T(9;22)
RDM Code: 2259479/R
Tests: 25
Reactions: 50
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and PCR amplification.
**the reagents for total RNA extraction are not supplied in the kit*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-015-25	
Mix oligonucleotides and probes	Mix PCR p210 BCR-ABL1 4X	1 x 250 µl	- 20 °C
Mix buffer and RT/Taq Polym. enzyme	Mix RT-PCR 4X	1 x 250 µl	- 20 °C
Deionized H_2O	Deionized H_2O	1 x 1 ml	- 20 °C
Recombinant DNA/RNA	CAL 1 p210/abl – 1,08 x10^6 copies	1 x 30 µl	- 20 °C
Recombinant DNA/RNA	CAL 2 p210/abl -1,08 x10^5 copies	1 x 30 µl	- 20 °C
Recombinant DNA/RNA	CAL 3 p210/abl -1,08 x10^4 copies	1 x 30 µl	- 20 °C
Recombinant DNA/RNA	CAL 4 p210/abl - 1,08 x10^3 copies	1 x 30 µl	- 20 °C
Recombinant DNA/RNA	CAL 5 p210/abl - 1,08 x10^2 copies	1 x 30 µl	- 20 °C
Recombinant DNA/RNA	CAL 6 p210/abl - 10,8 copies	1 x 30 µl	- 20 °C
Recombinant RNA	Positive control p210/abl	1 x 30 µl	- 20 °C
Recombinant RNA	Negative control	1 x 30 µl	- 20 °C
Reference RNA (IS conversion)	Reference M-bcr p210/abl	2 x 20 µl	- 20 °C -80°C if > 1 month

TECHNICAL CHARACTERISTICS

COD. ONC-015-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate
POSITIVE CONTROLS, NEGATIVE CONTROLS AND REFERENCE	ONC-015-25: RNA for at least 3 analytical sessions Reference RNA, calibrated in accordance with WHO Primary Reference Panel NIBSC 09/138.
STANDARD CURVE	Recombinant DNA/RNA p210, 6 standard points with concentration from 1,08 x10^6 to 10,8 copies (calibrated with ERM-AD623 standard curve, produced and certified in accordance with European Reference Materials guidelines)
TECHNOLOGY	RT-PCR ONE-STEP in Real-time; oligonucleotides and specific probes; 2 FAM and HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 25° C (2 min); 1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 50 cycles at 95 °C (5 sec) + 60 °C (45 sec). Reading at 60 °C
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 10,8 copies; ≥ 0,0032%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

BCR-ABL1 t(9;22) (mBCR and µBCR) QUANTITATIVE DETECTION p190/p230

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-016-25
CND Code: W01060208– t (9;22)
RDM Code: 1822476/R
Tests: 25
Reactions: 50 x 2
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and PCR amplification.
**the reagents for total RNA extraction are not supplied in the kit*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUANTITATIVE PCR-SOMATIC MUTATIONS**. Quantitative detection of BCR-ABL1 t (9;22) breakpoint **m-bcr (e1a3 e e1a2)** and **µ-bcr (e18a2, e18a3, e19a2 e e19a3)** transcripts by reverse transcription, amplification with oligonucleotides and specific probes and subsequent detection with qPCR-Real-time using plasmids for standard curve. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

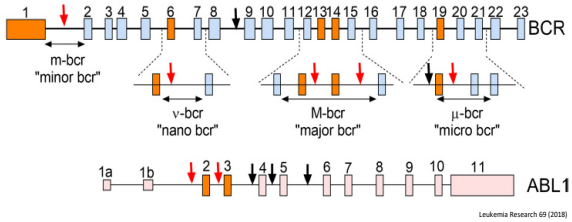
Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell. According to the 2016 World Health Organization criteria, the MPN classification includes seven subcategories: chronic myeloid leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), eosinophilic leukemia chronic - not otherwise specified and MPN, unclassifiable (MPN-U).

The Philadelphia chromosome (Ph) derived from the translocation between chromosomes 9 and 22 with subsequent BCR-ABL1 fusion, is present in about 95% of cases of chronic myeloid leukemia (CML), in 25-30% of cases of acute lymphoblastic leukemia (ALL) of adults and in 2-4% of ALL of children.

§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9; 129(6):667-679. doi: 10.1182/ blood-2016-10-695940. Epub 2016 Dec 27. Review.
§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan; 22(1):14-22. Epub 2007 Sep 20. Review.
§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19; 127(20): 2391-405. Epub 2016 Apr 11.
§ Guidelines for the measurement of BCR-ABL1 transcripts in chronic myeloid leukaemia. Br J Haematol. 2011 Apr; 153(2):179-90. doi: 10.1111/j.1365-2141.2011.08603.x. Epub 2011 Mar 8.
§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.
§ J Clin Oncol. 2009 Dec 10;27(35):6041-51. doi: 10.1200/JCO.2009.25.0779. Epub 2009 Nov 2. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet
§ Leukemia. 2009 Nov;23(11):1957-63. doi: 10.1038/leu.2009.168. Epub 2009 Aug 27. Harmonization of molecular monitoring of CML therapy in Europe
§ European LeukemiaNet (2009). Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. Journal of Clinical Oncology, 27, 6041–6051.
§ Leukemia. 2015 May;29(5):999-1003. doi: 10.1038/leu.2015.29. Epub 2015 Feb 5. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia

CLINICAL SIGNIFICANCE

The BCR-ABL1 rearrangement results in the generation of fusion proteins with constitutive tyrosine kinase activity. Based on the specific breakpoints of the rearrangement, different isoforms of the BCR-ABL1 fusion protein are generated, which correlate with different leukemic phenotypes. Three breakpoint regions in the BCR gene have been described: major (M-BCR), minor (m-BCR), and micro (µ-BCR). More than 95% of Ph+ CML patients have the rearrangement in the M-BCR region (p210 BCR-ABL1), with the e13a2 and e14a2 transcripts most represented. The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript mostly represented. A third BCR-ABL1 protein, p230 BCR-ABL1 (µBCR), can also be observed. This translocation is associated with CML characterized by granulocytic hyperplasia and, in general, with a more indolent clinical course.



