

UBA1 (c121 A>G; c121 A>C; c122 T>C) GENETIC VARIANTS (VEXAS SYNDROME)

ORDERING INFORMATIONS

REF: INF-005-25
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-RESEARCH USE ONLY**. Detection of the mutations c121 A>G; c121 A>C; c122 T>C of UBA1 gene (VEXAS SYNDROME) by Real-Time PCR technique. Kit optimized for Real-time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Thermofisher QuantStudio™ 5 Real-Time PCR System.

SCIENTIFIC BACKGROUND

VEXAS syndrome (vacuoles, enzyme E1, X-linked, autoinflammatory, somatic) is a monogenic disease of adulthood caused by somatic mutations in the UBA1 gene in hematopoietic progenitor cells. Patients develop inflammatory and hematological symptoms. Self-inflammation of myeloid origin and progressive bone marrow failure lead to considerable morbidity and mortality. The identification of such pathology has become more frequent since its first description at the end of 2020. There are several clinical manifestations associated with VEXAS syndrome, some intrinsically linked to the disease (for example, myelodysplastic syndrome) and other comorbidities attributable to the patient's age or resulting from the treatment of the disease. In fact, because the disease can be refractory to different lines of therapy, chronic immunosuppression can also contribute to complications, mainly infections, which makes treatment guidelines difficult.

§ Review Curr Res Transl Med. 2025 Jun 18;73(4):103524. Online ahead of print. Infections in VEXAS syndrome: a systematic review of the literature.
§ Review Oncotarget. 2024 Sep 30;15:644-658. UBA1 dysfunction in VEXAS and cancer Maki Sakuma, Torsten Haferlach, Wencke Walter.
§ Blood. 2021 Mar 9;137(26):3676-3681. doi: 10.1182/blood.2020010286 Novel somatic mutations in UBA1 as a cause of VEXAS syndrome.

CLINICAL SIGNIFICANCE

Functional analysis identified the loss of the cytoplasmic isoform UBA1b, whose transcription begins at residue p.Met41, and the subsequent acquisition of a new isoform, UBA1c. VEXAS mutations at residue M41 reduce the translation efficiency of UBA1b, favoring translation from an alternative start codon, M67, and producing a catalytically inactive isoform, UBA1c. Loss of function mutations of UBA1 in VEXAS result in distinct phenotypes including inflammation, cytopenias, thrombotic tendencies, clonality, and associations with blood cancer.

In VEXAS syndrome, mutated blood stem cells progressively replace healthy ones, i.e. those that have not acquired the mutation, through a mechanism called clonal hematopoiesis.

The causes and characteristics of clonal hematopoiesis underlying VEXAS syndrome remain unknown. As a consequence, inflammation occurs in various organs (fever, skin lesions, lung and blood vessel involvement, inflammation of the cartilage) and the ability of the bone marrow to generate a sufficient number of new blood cells is compromised, resulting in anemia and reduction of platelets.

In all cases of VEXAS, mutations acquired in the UBA1 gene, which encodes the main enzyme of cellular ubiquitylation, have been identified. The most frequent mutations are those in codon 41, Meth (c122 T>C; c121 A>G; c121 A>C).

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DESCRIPTION	LABEL	VOLUME	STORAGE
		INF-005-25	
Mix oligonucleotides	Mix c121 A>G 10X MIX 1	1 x 77,5 µl	-20°C
Mix oligonucleotides	Mix c121 A>C 10X MIX 2	1 x 77,5 µl	-20°C
Mix oligonucleotides	Mix c122 T>C 10X 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 ₂ O	Deionized H ₂ O	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2 c121 A>G	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2 c121 A>C	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 1, Control 2 c122 T>C	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. INF-005-25

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; 1 SYBR-GREEN/FAM fluorescence channels
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) + 63°C (40 sec) + 72°C (50 sec) + 1 dissociation cycle from 70 °C to 95°C with 0,2 °C increments
ANALYTICAL SPECIFICITY	Absence of non-specific pairings oligonucleotides; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 5 ng of genomic DNA; ≥ 5%
LIMIT OF BLANK (LOB)	< 100 -d(RFU)/dT (Opus Dx Biorad); < 10000 Derivative Reporter (-Rn) (QuantStudio™5 Real-TimePCR System.
REPRODUCIBILITY	99,9%
SPECIFICITY / SENSITIVITY	99,9%/98%