



Genetic variants PI*S and PI*Z of the ALPHA 1 ANTITRYPSIN gene

ORDERING INFORMATION

REF: GEN-053-25
Tests: 25 Reactions: 31 x 2
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

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

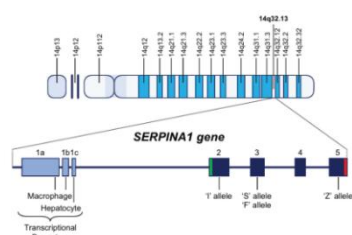
PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS- RESEARCH USE ONLY.** Detection of the genetic variants S (rs17580) and Z (rs28929474) of the coding for alpha 1 antitrypsin gene by Real-Time PCR technique. Kit optimized for Real-time PCR instruments Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx. Thermofisher QuantStudio™ 5 Real-Time PCR System.

SCIENTIFIC BACKGROUND

The SERPINA1 gene that encodes alpha-1 antitrypsin (AAT) is a highly polymorphic 12.2kb gene clustered with other serpin genes on the long arm of chromosome 14 at position 32.13 (14q32.13), and consists of three noncoding regions (1a-c) and four protein-coding regions.

AAT deficiency (AATD) is caused by variations/mutations in the SERPINA1 gene sequence, the different types of which lead to different changes in the AAT protein (conformational and concentration), and consequently, have different pathological implications. The normal AAT protease inhibitor (PI) is designated with the letter M and is encoded by the wild-type SERPINA1 sequences, also termed the M alleles; individuals with biallelic M alleles are therefore designated as PI*MM individuals.



CLINICAL SIGNIFICANCE

Alpha-1 antitrypsin deficiency (A1ATD) is an inherited metabolic disorder. The severity of A1ATD-associated liver disease is highly variable, necessitating further characterisation. The allele most commonly associated with severe AATD is the Z allele. Individuals that are homozygous for the Z allele (PI*ZZ) are at high risk of lung and liver disease, and have serum AAT levels that are approximately 10–20% of normal (20–45 mg/dL, or 2.5–7 µM). The S allele variant (Glu264Val related to AATD, causing a 40% decrease in circulating AAT protein, with mean serum levels in homozygous PI*SS subjects of 0.82 g/L (95% CI 0.73 to 100 g/L). The S allele has also been associated with a higher prevalence and increased severity of asthma. The PI*SZ genotype increases the risk of emphysema in smokers compared to the “normal” PI*MM population. Subjects with the PI*SS genotype have a significantly lower risk of lung disease compared with the PI*ZZ genotype. Since the PI*SZ genotype is considered a genetic risk factor for the development of lung disease in smokers, careful attention and strong anti-smoking counselling should also be given to PI*SS subjects that smoke.

For diagnostic testing of symptomatic patients, the 2016 US Clinical Practice Guidelines recommend genotyping for at least the S and Z alleles because >95% of all individuals with severe AATD have PI*ZZ or PI*SZ genotypes, with confirmatory testing considered using PI phenotyping, AAT level testing and/or expanded genotyping.

§ Risk of lung disease in the PI*SS genotype of alpha-1 antitrypsin: an EARCO research project. Martin et al. Respiratory Research (2024) 25:260 <https://doi.org/10.1186/s12931-024-02879-y>

§ Real-time PCR detection of PI*S and PI*Z alleles of SERPINA1 gene using SYBR green. Gene 921 (2024) 148540. <https://doi.org/10.1016/j.gene.2024.148540>

§ Alpha-1 Antitrypsin and Hepatocellular Carcinoma in Liver Cirrhosis: SERPINA1 MZ or MS Genotype Carriage Decreases the Risk. Int. J. Mol. Sci. 2021, 22, 10560. <https://doi.org/10.3390/ijms221910560>

§ Variants of SERPINA1 and the increasing complexity of testing for alpha-1 antitrypsin deficiency. Ther. Adv. Chronic Dis. 2021, Vol. 12: 33–48 <https://doi.org/10.1177/20406223211015954>



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DESCRIPTION	LABEL	VOLUME	STORAGE
		GEN-053-25	
Mix oligonucleotides and probes	Mix PI*S 10X	1 x 62 µl	-20°C
Mix oligonucleotides and probes	Mix PI*Z 10X	1 x 62 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 620 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2, Control 3 PI*S	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2, Control 3 PI*Z	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. GEN-053-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissues, cells
POSITIVE CONTROL	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Thermofisher QuantStudio™ 5 Real-Time PCR System.
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) + 62 °C (60 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 5 ng of genomic DNA
LIMIT OF BLANK (LOB)	>40 Cq
REPRODUCIBILITY	99,9%
SPECIFICITY / SENSITIVITY	99,9%/98%