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BioMol LABORATORIES

BCR-ABL1 t(9;22) (mBCR e µBCR) QUANTITATIVE DETECTION p190/p230

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-016-25
CND Code: W01060208– t (9;22)
RDM Code: 1822476/R
Tests: 25 x2
Reactions: 100
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and PCR amplification.
**the reagents for total RNA extraction are not supplied in the kit*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	LABEL	VOLUME	STORAGE
			ONC-016-25	
Mix oligonucleotides and probes	Mix PCR p190 BCR-ABL1 4X		1 x 250 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR p230 BCR-ABL1 4X		1 x 250 µl	- 20 °C
Mix buffer and RT/Taq polymerase enzyme	Mix RT-PCR 4X		1 x 500 µl	- 20 °C
Deionized H_20	Deionized H_20		1 x 1 ml	- 20 °C
Recombinant DNA	CAL 1 p190/abl – 1,08 x10^5 copies	CAL 1 p230/abl – 1,08 x10^5 copies	1 x 30 µl	- 20 °C
Recombinant DNA	CAL 2 p190/abl -1,08 x10^4 copies	CAL 2 p230/abl -1,08 x10^4 copies	1 x 30 µl	- 20 °C
Recombinant DNA	CAL 3 p190/abl -1,08 x10^3 copies	CAL 3 p230/abl -1,08 x10^3 copies	1 x 30 µl	- 20 °C
Recombinant DNA	CAL 4 p190/abl - 1,08 x10^2 copies	CAL 4 p230/abl - 1,08 x10^2 copies	1 x 30 µl	- 20 °C
Recombinant DNA	CAL 5 p190/abl – 10,8 copies	CAL 5 p230/abl – 10,8 copies	1 x 30 µl	- 20 °C
Recombinant RNA	Positive control p190/p230/abl		1 x 60 µl	- 20 °C
Recombinant RNA	Negative control housekeeping		1 x 60 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-016-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate
POSITIVE AND NEGATIVE CONTROLS	Recombinant RNA for 3 analytical sessions
STANDARD CURVE	Recombinant DNA p190 and p230, 5 points with known concentration from 10,8 to 1,085 copies, plasmid standard curve
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 25 °C (2 min); 1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 50 cycles at 95 °C (5 sec) + 60 °C (45 sec). Reading at 60°C
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	= 10 copies
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

BRAF V600E (T1799A) MUTATION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-021-25
CND Code: W01060299
RDM Code: 1703276/R
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-SOMATIC MUTATIONS.**
Qualitative detection of V600E mutation of the BRAF gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Oncogenic BRAF mutations are present in approximately 6% of human cancers and 40-50% of melanomas. BRAF mutations have also been identified in other common cancers, such as colorectal cancer (CRC) and non-small cell lung cancer (NSCLC), albeit at a lower frequency than melanoma (about 10% and 2-5%, respectively).

Other cancer types in which BRAF mutations are relatively common (> 5%) include: thyroid cancer, small bowel cancer, and gastrointestinal neuroendocrine cancer.

CLINICAL SIGNIFICANCE

The most frequently encountered activating BRAF mutation (approximately 90%) is a point mutation in exon 15 of the gene (c.1799T>A), which causes the substitution of a valine residue in glutamic acid at codon 600 (V600E) of the protein. This mutation confers two oncogenic properties to the BRAF protein: 1) increases the activity of the BRAF kinase domain (~500-fold compared to the wild-type one), 2) allows BRAF to be active as a monomer when RAS activity is reduced, independent of RAS-mediated activation. The result is a hyperfunctioning protein that continuously activates ERK, bypassing RAS activation and ignoring ERK-dependent negative feedback.

Other BRAF V600 variants found in less than 10% of malignant melanomas include valine to lysine (V600K), valine to aspartic acid (V600D), valine to methionine (V600M), and valine to arginine (V600R) substitutions at codon 600.

§ *Mutations in the Serine/Threonine Kinase BRAF: Oncogenic Drivers in Solid Tumors. Cancers 2024, 16, 1215. https://doi.org/10.3390/cancers16061215*

§ *Molecular Pathways and Mechanisms of BRAF in CancerTherapyClin Cancer Res 2022; 28:4618–28 doi: 10.1158/1078-0432.CCR-21-2138*

§ *Classifying BRAF alterations in cancer: new rational therapeutic strategies for actionable mutations. Oncogene. 2018 Mar 15. doi: 10.1038/s41388-018-0171-x. Review.*

§ *BRAF in non-small cell lung cancer (NSCLC): Pickaxing another brick in the wall. Cancer Treat Rev. 2018 Apr 24; 66:82-94. doi: 10.1016/j.ctrv.2018.04.006. Review.*

§ *Molecular testing for BRAF mutations to inform melanoma treatment decisions: a move toward precision medicine. Mod Pathol. 2018 Jan;31(1):24-38. doi: 10.1038/modpathol.2017.104.*

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BioMol LABORATORIES

BRAF V600E (T1799A) MUTATION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-021-25
CND Code: W01060299
RDM Code: 1703276/R
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*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-021-25	
Mix oligonucleotides and probes	Mix V600F BRAF 10X	1 x 77,5 µl	- 20 °C
Buffer and enzyme mix	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	Positive control **MUT** V600E BRAF	1 x 22 µl	- 20 °C
Genomic DNA or recombinant DNA	Negative control **WT** V600E BRAF	1 x 22 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-021-25	
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
NEGATIVE 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,Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
RUNNING TIME	110 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of genomic DNA; ≥ 2% B-RAF (MUT) VERSUS B-RAF (WT).
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

PML-RARα t (15; 17) (q22; q21) ONE-STEP RT-PCR QUALITATIVE DETECTION (bcr1, bcr2, bcr3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-030-25
CND Code: W01060299
RDM Code: 2256789/R
Tests: 25 Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS** medical devices.
Qualitative determination of the t(15; 17) PML-RARα translocation (bcr1, bcr2 and bcr3) by RT-PCR (Reverse transcriptase-polymerase chain reaction) technique and subsequent detection in PCR-Real-time.
Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

PML- RARα transcripts derive from the t (15; 17) (q22; q21) translocation and are associated with most cases of acute promyelocytic leukemia (APL).

