

APO-E (ARG158CYS) C4070T POLYMORPHISM

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

For in vitro diagnostic use

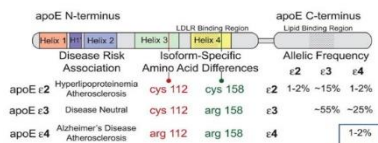


PRODUCT CHARACTERISTICS

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 $\epsilon 2$, $\epsilon 3$, and $\epsilon 4$, 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 ($\epsilon 2$, $\epsilon 3$ and $\epsilon 4$): APOE- $\epsilon 2$ (cys112, cys158), APOE- $\epsilon 3$ (cys112, arg158) and APOE- $\epsilon 4$ (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.



CLINICAL SIGNIFICANCE

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

- $\epsilon 2$ (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 $\epsilon 2/\epsilon 2$ combination may have an increased risk of early vascular disease. The $\epsilon 2$ allele has also been implicated in Parkinson's disease.
- $\epsilon 3$ (rs7412-C, rs429358-T) has an allele frequency of approximately 79%. It is considered the "neutral" Apo E genotype.
- $\epsilon 4$ (rs7412-C, rs429358-C) has an allele frequency of approximately 14%. $\epsilon 4$ 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.

- § Meta-analysis: BMC Neurosci. 2024 Jun 25;25(1):28. Diabetes mellitus and risk of incident dementia in APOE $\epsilon 4$ 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 $\epsilon 4$ and Alzheimer's Disease and Related Dementias Across Hispanic Regions of Origin
- § The APOE $\epsilon 4$ 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).



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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 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-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%