MPL W515L/K MUTATION (MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: ONC-013-25 RDM Code: 1772905/R
Tests: 25 Reactions: 31 x 2
REF: ONC-013-50 RDM Code: 2256722/R
Tests: 50 Reactions: 62 x 2
CND Code: W01060299
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

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

PRODUCT CHARACTERISTICS

Detection of W515L/K mutation of the MPL gene (myeloproliferative leukemia virus oncogene) by Real-Time PCR technique. Kit optimized for Real Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell.

The JAK (Janus Kinases) family of enzymes includes JAK1, JAK2, JAK3, and TYK2. These molecules bind to the cytosolic domains of cytokine receptors and are essential for the message transduction of cytokines and growth factors.

Polycythemia vera (PV), idiopathic myelofibrosis (PMF), and essential thrombocythemia (ET) show shared phenotypic features (MPN BCR/ABL neg) that result from direct or indirect constitutive activation of the related tyrosine kinase JAK2 to the hematopoietic growth factor receptors for erythropoietin (EPOR) and thrombopoietin (MPL) and to the G-CSF (granulocyte colony-stimulating factor) receptor.

CLINICAL SIGNIFICANCE

Direct activation of JAK2 is caused by a point mutation (V617F in JAK2 exon 14) or, less commonly, by insertions or deletions in exon 12 of the JAK2 gene. Indirect activation, on the other hand, is caused by point mutations in the thrombopoietin receptor, MPL, or by mutations in the CAL chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly. The MPL gene is located on chromosome 1p34 and encodes the thrombopoietin receptor, which binds to thrombopoietin, the cytokine that regulates megakaryocyte development and platelet production, as well as hematopoietic homeostasis of stem cells. Binding of thrombopoietin to its receptor causes the activation of JAK2, which phosphorylates MPL and initiates a cascade of transduction events that regulate cell survival, proliferation, and differentiation. Mutations in the MPL gene locate in exon 10 of the gene (G1544X) and cause a W515L/K amino acid substitution resulting in impaired function of the autoinhibitory region and subsequent ligand-independent activation of the thrombopoietin receptor. These mutations are present in 2-3% of cases of essential thrombocythemia (ET) and 3-5% of cases of primary myelofibrosis (PMF).

§ Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9;129(6):667-679 . doi: 10.1182/blood-2016-10-695940. Epub 2016 Dec 27. Review.

§ Mutations in MPNs: prognostic implications, window to biology, and impact on treatment decision. Hematology Am Soc Hematol Educ Program.2016 Dec 2;2016(1):552-560.

§ Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan;22(1):14-22. Epub 2007 Sep 20. Review.

§ The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-405. Epub 2016 Apr 11.

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ISO 9001:2015
ISO 13485:2016

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DESCRIPTION	LABEL	VOLUME		STORAGE
		ONC-013-25	ONC-013-50	
Mix oligonucleotides and probes	Mix W515L MPL 10 X	1 x 85 µl	1 x 170 µl	- 20 °C
Mix oligonucleotides and probes	Mix W515K MPL 10 X	1 x 85 µl	1 x 170 µl	- 20 °C
Mix buffer and Taq-polymerase	Mix Real-Time PCR 2X	1 x 850 µl	2 x 850 µl	- 20 °C
Deionized H_20	Deionized H_20	2 x 1 ml	2 x 1 ml	- 20 °C
Genomic DNA or recombinant DNA	Positive control 100% W515W MPL	1 x 50 µl	1 x 50 µl	- 20 °C
Genomic DNA or recombinant DNA	Positive control W515L MPL W515K MPL	1 x 50 µl	1 x 50 µl	- 20 °C

TECHNICAL CHARACTERISTICS

COD. ONC-013-25 / COD. ONC-013-50

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 4 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.
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 and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	< 2%
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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