GCG-Myelodysplastic Syndromes(MDS) / Myeloproliferative Neoplasm(MPN) Panel

Personal Information	Specimen Information	Test Information
Name: Jason Doe	Sample ID: 20230327-971-0000	Test reported: 2023-04-11
Date of Birth: 1996.01.01	Medical record No: -	Ordering physician: Dr. Smith
Sex: Male	Date received: 2023-03-27	Institution: Hospital A

Cancer Type R/O MDS/MPN

RESULT SUMMARY

	Tier 1	Tier 2	Tier 3
Variant	1	0	1
Gene	JAK2	-	KDM6A

TEST RESULT

Tier 1 : Variants of Strong Clinical Significance 1

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	JAK2	c.1849G>T	p.Val617Phe	18	978	COSM12600

INTERPRETATION

The c.1849G>T (p.Val617Phe) variant in the JAK2 gene has been previously reported mainly in hematologic malignancy (N=42,773, COSM12600), and the V617F variant is classified as oncogenic. The JAK2 gene is a type of intracellular kinase, mainly found in MPN, and the V617F mutation is found in polycythemia vera (PV, >95%), essential thrombocythemia (ET, 50-60%), and primary myelofibrosis (PMF, 50-60%). In PMF, the JAK2 V617F mutation corresponds to intermediate prognosis. The JAK2 inhibitor, ruxolitinib, is FDA approved for the treatment of polycythemia vera that is inadequate or intolerant to hydroxyurea, intermediate-risk or high-risk myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. A JAK2 V617F mutation can be also found in MDS with isolated del(5q) and does not affect the prognosis.

Tier 2 : Variants of Potential Clinical Significance 0

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
No variant						

INTERPRETATION

No tier 2 (Potential clinical significance) mutations were identified.

Tier 3 : Variants of Unknown Clinical Significance 1

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	KDM6A	c.799A>G	p.Ser267Gly	100	502	-

INTERPRETATION

The c.799A>G (p.Ser267Gly) variatn in KDM6A gene has not been previously reported in cancer tissues including hematologic malignancy and its clinical significance is unclear due to unknown oncogenicity of the variant.

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Lab Director(medical doctor)
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TEST INFORMATION

1. TEST METHOD

Target Region	49 genes(essential : 11 genes, additional : 38 genes)
Tested Panel	Myelodysplastic syndromes (MDS) Panel
Target Enrichment Method	Hybridization with oligonucleotide probes (HEMA v.2301.1)
Massively Parallel Sequencing	Sequencing by synthesis (illumina)
Bioinformatic Pipeline	BI_Hema_v2.0 (Alignment: BWA, Variant calling: VarScan2_GATK)
Reference Genome	GRCh37/hg19

2. QC DATA

Sample(DNA) QC	Pass	Mean Coverage of Depth(X)	1126X
Library QC	Pass	% of Target Bases ≥ 50X	100%
Sequencing QC	Pass		

3. TEST LIMITATIONS

- This test was performed using sequencing analysis, and can detect SNP and small-indel variants within the analyzed region, but not structural variations such as copy number variation (CNV) and gene rearrangement.
- The limit of detection for SNV and small-indel variants is approximately 5%.
- The detected variants in this test are not re-confirmed by Sanger sequencing, ddPCR or other confirmation methods.
- This test does not distinguish between germline and somatic variants. If the variant allele frequency of the mutation is close to 50% or 100%, the possibility of germline variant cannot be excluded.
- The variants detected in this test are classified into four (tier 1~4) according to the 2017 JMD guideline (J Mol Diagn 2017;19:313-327), and tier 4 variants are not reported.

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4. CLASSIFICATIONS

Somatic Variants are classified into four stages according to the evidence level and clinical significance of the mutation.
Tier 4 is not reported.