The two genes fused in the t (15; 17) translocation are the PML (Promyelocytic leukemia) gene, located on chromosome 15, and the retinoic acid receptor α (RARα) gene located on chromosome 17. The chimeric protein PML- RARα it is a transcriptional repressor. In the absence of the ligand (retinoic acid, RA), it binds to DNA together with the co-repressors SMRT (silencing mediator for RAR and TR) and N-CoR (nuclear receptor corepressor) making chromatin inaccessible to transcriptional activators or various machinery for basal transcription.

§ Oncol Lett. 2024 Jan 22;27(3):114. doi: 10.3892/ol.2024.14246. eCollection 2024 Mar. Acute promyelocytic leukemia with PML/RARA (bcr1, bcr2 and bcr3) transcripts in a pediatric patient

§ Transpl Immunol. 2023 Dec:81:101919. doi: 10.1016/j.trim.2023.101919. Epub 2023 Aug 19. PML/RARa leukemia induced murine model for immunotherapy evaluation

§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

§ Reiter A, Saubele S, Grimwade D, Wiesmels JL, Segal M, Lafage-Pochitaloff M et al. Genomic anatomy of the reciprocal translocation t(15;17) in acute promyelocytic leukemia. Gene Chromosome Cancer 2003; 36: 175–188.

§ Zelent A, Guidez F, Melnick A, Waxman S, Licht JD. Translocations of the RARalpha gene in acute promyelocytic leukemia. Oncogene 2001; 20: 7186–7203.

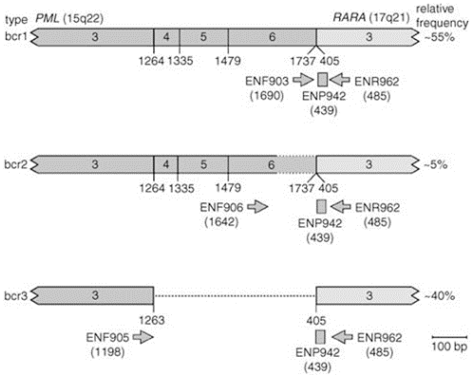
§ Grimwade D. The pathogenesis of acute promyelocytic leukaemia: evaluation of the role of molecular diagnosis and monitoring in the management of the disease. Br J Haematol 1999; 106: 591–613.

§ Longo L, Pandolfi PP, Biondi A, Rambaldi A, Mencarelli A, Lo Coco F et al. Rearrangements and aberrant expression of the retinoic acid receptor alpha gene in acute promyelocytic leukemias. J Exp Med 1990; 172: 1571–1575.

§ Lemons RS, Eilender D, Waldmann RA, Rebentisch M, Frej AK,Ledbetter *DH et al. Cloning and characterization of the t(15;17) translocation breakpoint region in acute promyelocytic leukemia. Genes Chromosomes Cancer 1990; 2: 79–87.*

CLINICAL SIGNIFICANCE

RARα breakpoints always occur in intron 2 which is 17 kb long while for the PML locus, in the t(15;17) translocation breakpoints three regions are involved: intron 6 (bcr1; 55% of cases) , exon 6 (bcr2; 5% of cases) and intron 3 (bcr3; 40% of cases). As a result, therefore, there are three possible PML- RARα isoforms: the long isoform L (bcr1), the variant isoform V (bcr2), and the short isoform S (bcr3).



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BioMol LABORATORIES

PML-RARα t (15; 17) (q22; q21) ONE-STEP RT-PCR QUALITATIVE DETECTION (bcr1, bcr2, bcr3)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-030-25
CND Code: W01060299
RDM Code: 2256789/R
Tests: 25 Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-030-25	
Mix oligonucleotides and probes	Mix PCR PML-RARα bcr1 4X	1 x 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR PML-RARα bcr2 4X	1 x 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR PML- RARα bcr3 4X	1 x 155 µl	- 20 °C
Mix buffer and Taq-polymerase	Mix RT-PCR 4X	1 x 465 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	- 20 °C
Recombinant RNA Positive control	Positive control bcr1 - bcr2- bcr3- abl	1 x 90µl	- 20 °C
Recombinant RNA Negative control	Negative control	1 x 90 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-030-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions; single positive control for bcr1, bcr2, bcr3; negative control for abl
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels.
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles at 95 °C (5 sec) + 60 °C (45 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of RNA; ≥1%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

AML1-ETO t (8; 21) (Q22; Q22) ONE-STEP RT-PCR QUALITATIVE DETECTION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-031-25
CND Code: W01060299
RDM Code: 2256801/R
Tests: 25 Reactions: 31
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

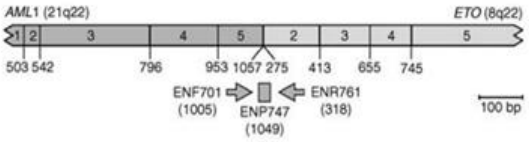
Device belonging to the family of in vitro **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS** medical devices.
Qualitative detection of AML1-ETO t(8;21) translocation by RT-PCR technique (Reverse transcriptase-polymerase chain reaction) and subsequent detection in Real-time-PCR. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Current treatment protocols for acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) are based on prognostic factors, which contribute to therapy stratification. Key prognostic factors identified in leukemia over the years include pretreatment characteristics such as age, WBC count, immunophenotypic profiles, specific chromosomal abnormalities, aberrant fusion genes (FGs), and mutations. The AML1/ETO fusion transcript is expressed in all patients with acute myeloid leukemia (AML) t (8; 21) (q22; q22).

