

# JAK2 (Janus kinase 2) V617F mutation, qualitative detection

## ORDERING INFORMATIONS

REF: *ONC-011-25 RDM Code: 1699886/R*  
Tests: 25 Reactions: 31  
REF: *ONC-011-50 RDM Code: 2256590/R*  
Tests: 50 Reactions: 62  
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*

For in vitro diagnostic use



## PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS**.  
Qualitative detection of the V617F mutation of the JAK2 gene (Janus kinase 2) by Real-Time PCR technique. Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, 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.

§ *Cancers (Basel). 2024 Apr 26;16(9):1679. doi: 10.3390/cancers16091679. Advances in Molecular Understanding of Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis: Towards Precision Medicine*

§ *Front. Pharmacol. 22 July 2024 Sec. Pharmacogenetics and Pharmacogenomics Volume 15 - 2024*

§ *Myelofibrosis Blood. 20 APRIL 2023 | VOLUME 141, NUMBER 161*

§ *Diagnostics (Basel). 2023 Jan 31;13(1):163. doi: 10.3390/diagnostics13010163.*

*Molecular Genetics of Thrombotic Myeloproliferative Neoplasms: Implications in Precision Oncology*

§ *Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9;129(6):667-679. 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.*

§ *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.*

## 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 CALR chaperone calreticulin (CALR) gene that allow MPL to bind and activate JAK2 indirectly.

The JAK2 V617F mutation results from a guanine-to-thymine substitution at nucleotide 1849 of exon 14 of the JAK2 gene, resulting in a single amino acid valine/phenylalanine substitution at codon 617. The mutation results in ligand-independent JAK2 kinase activity. This mutation can be found in approximately 70% of Philadelphia chromosome-negative MPNs (Ph-MPDs): it is present in 65-95% of PV patients, 23-57% of ET patients, and 35-50 % of patients affected by PMF.

20-30% of patients with polycythemia vera become homozygous for the mutation through a loss-of-heterozygosity mechanism.

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## Qualitative detection

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|------------------------------------------|-------------------------------------------|-------------|-------------|---------|
|                                          |                                           | ONC-011-25  | ONC-011-50  |         |
| Mix oligonucleotides and probes          | Mix V617F JAK2 10X                        | 1 x 77,5 µl | 2 x 77,5 µl | - 20 °C |
| Mix buffer and Taq-polymerase            | Mix Real-Time PCR 5X                      | 1 x 155 µl  | 2 x 155 µl  | - 20 °C |
| Deionized H <sub>2</sub> O               | Deionized H <sub>2</sub> O                | 1 x 1 ml    | 2 x 1 ml    | - 20 °C |
| Genomic DNA or recombinant DNA Control 1 | <b>Control 1</b><br>MUT 40-70% V617F JAK2 | 1 x 22 µl   | 2 x 22 µl   | - 20 °C |
| Genomic DNA or recombinant DNA Control 2 | <b>Control 2</b><br>MUT 100% V617F JAK2   | 1 x 22 µl   | 2 x 22 µl   | - 20 °C |
| Genomic DNA or recombinant DNA Control 3 | <b>Control 3</b><br>WT 100% V617F JAK2    | 1 x 22 µl   | 2 x 22 µl   | - 20 °C |

### TECHNICAL CHARACTERISTICS

COD. ONC-011-25 / COD. ONC-011-50

|                                                 |                                                                                                                                                                                                                                                                                                              |
|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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 (ONC-011-25)<br>Recombinant DNA for at least 6 analytical sessions (ONC-011-50)                                                                                                                                                                           |
| TECHNOLOGY                                      | Real-time PCR; oligonucleotides and specific probes; for the wt allele and the mutated allele in multiplex PCR; a single reaction for both alleles; 2 FAM/HEX fluorescence channels                                                                                                                          |
| VALIDATED INSTRUMENTS                           | Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris b-CUBE and Hyris b-CUBE3 with Hyris bAPP                                                                                                                                                                                                              |
| RUNNING TIME                                    | 110 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<br>≥ 0,025 ng of genomic DNA; ≥ 2% JAK2 (MUT) versus JAK2 (WT); validated with the WHO 1st International Reference Panel for Genomic JAK2 V617F (National Institute for Biological Standards and Control NIBSC) |
| LIMIT OF DETECTION (LOD)                        |                                                                                                                                                                                                                                                                                                              |
| LIMIT OF BLANK (LOB)                            | 0% NCN                                                                                                                                                                                                                                                                                                       |
| REPRODUCIBILITY                                 | 99,9%                                                                                                                                                                                                                                                                                                        |
| DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY | 100%/98%                                                                                                                                                                                                                                                                                                     |