MAYO CLINIC

1-800-533-1710

Comprehensive NGS Myeloid Panel

NGSMC

PATIENT NAME				ORDER NUMBER
PATIENT, ATLAS T				**M124015713**
PATIENT ID M206139800	DATE OF BIRTH 05/13/2010	AGE 15 Y	SEX Male	REQUESTED BY PROVIDER UNKNOWN
COLLECTED 2/24/2026, 10:39 AM	RECEIVED 2/24/2026, 10:39 AM	REPORTED 2/24/2026, 10:42 AM		

The collected, received, and reported dates and times on the report are in the time zone of the performing location.

7028845
MCL Jacksonville Campus
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CLIENT MRN
321

Specimen Type	**Bone marrow**
Indication for Test	**r/o AML**
Reviewed By	**SONIA RODRIGUEZ**

INTERPRETATION

A full copy of the interpretative report is available as a PDF appended to this cover sheet and is ready to review.

This result should be interpreted within the context of the hematopathology report and correlated with other laboratory testing results for disease classification, monitoring and therapy selection.

Code : MCF Laboratory : Mayo Clinic Jacksonville, Clinical Laboratory Address : 4500 SAN PABLO ROAD
Lab Director : JEFFREY SAMUEL DLOTT MD CLIA Certificate : 10D0269502 JACKSONVILLE FL 32224--186

Patient Name:
Specimen ID:

Order Number:

Sample Cancer Type: Other Hematological Cancer

PATHOGENIC MUTATIONS DETECTED

DNA Sequence Variants

Gene	Locus	Transcript	Coding	Amino Acid Change	Allele Frequency	Coverage
JAK2	chr9:5073770	NM_004972.4	c.1849G>T	p.(V617F)	69.70%	1983
ASXL1	chr20:31023112	NM_015338.6	c.2598_2599insA	p.(G867Rfs*13)	11.60%	1979
SRSF2	chr17:74732959	NM_003016.4	c.284C>T	p.(P95L)	33.50%	765

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INTERPRETATION

JAK2 p.(V617F) c.1849G>T

Janus kinase 2

Background: The JAK2 gene encodes Janus kinase 2, a non-receptor protein tyrosine kinase (PTK)[1,2]. JAK2 is a member of the Janus kinase (JAK) family, which includes JAK1, JAK2, JAK3, and TYK2[2]. Janus kinases are characterized by the presence of a second phosphotransferase-related or pseudokinase domain immediately N-terminal to the PTK domain[3]. JAK kinases function with signal transducer and activator of transcription (STAT) proteins to facilitate intracellular signal transduction required for cytokine receptor and interferon-alpha/beta/gamma signaling[3,4,5]. Since JAK2 functions in interferon receptor signaling, inactivation of JAK2 is proposed to inhibit the presentation of tumor antigens and contribute to immune evasion[6,7].

Alterations and prevalence: Clonal expansion of hematopoietic cells in myeloproliferative neoplasms (MPNs) is associated with loss of heterozygosity on chromosome 9p and subsequently the acquisition of a dominant somatic gain-of-function V617F mutation in the pseudokinase domain of JAK2[8,9]. The JAK2 V617F mutation is rarely observed in acute myeloid leukemia (AML)[10,11]. Mutations in the pseudokinase domain of JAK2, including R683G, have been detected in 8% of ALL[12,13]. JAK2 fusions are observed in myeloid and lymphoid leukemias with partner genes including TEL, PCM1, and BCR[14,15,16,17]. JAK2 fusions are infrequently observed in solid tumors[18]. As with JAK1, truncating mutations in JAK2 are common in solid tumors and particularly enriched in uterine cancers[18]. JAK2 is amplified in 4% of sarcoma, diffuse large B-cell lymphoma, and head and neck squamous cell carcinoma, 3% of ovarian serous cystadenocarcinoma, and 2% of esophageal adenocarcinoma, uterine corpus endometrial carcinoma, stomach adenocarcinoma, bladder urothelial carcinoma, and uterine carcinosarcoma[18,19]. Alterations in JAK2 are also observed in pediatric cancers[18,19]. Somatic mutations are observed in 6% of B-lymphoblastic leukemia/lymphoma, 3% of soft tissue sarcoma, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of leukemia (3 in 354 cases), bone cancer (2 in 327 cases), glioma (1 in 297 cases), Wilms tumor (1 in 710 cases), and peripheral nervous system tumors (1 in 1158 cases)[18,19]. JAK2 fusions are observed in 10% of B-lymphoblastic leukemia/lymphoma and 1% of leukemia (1 in 107 cases)[18,19]. JAK2 is amplified in 1% of Wilms tumor (2 in 136 cases) and less than 1% of B-lymphoblastic leukemia/lymphoma (4 in 731 cases)[18,19].