CLINICAL SIGNIFICANCE

The translocation between chromosomes 8 and 21, t(8;21) (q22; q22), is one of the most frequent recurrent cytogenetic abnormalities in acute myeloid leukemia (AML). The t(8;21) causes the fusion of the AML1 gene on chromosome 21 with the ETO gene on chromosome 8. The new chimeric gene (AML1/ETO) produces a transcript that appears to be important for maintaining the leukemic phenotype in leukemic cell lines. It is associated with a good response to chemotherapy, with a high rate of remission and survival.



Identification scheme of the three AML1/ETO translocation points through the different combination of primers. (*Leukemia. Blood 1996;88:2183–2191.*)

§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

§ Appelbaum FR. Perspectives on the future of chronic myeloid leukemia treatment. Semin Hematol 2001; 38: 35–42.

§ Kottaridis PD, Gale RE, Frew ME, Harrison G, Langabeer SE, Belton AA et al. The presence of a FLT3 internal tandem duplication in patients with acute myeloid leukemia (AML) adds important prognostic information to cytogenetic risk group and response to the first cycle of chemotherapy: analysis of 854 patients from the United Kingdom Medical Research Council AML 10 and 12 trials. Blood 2001; 98: 1752–1759.

§ Lowenberg B, Downing JR, Burnett A. Acute myeloid leukemia. N Engl J Med 1999; 341: 1051–1062.

§ Grimwade D, Walker H, Oliver F, Wheatley K, Harrison C, Harrison G et al. The importance of diagnostic cytogenetics on outcome in AML: analysis of 1,612 patients entered into the MRC AML 10 trial. The Medical Research Council Adult and Children's Leukaemia Working Parties. Blood 1998; 92: 2322–2333.

§ Jurlander J, Caligiuri MA, Ruutu T, Baer MR, Strout MP, Oberkircher AR et al. Persistence of the AML1/ETO fusion transcript in patients treated with allogeneic bone marrow transplantation for t(8;21) leukemia. Blood 1996; 88: 2183–2191.

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BioMol LABORATORIES

AML1-ETO t (8; 21) (Q22; Q22) ONE-STEP RT-PCR QUALITATIVE DETECTION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-031-25
CND Code: W01060299
RDM Code: 2256801/R
Tests: 25 Reactions: 31
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-031-25	
Mix oligonucleotides and probes	Mix PCR AML1-ETO 4X	1 x 155 µl	- 20 °C
Mix buffer and enzyme RT and Taq polymerase	Mix RT-PCR 4X	1 x 155 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	- 20 °C
Recombinant RNA Positive control	Positive control AML1-ETO-abl	1 x 30 µl	- 20 °C
Recombinant RNA Negative control	Negative control	1 x 30 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-031-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions; positive control and negative control.
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels.
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles at 95 °C (5 sec) + 60 °C (45 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of RNA; ≥1%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

CBFB-MYH11 INV (16) (p13q22) ONE-STEP RT-PCR QUALITATIVE DETECTION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-032-25
CND Code: W01060211
RDM Code: 2256822/R
Tests: 25 Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

PRODUCT CHARACTERISTICS

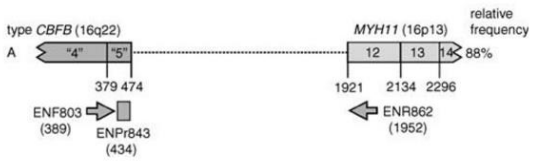
Device belonging to the family of in vitro **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS** medical devices.
Qualitative detection of pericentric inversion INV 16, CBFB-MYH11 and identification of transcripts A, D and E by RT-PCR technique (Reverse transcriptase-polymerase chain reaction) and subsequent detection by PCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

Current treatment protocols for acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) are based on prognostic factors, which contribute to therapy stratification. Key prognostic factors identified in leukemia over the years include pretreatment characteristics such as age, WBC count, immunophenotypic profiles, specific chromosomal abnormalities, aberrant fusion genes (FGs), and mutations. In most studies of adult primary AML, the presence of chromosomal abnormalities involving genes encoding central binding factor (CBF) α or β subunits, t(8;21) (q22;q22) or inv(16)(p13q22), respectively, is associated with a very high complete remission rate.

CLINICAL SIGNIFICANCE

In most studies of adult primary AML, the presence of chromosomal abnormalities involving genes encoding central binding factor (CBF) α or β subunits, t(8;21)(q22;q22) or inv(16)(p13q22), respectively, is associated with a very high complete remission rate. At the molecular level, inv(16)(p13q22) results in the fusion gene of CBFβ in chromosomal band 16q22 with the MYH11 gene in chromosomal band 16p13, creating a new chimeric gene, CBFβ/MYH11.4 Since the breakpoints genomes within the CBFβ and MYH11 genes are variable, at least eight different types of CBFβ/MYH11 fusion transcripts are encoded. The most common of these fusion transcripts is referred to as "type A" and is detected in approximately 85% of patients with AML and inv (16) (p13q22).



§ Eur J Haematol 2024 Jun;112(6):964-974. doi: 10.1111/ejh.14192. Epub 2024 Feb 22. Clinical implications of additional chromosomal abnormalities in adult acute myeloid leukemia with inv (16)/t(16;16)/CBFB::MYH11

§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

§ Kottaridis PD, Gale RE, Frew ME, Harrison G, Langabeer SE, Belton AA et al. The presence of a FLT3 internal tandem duplication in patients with acute myeloid leukemia (AML) adds important prognostic information to cytogenetic risk group and response to the first cycle of chemotherapy: analysis of 854 patients from the United Kingdom Medical Research Council AML 10 and 12 trials. Blood 2001; 98: 1752–1759.

