

MYD88 L265P (T>C) MUTATION

ORDERING INFORMATIONS

REF: *ONC-017-25*
Tests: *25 Reactions: 31*
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-SOMATIC MUTATIONS- RESEARCH USE ONLY.**

Determination of the L265P mutation of the MYD88 gene by Polymerase chain Reaction PCR technique and subsequent detection in real-time PCR. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, ThermoFisher QuantStudio™ 5 Real-Time PCR System.

SCIENTIFIC BACKGROUND

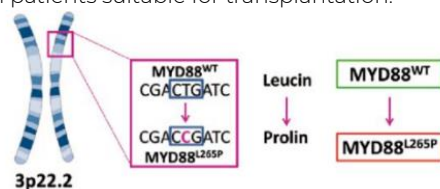
Myeloid differentiation factor 88 (MYD88) was discovered in the 1990s as a primary differentiation response gene in myeloid precursors that was activated following terminal differentiation and growth arrest induced by IL6. As a general adaptor protein, MYD88 contains three main structures: a death domain (DD) at the N terminus, an intermediate linker domain (ID), and a Toll/interleukin-1 receptor domain (TIR) at the C terminus.

Whole genome sequencing in WM allowed the identification of a somatic variant (T>C) at position 38182641 in chromosome 3p22.2 that results in an amino-acid change from leucine to proline (L265P) in the MYD88 gene.

This missense mutation (L265P) is found in ~90% of Waldenström macroglobulinemia (WM) cases and in significant portions of activated B-cell diffuse large B-cell lymphomas and IgM monoclonal gammopathy of undetermined significance.

CLINICAL SIGNIFICANCE

The identification of specific genetic mutations in patients with Waldenström macroglobulinemia may lead to advances in the diagnosis and treatment of this lymphocytic lymphoplasm. MYD88 L265P can therefore be useful to distinguish lymphoplasmic lymphoma from marginal zone lymphoma and multiple myeloma. Waldenström macroglobulinemia is a form of lymphoma in which IgM are secreted; lymphocyte cells insert themselves into the bone marrow resulting in high blood viscosity. The molecule expressed by MYD88 plays a role in signalling between toll-like receptors (TLRs) and the receptor for interleukin-1. When stimulated, MYD88 upregulates the IRAK signaling pathway, which in turn activates the NF-κB signaling pathway, which is necessary for cell proliferation in Waldenström's macroglobulinemia. The blocking of this signaling pathway by the proteasome inhibitor Bortezomib (Velcade) has also been shown to be effective in refractory cases of Waldenström's disease. Bortezomib therapies produce rapid responses, and it is generally well tolerated. It appears to have no adverse effects on stem cell collection and rooting, making it a feasible therapeutic option in patients suitable for transplantation.



- § Hum Pathol 2024 Dec 17:105708. Lymphoplasmacytic lymphoma and Waldenström macroglobulinemia, a decade after the discovery of MYD88^{L265P}
- § Inflamm Res. 2023 Nov;72(10-11):2023-2036. Targeting MyD88: Therapeutic mechanisms and potential applications of the specific inhibitor ST2825
- § Single-cell analysis of MYD88^{L265P} and MYD88^{WT} Waldenström macroglobulinemia patient. HemaSphere. 2024;8:e27. <https://doi.org/10.1002/hem3.27>
- § Cancer Res 2018 May 15;78(10):2457-2462. doi: 10.1158/0008-5472.CAN-18-0215. Epub 2018 Apr 27. MYD88 L265P Mutation in Lymphoid Malignancies
- § Prevalence and clinical significance of the MYD88 (L265P) somatic mutation in Waldenström's macroglobulinemia and related lymphoid neoplasms. BLOOD, 28 MARCH 2013 x VOLUME 121, NUMBER 13
- § MYD88 L265P mutation in Waldenström macroglobulinemia. BLOOD, 30 MAY 2013 x VOLUME 121, NUMBER 22
- § MYD88 L265P Somatic Mutation in Waldenström's Macroglobulinemia. n engl j med 367:9 nejm.org august 30, 2012
- § Multicenter Clinical Trial of Bortezomib in Relapsed/Refractory Waldenström's Macroglobulinemia: Results of WMCTG Trial 03-248 Clin Cancer Res 2007;13(11) June 1, 2007

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DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-017-25	
Mix oligonucleotides and probes	Mix L256P MYD88 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H ₂ O	Deionized H ₂ O	1 x 1 ml	-20°C
Recombinant DNA	Positive control	1 x 30 µl	-20°C
Recombinant DNA	Negative control	1 x 30 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. **ONC-017-25**

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood or tissue
POSITIVE CONTROL	Recombinant DNA for at least 3 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx, Thermofisher QuantStudio™ 5 Real-Time PCR System.
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 50 cycles at 95 °C (15 sec) + 60 °C (1 min)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 5 ng of genomic DNA; ≥ 2% (MUT) VERSUS (WT).
LIMIT OF BLANK (LOB)	>40 Cq
REPRODUCIBILITY	99,9%
SPECIFICITY / SENSITIVITY	100%/98%