



MTHFR A1298C POLYMORPHISM

ORDERING INFORMATION

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.

For in vitro diagnostic use



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-adenosylmethionine (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 methylenetetrahydrofolate 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 cytotoxicity 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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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 ₂ O	Deionized H ₂ O	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%