§ Marcucci G, Caligiuri MA, Dohner H, Archer KJ, Schlenk RF, Dohner K et al. Quantification of CBFbeta/MYH11 fusion transcript by real time RT-PCR in patients with INV(16) acute myeloid leukemia. Leukemia 2001; 15: 1072–1080.

§ Appelbaum FR. Perspectives on the future of chronic myeloid leukemia treatment. Semin Hematol 2001; 38: 35–42.

§ Lowenberg B, Downing JR, Burnett A. Acute myeloid leukemia. N Engl J Med 1999; 341: 1051–1062.

§ Grimwade D, Walker H, Oliver F, Wheatley K, Harrison C, Harrison G et al. The importance of diagnostic cytogenetics on outcome in AML: analysis of 1,612 patients entered into the MRC AML 10 trial. The Medical Research Council Adult and Children's Leukaemia Working Parties. Blood 1998; 92: 2322–2333.

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BioMol LABORATORIES

CBFB-MYH11 INV (16) (p13q22) ONE-STEP RT-PCR QUALITATIVE DETERMINATION

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-032-25
CND Code: W01060211
RDM Code: 2256822/R
Tests: 25 Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for reverse transcription and Real-Time PCR amplification
**the reagents for RNA extraction are not supplied in the kit.*

CONTENTS OF THE KIT

DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-032-25	
Mix oligonucleotides and probes	Mix PCR CBFB MYH11 A 4X	1 x155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR CBFB MYH11 D 4X	1 x 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR CBFB MYH11 E 4X	1x 155 µl	- 20 °C
Mix buffer and enzyme RT and Taq polymerase	Mix RT-PCR 4X	1 x 465 µl	- 20 °C
Deionized H_20	Deionized H_20	1 x 1 ml	- 20 °C
Recombinant RNA Positive control	Positive control CBFB MYH11 A, D, E and abl	1 x 90 µl	- 20 °C
Recombinant RNA Negative control	Negative control	1 x 90 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-032-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions; single positive control for CBFB/MYH11 A, D, E negative control for abl
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes for the translocation and for the ABL gene; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles at 95 °C (5 sec) + 60 °C (45 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,025 ng of RNA; ≥1%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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BioMol LABORATORIES

INSTRUMENTS

TECHNICAL DATA SHEET

Auto-Pure 32

REF: AS-17040-00

For in vitro diagnostic use

CE IVD

VER.1 of 08/06/2023

Auto-Pure 32 nucleic acid purification system is a device for extracting and purifying nucleic acid by using magnetic bead method. It has the advantages of high automation, fast extraction, stable results, and easy operation. Using the 96 deepwell plate kit, 1-32 samples can be purified in one run. With different types of magnetic bead nucleic acid reagent sets, it can quickly extract DNA and RNA from animal and plant tissues, blood, body fluids, criminal specimens and other samples. It is widely used in scientific research, disease control system, food safety, forensics, clinical monitoring and other fields.

·Stand-alone operation, 7-inch color touch screen display, easy to use

·Customize the temperature and program according to the requirements

·Short operation time, 15-30 min/time, can extract up to 32 samples in one run

·High yield of nucleic acid, low loss of magnetic beads, and good reproducibility of results

·UV sterilization function to avoid cross-contamination

·Open system, suitable for various magnetic bead extraction reagents

·Drawer design to prevent possible injuries

·APP software will be configured to monitor the system in real time through mobile devices

COD. AS-17040-00

DIMENSION	400 x 470 x 450 mm
WEIGHT	28 KG
THROUGHPUT	1 ~32
PROCESS VOLUME	50 ~1000µl
TEMPERATURE	R.T.. ~120°C
OPERATION	7-inch touch screen – Mouse
STORAGE CAPACITY	Preset 8 programs; max store 100 programs
EXTENSION INTERFACE	Standard Usb, Ethernet port
POLLUTION CONTROL	Fan exhaustion, UV sterilization

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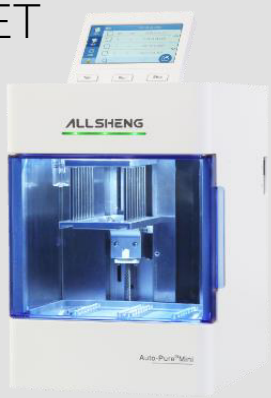
TECHNICAL DATA SHEET

Auto-Pure Mini

REF: AS-17170-00



For in vitro diagnostic use

CE IVD

VER.1 of 08/06/2023

Auto-Pure Mini automatic nucleic acid purification system is a product that is further miniaturized on the basis of the existing nucleic acid extractor by using magnetic bead method. It offers nucleic acid purification of up to 16 samples per run and it is characterized by mini size and powerful function to meet the daily testing requirement of small labs. It is a compact device that easily fits on a bench and its low weight makes it easy to carry. It is possible to connect Auto-pure Mini to your smartphone or tablet by app and collect all data on other devices.