Potential relevance: Currently, no therapies are approved for JAK2 aberrations. JAK2 V617F and JAK2 exon 12 mutations are considered major diagnostic criteria of polycythemia vera (PV)[20,21]. Ruxolitinib[22] (2011) is a JAK1/2 inhibitor FDA approved for PMF and PV, although specific JAK2 alterations are not indicated. Other JAK inhibitors including tofacitinib (2012) and baricitinib (2018) are approved for the treatment of rheumatoid arthritis. JAK2 mutations and fusions are associated with poor risk in acute lymphoblastic leukemia[23]. Clinical cases associated with high tumor mutational burden (TMB) but failure to respond to anti-PD1 therapy were associated with loss of function mutations in JAK1/2[24]. Some case studies report efficacy with ruxolitinib in myeloid and lymphoid leukemias, although duration of complete response was limited[14,15,16,17].

ASXL1 p.(G867Rfs*13) c.2598_2599insA

additional sex combs like 1, transcriptional regulator

Background: The ASXL1 gene encodes the ASXL transcriptional regulator 1 protein, a ligand-dependent co-activator and epigenetic scaffolding protein involved in transcriptional regulation[1,41]. ASXL1 belongs to the ASXL gene family, which also includes ASXL2 and ASXL3[41]. ASXL proteins contain a conserved c-terminal plant homeodomain (PHD) which facilitates interaction with DNA and histones[41,42]. ASXL1 influences chromatin remodeling and transcription through interaction with BAP1 and polycomb repressive complex (PRC) proteins, as well as other transcriptional activators and repressors[41,43]. In cancer, ASXL1 is the target of somatic mutations which often result in a truncated ASXL1 protein and loss of its PHD[44,45,46]. Such mutations can lead to impaired protein function and consequent upregulation of HOXA gene expression, supporting a tumor suppressor role for ASXL1[47].

Alterations and prevalence: Missense, nonsense, and frameshift mutations in ASXL1 are reported in 3-6% of de novo acute myeloid leukemia (AML), up to 36% of secondary AML, approximately 15% of myelodysplastic syndromes (MDS), up to 23% of myeloproliferative neoplasms (MPN), up to 30% of systemic mastocytosis (SM), and approximately 45% of chronic myelomonocytic leukemia (CMML)[18,37,43,48,49,50,51,52,53]. The ASXL1 G646Wfs*12 mutation accounts for over 50% of ASXL1 mutated cases in myeloid malignancies[45,50,54]. This mutation results from a single nucleotide expansion that occurs within an eight base pair guanine repeat that extends from c.1927 to c.1934. It is proposed that the high prevalence of the G646Wfs*12 variant is due to replication slippage which can occur in areas of repetitive sequence[55]. As a consequence, detection of G646Wfs*12 may result as an artifact of PCR and/or sequencing[56]. However, multiple studies observe an increase in the frequency of G646Wfs*12 in myeloid cancer relative to normal suggesting that G646Wfs*12 is a bona fide somatic mutation[48,55,57].

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INTERPRETATION (continued)

Potential relevance: The majority of frameshift and nonsense mutations in ASXL1 that result in protein truncation and removal of the PHD domain are considered pathogenic[58]. Mutations in ASXL1 confer poor/adverse risk in AML[37,39]. Additionally, ASXL1 nonsense or frameshift mutations are independently associated with poor prognosis in MDS and CMML[35]. Moreover, ASXL1 mutations are independently associated with inferior overall survival (OS) in patients with MPN or SM[20,36].

