

PAI-1 4G/5G POLYMORPHISM

ORDERING INFORMATION

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

For in vitro diagnostic use



PRODUCT CHARACTERISTICS

Detection of 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.

§ 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 Dement.* 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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DESCRIPTION	LABEL	VOLUME		STORAGE
		GEN-005-25	GEN-005-50	
Oligonucleotide Mix	Mix PAI-1 5G 10X	1 x 85 µl	1 x 170 µl	-20°C
Oligonucleotide Mix	Mix PAI-1 4G 10X	1 x 85 µl	1 x 170 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 850 µl	2 x 850 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	2 x 1 ml	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control +1 HOMO 5G	1 x 35 µl	1 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control +2 HET 4G/5G	1 x 35 µl	1 x 35 µl	-20°C
Genomic DNA or recombinant DNA	Control +3 HOMO 4G	1 x 35 µl	1 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 CONTROL	Recombinant DNA for at least 3 analytical sessions
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 at 70 °C with 0.2 °C increase.
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	≥ 0,016 ng of DNA
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%