·Simple and intelligent operation

Built-in lighting LED, real-time observation of the operating status of the instrument
Graphical interface design makes the operation of the instrument easier
Configure mobile phone APP software, edit, set, and manage programs more easily

·Field experiment

Special design of the instrument, small size, easy to carry
Support low power consumption mode, such as when the battery is used for power supply, the display will automatically stop when it is not used for a long time
External power supply, DC24V/5A, allowing battery power supply

·High-quality fast extraction

Up to 16PCS 1mL samples can be processed simultaneously
The use of lead screw drive to achieve lifting movement, high precision
UV sterilization function to avoid cross-contamination

·Open design, free editing of programs

Accurate temperature control of room temperature +5℃~120℃
Open software design, simple setting can complete the program setting
Complete software functions, suitable for all kinds of magnetic bead reagents
Diversified mixing and magnetic absorption methods are conducive to reagent optimization

COD. AS-17170-00

DIMENSION	200 x 260 x 300 mm
WEIGHT	7 KG
THROUGHPUT	1 ~16
PROCESS VOLUME	20 ~1000 µl
TEMPERATURE	R.T. ~120 °C.
OPERATION	4.3-inch touch screen, 3 shortcut keys, external mouse, barcode reader
STORAGE CAPACITY	Preset 6 programs, max store 100 programs
EXTENSION INTERFACE	Standard Usb, Ethernet port, Wi-Fi, Bluetooth
POLLUTION CONTROL	Fan exhaustion, UV sterilization

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BioMol LABORATORIES

TECHNICAL DATA SHEET

JOAN LAB MINI CENTRIFUGE MC-7S

VER.1 of 08/06/2023

Joanlab MC-7S Mini Laboratory Centrifuge is equipped with a 3-in-1 rotor. The operation is smooth, with low noise and low vibration. It is equipped with safety protection: low voltage input, robust lid that reduces the risk of liquid splashes into the device and rotor safety buckle. With a quiet motor and vibration-absorbing rubber base, the JOANLAB MC-7S mini centrifuge keeps operating noise to a minimum (less than 47dB) and reduces interference in the laboratory. The automatic lid lock feature keeps the lid locked during operation, protecting the operator from injury from the rapidly spinning rotors.

DESCRIPTION	JOANLAB
Relative Centrifugal Force	3286 x g
Rotating speed	7000rpm +/- 5%
Max acceleration/reduction speed	≤ 12s / ≤ 15s
Noise	≤ 47db(A)
Input power	25 W
Control mode	Direct drive power
Multirotor	0.2/0.5/1.5/2ml micro tubes *12 + 0.2ml 8 PCR strip*4
Voltage	230V

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MINI CENTRIFUGE MC-700 SERVICEBIO

VER.1 of 08/06/2023

The Mini centrifuge (also known as microcentrifuge) is simple and convenient to operate. Just put the microtube, cover the lid and start it. The rotor can reach the highest speed in a few seconds, and its centrifugal force is evenly and quickly applied to the microtube. It is especially suitable for handling PCR tubes and microfiltration, quickly throwing off reagents from the tube wall or tube cap, and slow centrifugation of the test tube or tube. The MC-700 Mini centrifuge is smart and versatile. It is equipped with three types of centrifugal rotors, suitable for 1.5 mL, 2.0 mL, 0.5 mL, 0.2 mL centrifuge tubes and 0.2 mL, 8-strip centrifuge tubes for PCR. Fully transparent round cover, equipped with multiple rotors.

0,5 mL rotor

0,2 mL rotor

DESCRIPTION	Servicebio
Rotating speed	7000rpm +/- 5%
Acceleration/reduction speed	≤ 12s / ≤ 15s
Noise	≤ 47db(A)
Input power	24 W
Control mode	Direct drive power
Multirotor	10x0.5/8x1.5 ml micro tubes + 4x0.2ml 8 PCR strip
Voltage	230V

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VORTEX MIXER MV-100 SERVICEBIO

VER.1 of 08/06/2023

The Vortex Mixer MV-100 is suitable for short or long term operation. It is a stable and reliable instrument, with a compact design, which features a shockproof silicone base that facilitates high-speed operations. It mixes all sample types evenly and thoroughly.

DESCRIPTION	Servicebio
Dimension (l * w * h)	210mm * 210mm * 180mm
Oscillation mode	Circumferential
Power	60 W ± 5%
Rotating speed	2850 rpm
Voltage	220-230 (VAC)
Frequency	50 / 60Hz.
Weight	1.7 kg

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OPTIPETTE PIPETTE SERIES

VER.1 of 08/06/2023

Model	Cat. no.	Colour code	Volume (µL)	A (%)	P (%)	Standard tips non-filtered
OP2*	5601	●	0.2 1.0 Max 2.0	± 12.0 ± 2.7 ± 1.5	± 6.0 ± 1.3 ± 0.7	10 µL
OP10	5602	●	Min 0.5 5.0 Max 10.0	± 4.0 ± 1.0 ± 0.5	± 2.8 ± 0.6 ± 0.4	
OP20	5603	●	Min 2 10 Max 20	± 3.0 ± 1.0 ± 0.8	± 1.5 ± 0.5 ± 0.3	200 µL
OP50	5607	●	Min 5 25 Max 50	± 2.5 ± 1.0 ± 0.8	± 2.0 ± 0.6 ± 0.4	
OP100	5604	●	Min 10 50 Max 100	± 1.6 ± 0.8 ± 0.8	± 0.80 ± 0.24 ± 0.20	
OP200	5605	●	Min 20 100 Max 200	± 1.2 ± 0.8 ± 0.6	± 0.60 ± 0.25 ± 0.20	
OP250	5600	●	Min 50 125 Max 250	± 1.0 ± 0.8 ± 0.6	± 0.4 ± 0.3 ± 0.3	300 µL
OP1000	5606	●	Min 100 500 Max 1,000	± 1.6 ± 0.7 ± 0.6	± 0.40 ± 0.20 ± 0.15	1,000 µL
OP5000	5608	○	Min 500 2,500 Max 5,000	± 1.2 ± 0.6 ± 0.5	± 0.5 ± 0.20 ± 0.15	5,000 µL
OP10000	5609	○	Min 1,000 5,000 Max 10,000	± 2.5 ± 0.8 ± 0.5	± 0.6 ± 0.3 ± 0.2	10,000 µL