SRSF2 p.(P95L) c.284C>T

serine and arginine rich splicing factor 2

Background: The SRFS2 gene encodes the serine/arginine (SR)-rich splicing factor 2, a member of the SR-rich family of pre-mRNA splicing factors which make up part of the spliceosome. SRFS2 contains an RNA recognition motif (RRM) that recognizes and binds exonic splicing enhancers (ESE) in a sequence-specific manner[25]. SR proteins are essential regulators of alternative RNA splicing due to their ability to bind RNA and interact with other splicing factors. These proteins can influence the exclusion of cassette exons, a form of alternative splicing also known as exon skipping, which allows for the production of different protein isoforms[25,26]. SRSF2 is the target of somatic missense mutations and in-frame deletions in hematological malignancies, particularly myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), and myeloproliferative neoplasms (MPN)[27,28,29]. Such mutations in SRSF2 result in a differential gain of function which influences cassette exon exclusion, thereby supporting an oncogenic role in cancer[30].

Alterations and prevalence: Mutations in SRSF2 are observed in approximately 10% of MDS cases and 30-40% of CMML[28,31,32]. Missense mutations at P95 are most recurrent, which leads to an amino acid change from proline to histidine (H), leucine (L), or arginine (R)[32]. Specifically, the P95H substitution alters SRSF2 affinity for ESEs and drives preferential recognition of cassette exons containing C- versus G-rich ESEs[29,30]. Although less prevalent, recurrent in-frame deletions (P95H_R102del) are observed in primary myelofibrosis (PMF)[33]. This mutation results in the deletion of 8 amino acids which has been shown to exhibit greater variation of splicing events relative to the P95 missense mutation alone[34].

Potential relevance: Mutation of SRSF2 considered is one of the molecular abnormalities that defines acute myeloid leukemia, myelodysplasia related (AML-MR) according to the World Health Organization (WHO)[21]. SRSF2 mutations confer poor prognosis and risk in MDS, systemic mastocytosis (SM), and acute myeloid leukemia (AML) and are associated with decreased overall survival (OS)[35,36,37,38,39]. In MPN, SRSF2 mutations are considered high-risk mutations and are independently associated with inferior OS as well as leukemia-free survival[20,40]. Additionally, SRSF2 mutations are predictive of leukemic transformation in patients with PMF[20].

Variants of Unknown Significance

DNA Sequence Variants

Gene	Locus	Transcript	Coding	Amino Acid Change	Allele Frequency
CEBPA	chr19:33792597	NM_004364.4	c.724G>A	p.(G242S)	50.60%

CLINICAL TRIALS

Information regarding possible clinical trials for this patient can be found at the following sites:

1). ClinicalTrials.gov:
http://clinicaltrials.gov/ct2/search/advanced

2). Mayo Clinic:
http://www.mayo.edu/research/clinical-trials

3). National Cancer Institute:
http://www.cancer.gov/clinicaltrials/search

4). The Leukemia & Lymphoma Society's Clinical Trial Support Center
htt s://www.hematolog .or /education/clinicians/clinical-trial-Su ort-center

METHOD SUMMARY

This assay includes DNA based sequencing for 52 genes including the hotspots of 32 genes and 20 full genes, and RNA based sequencing for 35 fusion driver genes which allows to detect > 700 unique fusions.

DNA and RNA are extracted from blood or bone marrow samples. After library preparation using Ion AmpliSeq™ technology, the samples are subjected to Ion Torrent next generation sequencing (NGS) with post-sequencing analysis on an NGS instrument, Genexus. NGS bioinformatics is performed using the software provided by Thermo Fisher.

Genomic alterations are called according to the Genome Reference Consortium Human Build 37 (GRCh37), hg19 and described using the standard nomenclature and interpreted using the current standards and guidelines recommended by Association of Molecular pathology (AMP), American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP).

Our validation has shown >99% of accuracy, 100% (intra- and interassay) reproducibility and a sensitivity of detection of 5% variant allele fraction (VAF) with a minimum depth coverage of 250X for single base substitutions, insertion/deletion events including FL T3-ITDs and gene fusions for the targeted gene mutations and fusions included in the validation design.

