Patient Name:	DUMMY	**CRM ID:**	NA
Age/DOB:	NA	**Sample Type:**	NA
Sex:	NA	**Collection Date:**	DD-MM-YYYY
Referring Clinician:	NA	**Received Date:**	DD-MM-YYYY
Test Requested:	JAK2 Exon 12 Mutation	**Reporting Date:**	DD-MM-YYYY

JAK-2 (Exon12) Mutation Analysis by Sanger Seq.

CLINICAL DIAGNOSIS/SYMPTOMS

NA

RESULTS

RESULTS	
Jak-2 (Exon 12)	No variant Identified

CLINICAL SIGNIFICANCE

JAK2 gene mutations are important diagnostic markers for the Myeloproliferative disorder Polycythemia vera (PV). A single mutation (V617F) is found in approximately 95% of cases. Of the PV cases that are V617F-negative (approximately 5%), most are associated with mutations in a different region of the JAK2 gene within exon 12. Patients with exon 12 mutations frequently present erythrocytosis as the predominant feature, but without concurrent elevations in the megakaryocytic or granulocytic lineages as seen in V617F-positive PV. Consequently, many exon 12 positive cases are considered clinically as Idiopathic erythrocytosis. Unlike the V617F mutation that is found in several Myeloproliferative neoplasms (PV, Essential thrombocythemia & Primary myelofibrosis), JAK2 exon 12 mutations are restricted only to cases of PV. JAK2 exon 12 mutation screening in patients who present with a suspicion for PV that is V617F negative.

METHODOLOGY

Targeted sequencing and mutation analysis was performed by Polymerase Chain Reaction (PCR) followed by automated DNA sequencing of the amplicon using BigDye Terminator Chemistry on an ABI Genetic Analyzer 3500XL platform. Sequencing data were aligned to NCBI database to analyze the mutations.

COMMENT

More than 10 different sequence variations have been found in exon 12 of the *JAK2* gene, most of which are in the region between codons 536 and 544. All Mutation will be covered through this test as F537-K539delinsL H538QK539L, H538-K539delinsL, K539L, I540-E543delinsMK ,R541-E543delinsK, N542-E543del ,E543-D544del ,V536-I546dup11 ,F537-I546dup10+F547L. Results of this test must always be interpreted in the context of clinical and other relevant laboratory data such as erythropoietin level exclusion of other causes of elevated hemoglobin, and should not be used alone for a diagnosis of polycythemia vera which is a form of malignancy i.e myeloproliferative disorder. Many MPD cases negative for exon 14 mutations have been observed to carry mutations in exon 12 of *JAK2*. Somatic mutations in exon 12 of *JAK2* have been found in 5% cases of suspected PV.

LIMITATIONS

- A positive result is not specific for a particular Myeloproliferative neoplasm (MPN) diagnosis and clinicopathologic correlation is necessary in all cases.
- A negative result does not exclude the presence of MPN or other neoplastic processes.
- The sensitivity of detection for Sanger sequencing is generally recognized as being approximately 15% to 20% mutant allele frequency.
- PCR is a highly sensitive technique, however inherent PCR inhibitors in the specimen result in amplification failure.

REFERENCES:

1. Pardanani A, Lasho TL, Finke C, Hanson CA, Tefferi A.Prevalence and clinicopathologic correlates of JAK2 exon 12 mutations in JAK2V617F-negative polycythemia vera. Leukemia 2007;21:1960-3.1-9

2. Martínez-Aviles L, Besses C, Alvarez-Larran A, Cervantes F, Hernandez-Boluda JC, Bellosillo B. JAK2 exon 12 mutations in patients with polycythemia vera or idiopathic erythrocy- tosis. Haematologica 2007;92:1717-18.

3. Pietra D, Li S, Brisci A, Passamonti F, Rumi E, Theocharides A, et al. Somatic mutations of JAK2 exon 12 in patients with JAK2 (V617F)-negative myeloproliferative disorders. Blood 2007 Nov 6; [Epub ahead of print].

4. Williams DM, Kim AH, Rogers O, Spivak JL, Moliterno AR. Phenotypic variations and new mutations in JAK2 V617F- negative polycythemia vera, erythrocytosis, and idiopathic myelofibrosis. Exp Hematol 2007; 35:1641-6

Conditions of Reporting

- Test results released pertain to the specimen submitted.
- All test results are dependent on the quality of the sample received by the Laboratory.
- Laboratory investigations are only a tool to facilitate arriving at a diagnosis and should be clinically correlated by the Referring Physician.
- Certain tests may require further testing at additional cost for derivation of exact value. Kindly submit the request within 72 hours of postreporting.
- Test results may show inter laboratory variations.
- If Sample collection date is not stated on test requisition form, the current date will be printed by default as the date of collection.
- Test results are not valid for medico legal purposes.

Disclaimer: Method given in report are only indicative and can be changed depending upon type of machine and kit available at time of testing.

Not all tests at all locations are under NABL scope. Availability of tests under NABL scope varies from lab to lab.

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2. It is to be presumed that the tests performed pertain to the specimen/sample attributed to the Customer's name or identification. It is presumed that the verification particulars have been cleared out by the customer or his/her representation at the point of generation of said specimen / sample. It is hereby clarified that the reports furnished are restricted solely to the given specimen only.

3. It is to be noted that variations in results may occur between different laboratories and over time, even for the same parameter for the same Customer. The assays are performed and conducted in accordance with standard procedures, and the reported outcomes are contingent on the specific individual assay methods and equipment(s) used, as well as the quality of the received specimen.

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