Additional spacers enable ejector height adjustment

Rotating pipetting pushbutton prevents accidental volume change

Calibration key provided with each pipette allows user-calibration

- Ergonomic handle design
- Easy calibration
- Excellent accuracy & precision
- Soft spring system reducing pipetting forces
- Colour-coded rings for volume identification
- UV resistant body
- Autoclavable lower parts
- Available in 8- &12-channel version

Product	Cat. no.	Model	Accessories
OPTIPETTE STARTER 4 PACK 	7902	OP10 OP20 OP200 OP1000	Plexi 4-position stand Tips 10 µL, 96 pcs Tips 200 µL, 96 pcs Tips 1,000 µL, 96 pcs Calibration tool x 4 Instruction manual
OPTIPETTE COLOR STARTER 4 PACK 	7912	OP10 OP20 OP200 OP1000	Plexi 4-position stand Tips 10 µL, 96 pcs Tips 200 µL, 96 pcs Tips 1,000 µL, 96 pcs Calibration tool x 4 Instruction manual

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CFX OPUS 96 REAL-TIME PCR SYSTEM

For in vitro diagnostic use

CE IVD

VER.1 of 08/06/2023

Integrated Workflow for the Modern Lab

BIO-RAD

The CFX Opus 96 Real-Time PCR System puts you on the road to an efficient workflow. Quickly set up runs and easily monitor run progress and analyze data using the comprehensive data management and analysis tools of CFX Maestro Software.

From your BR.io account, set up a run and access your results any time and anywhere you have internet access.

Benefits

Flexible connectivity and data management options for access and transfer of runs and experiment protocols.

- Operate in stand-alone mode through flexible connectivity options of wireless network (WiFi), Ethernet, and USB
- Access BR.io cloud platform for experimental setup and data management at any convenient location with internet access
- Enjoy continued support for and control of up to 4 CFX instruments with CFX Maestro Software for Windows 7 (64-bit), Windows 10 (64-bit), and Security Edition
- Email your completed run
- Save protocols and completed runs in a network folder

Intuitive touch-screen user interface for both experienced and new real-time PCR users.

- Create new real-time PCR protocols or easily modify existing protocols
- Set up unique User Names, with optional passwords, to easily organize and find your protocols and experiments

Specifications

System	
Licensed for real-time PCR	Yes
Sample capacity	96 wells
Sample size	1–50 µl (10–50 µl recommended)
Dimensions (W x D x H)	33 x 56 x 36 cm (13 x 22 x 14 in.)
Weight	22 kg (48 lb)
Touch-screen user interface	Adjustable, with angle of rotation 12–55º
Communications	USB 2.0 or above, Ethernet, WiFi
Electrical approvals	IEC, CE
Operating system	Windows 10 IoT
Optical Detection System	
Excitation	6 filtered LEDs
Detection	6 filtered photodiodes
Range of excitation/ emission wavelengths	450–730 nm
Scan time	
All channels	12 sec
Single channel	3 sec
Dynamic range	10 orders of magnitude
Sensitivity	Detects 1 copy of target sequence in human genomic DNA
Multiplex analysis	Up to 5 targets per well
96-Well Reaction Block	
Sample block type	Fixed 96-well sample block
Heating and cooling method	Peltier
Lid heating	30–110ºC
Temperature range	4–100ºC
Maximum ramp rate	5ºC/sec
Average ramp rate	3.3ºC/sec
Thermal accuracy	±0.2ºC
Thermal uniformity	±0.3ºC (max–min) 0.6ºC, measured 10 sec after the block reaches the target temperature
Gradient	
Operational range	30–100ºC
Programmable span	1–24ºC

continues

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Specifications

CFX Maestro Data Management and Analysis Software

Operating system	Windows 7 (64-bit), Windows 10 (64-bit), macOS (10.14, for analysis only)
Memory	Minimum of 1 GB
Data analysis modes	PCR quantification with standard curve
	Melt curve analysis
	Gene expression analysis by relative quantity (ΔCq) or normalized expression (ΔΔCq)
	Multiple-file gene expression analysis for comparison of an unlimited number of Cq values
	Allelic discrimination
	End-point analysis
	Data analysis options include bar charts, box-and-whisker plots, dot plots, clustergrams, scatter plots, and volcano plots
	Statistics include *t*-test and analysis of variance (ANOVA)
Data export	Save, copy, and print all graphs and spreadsheets from right-click menu
	Export specified data in multiple formats
	Copy and paste into a Microsoft Excel, Word, or PowerPoint file
	Print directly or save as PDFs customizable reports containing run settings, data graphs, and spreadsheets
	Export to RDML
Image export	Export images at any pixel size and at a resolution up to 600 dpi
	Save images as .bmp, .jpg, or .png files

Ordering Information

All software for Windows unless otherwise noted.

Catalog #	Description
12011319	**CFX Opus 96 Real-Time PCR System**, includes power cord, USB cable, and Ethernet cable; does not include CFX Maestro Software 2.0 or WiFi adaptor
17005940	**CFX Opus 96 Real-Time PCR System with Starter Pack**, includes CFX Opus 96 System, CFX Maestro Software 2.0, license for qbase+ Software, power cable, USB cable, Ethernet cable, reagents, consumables
12013758	**CFX Maestro Software 2.0**
12004128	**CFX Maestro Software for Mac**
12012832	**CFX Maestro Software 2.0, Security Edition**, 1 license
12013028	**CFX Maestro Software 2.0, Security Edition**, 5 licenses
12012833	**CFX Maestro Software 2.0, Russian Edition**
12012834	**CFX Maestro Software 2.0, Chinese Edition**
1845025	**Precision Melt Analysis Software**, includes 2 user licenses, installation CD, 2 HASP HL keys, melt calibration kit