DISCLAIMER

CLINICAL DISCLAIMER
This assay is designed mainly to detect currently known clinically significant somatic mutations and fusions in the genes associated with myeloid neoplasms. However, this assay may detect genomic variants of unknown significance. In some cases, mutations detected may represent CHIP (Clonal Hematopoiesis of Indeterminate Potential) mutations with no detectable hematological malignancies. In addition, patients with unexplained cytopenias may also harbor similar myeloid neoplasm-associated gene mutations (clonal cytopenias of uncertain significance, CCUS). Prior treatment for hematologic malignancy, particularly allogeneic hematopoietic stem cell transplant (HSCT) can affect the results obtained in this assay, as this assay may not distinguish between the donor and the recipient genomes. This assay does not distinguish between somatic and germ line alterations in analyzed gene regions, particularly with VAF near 50% or 100%. If nucleotide alterations in genes associated with germline mutation syndromes are present and there is also a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. This report interpretation is based on current medical and scientific literature, but clinical significance may not be completely established for all reported target gene abnormalities identified. The sequencing results should be interpreted

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in the context of clinical setting of a disease and correlated with the clinical, morphologic, and immunological features as well as other laboratory findings. The final interpretation of the NGS results for clinical management of the patient is the responsibility of the managing physician.

TECHNICAL DISCLAIMER
This assay is a targeted sequencing for the mutations in the genes or the hotspot of the genes known to be associated with myeloid neoplasms. The depth of sequencing coverage may be variable for some target regions. It is known that regions containing extended stretches of a repetitive nucleotide can be difficult for sequencing and thus mutations in such regions may be reported lower than expected. For example, a lower than expected VAF for the ASXL 1 c.1934dupG mutation may occur due to presence of homopolymers in the region, as noted by this lab and other users of this assay. A low tumor cell percentage in the sample may impact on the determination of VAF and/or mutation detection sensitivity. Suboptimal-performing regions (i.e. less than the expected minimum depth of coverage) may affect analytic sensitivity for detecting lower level mutations. This is a qualitative assay and therefore the VAF represents a relative proportion but not a precise measurement of mutant alleles. This assay detects FL T3-ITD up to 150 bp insertions as determined by our validation and published data. Some genomic alterations, such as very large insertions/deletions and copy number alterations (CNA) at the exon or gene level are not detected by this assay. This assay detects currently known gene fusions associated with myeloid neoplasms but not the other types of chromosome structural abnormalities.

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CUA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ANKRD26, ASXL1, BCOR, BCORL1, BRAF, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, HRAS, IDH1, IDH2, IKZF1, JAK2, KIT, KRAS, MPL, MYD88, NF1, NPM1, NRAS, PHF6, PPM1D, PRPF8, PTPN11, RAD21, RB1, RUNX1, SETBP1, SF3B1, SH2B3, SMC1A, SMC3, SRSF2, STAG2, STAT3, STAT5B, TET2, TP53, U2AF1, UBA1, WT1, ZRSR2