Catalog #	Description
1845098	**CFX Qualification Plate**, 96-well
1814000	**PX1 PCR Plate Sealer**, includes heat sealing instrument
1814030	**PCR Plate Heat Seal**, pkg of 100, optically clear seals for use with the PX1 PCR Plate Sealer
MSB1001	**Microseal 'B' PCR Plate Sealing Film**, pkg of 100, optically clear seals for PCR plates
HSP9655	**Hard-Shell 96-Well PCR Plates**, pkg of 50, low profile, thin wall, skirted, white shell/white wells
HSP9955	**Hard-Shell 96-Well PCR Plates**, pkg of 50, low profile, thin wall, skirted, white shell/white wells, barcoded
1708840	**iScript Reverse Transcription Supermix for RT-qPCR**, 25 x 20 µl reactions
1725037	**iScript Advanced cDNA Synthesis Kit for RT-qPCR**, 25 x 20 µl reactions
1725270	**SsoAdvanced Universal SYBR® Green Supermix**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
1725280	**SsoAdvanced Universal Probes Supermix**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
1725120	**iTaq Universal SYBR® Green Supermix**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
1725130	**iTaq Universal Probes Supermix**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
1725200	**SsoFast EvaGreen® Supermix**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
1725210	**SsoFast EvaGreen® Supermix with Low ROX**, 2 ml (2 x 1 ml), 200 x 20 µl reactions
12010176	**Reliance One-Step Multiplex RT-qPCR Supermix**, 1 ml (1 x 1 ml), 200 x 20 µl reactions
1725150	**iTaq Universal SYBR® Green One-Step Kit**, 100 x 20 µl reactions
1725140	**iTaq Universal Probes One-Step Kit**, 100 x 20 µl reactions
1725848	**iQ Multiplex Powermix**, 50 x 50 µl reactions
1725095	**SingleShot SYBR® Green One-Step Kit for Cell Lysis and RT-qPCR**, 100 x 50 µl reactions
1725160	**SsoAdvanced PreAmp Supermix**, 1.25 ml (1 x 1.25 ml), 50 x 50 µl reactions
17005726	**SEQuoia Complete Stranded RNA Library Prep Kit**, 24 reactions
17005710	**SEQuoia Complete Stranded RNA Library Prep Kit**, 96 reactions
12011928	**SEQuoia Dual Indexed Primers Set**, 12 vials of unique dual indexes, 96 reactions
12011930	**SEQuoia Dual Indexed Primers Plate**

Visit **bio-rad.com/CFXOpus** for more information.

BIO-RAD

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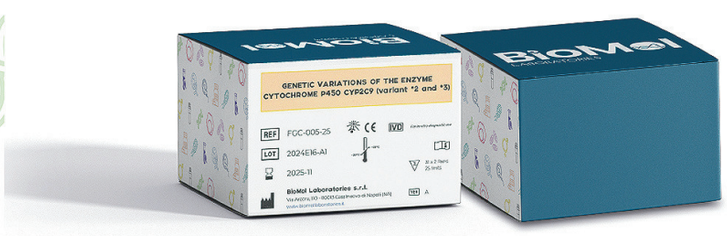
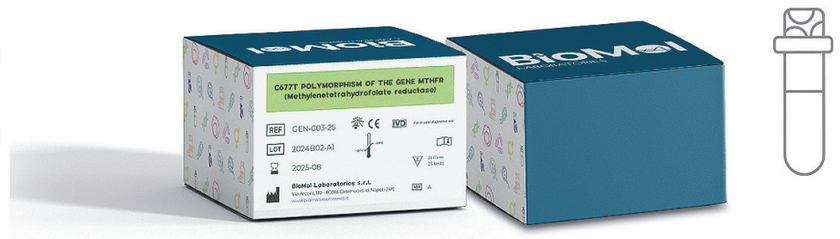
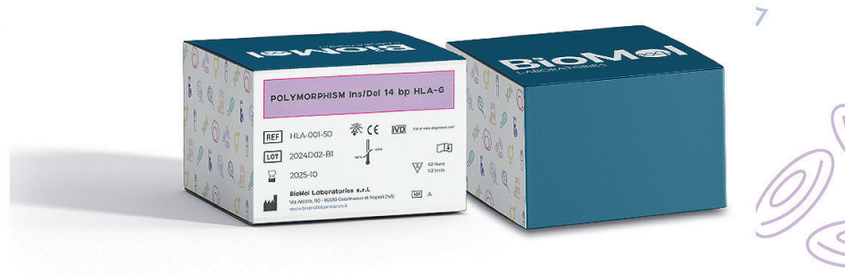
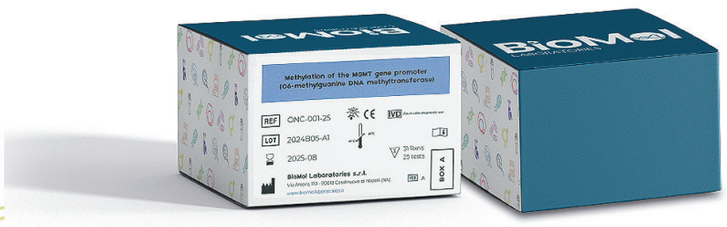
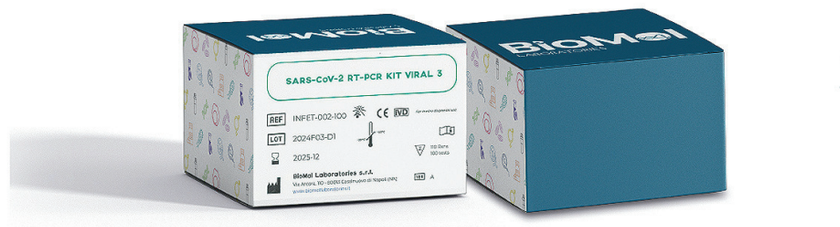
Innovative Company Specializing in Molecular Biology applied to “in vitro” diagnostics.











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