Genes Assayed for the Detection of Fusions

ABI1, ABI2, ABL1, ABL2, ACACA, ACER1, ACSL6, ACTN4, ADAM32, ADAMTS17, ADARB2, ADD3, AFF1, AFF3, AFF4, AGAP3, AGK, AGTRAP, AKAP9, ALK, ANLN, AP3B1, APBB1IP, ARHGAP26, ARHGEF12, ARHGEF17, ARMC10, ARNT, ATF7IP, ATG16L2, ATG7, ATP2B1, BAALC, BAG4, BCL2, BCL2L11, BCOR, BCR, BICD2, BIN2, BPTF, BRAF, BTBD18, BTF3L4, C11orf88, C7orf73, C8orf34, CABIN1, CAPRIN1, CASC5, CASP8AP2, CBFA2T2, CBFA2T3, CBFB, CBL, CCDC28A, CCDC6, CCDC88C, CCDC91, CCND1, CCNY, CCT8, CDC27, CDK5RAP2, CDK6, CDX2, CEP170B, CEP76, CEP85L, CEP89, CHIC2, CLCA2, CLCN6, CNTRL, COX5A, CPSF6, CREBBP, CT45A2, CUL1, CUX1, DAB2IP, DCP1A, DCPS, DDIT3, DDX10, DDX3X, DEK, DTD1, DUSP16, DYNC1I2, EBF1, EGFR, EIF2B1, ELL, EML1, ENAH, EP300, EPS15, ERC1, ERVK3-1, ETV6, EVX1, FAM114A2, FAM131B, FBXW2, FCHSD1, FGFR1, FGFR1OP, FGFR1OP2, FGFR2, FGFR3, FHIT, FIP1L1, FLNA, FLT3, FN1, FNBP1, FOXO3, FOXO4, FOXP1, FRK, FRYL, FSTL3, FUS, GAS7, GATM, GHR, GIT2, GMPS, GNAI1, GOLGA4, GOLGB1, GOT1, GPHN, GRIPAP1, GSX2, GTF2I, HERPUD1, HHEX, HIP1, HLF, HMGA2, HMGB3, HNRNPH1, HOOK3, HOXA11, HOXA13, HOXA9, HOXC11, HOXC13, HOXD11, HOXD13, INO80D, INPP5D, IQCG, IRF2BP2, ITPR2, JAK2, KANK1, KAT6A, KAT6B, KAT7, KCTD7, KDM5A, KDM7A, KDR, KIAA1524, KIAA1549, KIAA1549L, KIF5B, KLHL7, KMT2A, LASP1, LNP1, LPP, LPXN, LRP6, LRRFIP1, LSM12, LSM14A, LYN, MACF1, MACROD1, MAD1L1, MAML2, MAPRE1, MECOM, MEF2C, MET, MKL1, MKRN1, MLLT1, MLLT10, MLLT11, MLLT3, MLLT4, MLLT6, MN1, MPRIP, MROH2B, MRPS6, MYBL1, MYC, MYH11, MYO18A, MYO1F, MYRIP, MZT1, NABP1, NAP1L1, NCKIPSD, NCOA2, NDE1, NEBL, NIN, NKAIN2, NOL4L, NPM1, NRIP3, NSD1, NTRK2, NTRK3, NUB1, NUDCD3, NUMA1, NUP214, NUP98, OFD1, PAPSS1, PAX5, PBX1, PCM1, PDE4DIP, PDGFRA, PDGFRB, PDS5A, PER1, PHF23, PICALM, PLIN3, PML, POU1F1, PPFIBP1, PRDM12, PRDM16, PRDX4, PRKAR1A, PRKG2, PRRX1, PRRX2, PSIP1, PSMB2, PSMD2, PTPRR, PUM1, RABEP1, RABGAP1L, RAD18, RAD51B, RALGPS1, RANBP2, RAP1GDS1, RARA, RARG, RBM15, RBMS3, RCSD1, RNF115, RNF130, RP2, RPL22, RPS3, RUNX1, RUNX1T1, SARNP, SART3, SCAF11, SEC31A, SEPT11, SEPT2, SEPT5, SEPT6, SEPT9, SET, SETBP1, SFPQ, SH3D19, SH3GL1, SLC12A7, SLC45A3, SMAP1, SMC1A, SND1, SNX2, SORBS2, SOX6, SPAG9, SPECC1, SPECC1L, SQSTM1, SSBP2, STAT5B, STRN, STRN3, SYK, TACC1, TANK, TAX1BP1, TBL1XR1, TCF3, TECR, TERF2, TET1, TFE3, TFPT, TIRAP, TMEM178B, TMPRSS2, TNIP1, TNKS2, TOP1, TOP2B, TOP3A, TP53BP1, TPM3, TPR, TRIM24, TRIM27, TRIM4, TRIP11, TRPS1, UBN2, USP16, USP2, USP42, UVRAG, VRK1, WDR48, WHSC1L1, WT1, XKR3, YTHDF2, ZBTB16, ZC3HAV1, ZEB2, ZFPM2, ZFYVE19, ZKSCAN5, ZMIZ1, ZMYM2, ZNF384, ZNF687, ZSCAN30

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