Tier1	Strong clinical significance	Level A or B evidence
Tier2	Potential clinical significance	Level C or D evidence
Tier3	Unknown clinical significance	Not observed at a significant allele frequency in the general or specific subpopulation databases, or no convincing published evidence of cancer association.
Tier4	Benign or likely benign	Observed at significant allele frequency in the general databases. No existing published evidence of cancer association.

EVIDENCE LEVEL

Level A	Biomarkers related to predicting therapeutic response or resistance to FDA-approved therapies in specific cancer types or biomarkers included in professional guidelines as being related to therapeutic response or resistance to drugs, diagnosis or prognosis of cancer.
Level B	A biomarker with a consensus among experts in a well-designed study that is associated with the treatment response or resistance to a drug, the diagnosis or prognosis in a specific cancer type.
Level C	Predictive biomarkers of therapeutic response or resistance to FDA-approved drugs in other cancer types or biomarkers eligible for clinical trial participation, and biomarkers reported to be associated with cancer diagnosis or prognosis in several small studies.
Level D	Biomarkers with preclinical trials or small studies or several case reports.

REFERENCES

- COSMIC(http://cancer.sanger.ac.uk)
- c-bioportal(http://www.cbioportal.org)
- Cancer Hotspots(http://cancerhotspots.org)
- OncoKB(http://oncokb.org)
- My Cancer Genome(https://www.mycancergenome.org/)
- The Clinical Knowledgebase(https://ckb.jax.org/)
- WHO classification of tumours of haematopoietic and lymphoid tissues(revised 4th edition)
- NCCN guidelines®

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5. GENE INFORMATION

ESSENTIAL GENE LIST

Gene	Target Exon No.	Reference Transcript	Gene	Target Exon No.	Reference Transcript	Gene	Target Exon No.	Reference Transcript
ASXL1	12	NM_015338	CALR	All coding exons	NM_004343	CSF3R	14, 17	NM_156039
DNMT3A	All coding exons	NM_022552	JAK2	12, 14	NM_004972	MPL	10	NM_005373
RUNX1	All coding exons	NM_001754	SETBP1	4*	NM_015559	SF3B1	6-8, 12-17	NM_012433
SRSF2	1	NM_003016	TET2	All coding exons	NM_001127208			

ADDITIONAL GENE LIST

Gene	Target Exon No.	Reference Transcript	Gene	Target Exon No.	Reference Transcript	Gene	Target Exon No.	Reference Transcript
ANKRD26	5'UTR	NM_014915	ATRX	8-10, 17-31	NM_000489	BCOR	All coding exons	NM_001123385
BCORL1	All coding exons	NM_021946	BRAF	15	NM_004333	CBL	8-9	NM_005188
CBLB	9-10	NM_170662	CEBPA	All coding exons	NM_004364	DDX41	All coding exons	NM_016222
ETV6	All coding exons	NM_001987	EZH2	All coding exons	NM_004456	FLT3	14-20	NM_004119
GATA1	All coding exons	NM_002049	GATA2	All coding exons	NM_001145661	HRAS	2-3	NM_005343
IDH1	4	NM_005896	IDH2	4	NM_002168	JAK3	13	NM_000215
KDM6A	All coding exons	NM_021140	KIT	8-14, 17-18	NM_000222	KRAS	2-4	NM_004985
NOTCH1	26-28, 34	NM_017617	NPM1	10-11	NM_002520	NRAS	2-4	NM_002524
PDGFRA	12, 14, 18	NM_006206	PHF6	All coding exons	NM_001015877	PPM1D	6	NM_003620
PTPN11	3-4, 12-13	NM_002834	RAD21	All coding exons	NM_006265	SMC1A	2, 11, 16-17	NM_006306
SMC3	All coding exons	NM_005445	STAG1	All coding exons	NM_005862	STAG2	All coding exons	NM_001042749
STAT3	20-21	NM_139276	TP53	All coding exons	NM_000546	U2AF1	2, 6	NM_006758
WT1	2-10	NM_024426	ZRSR2	All coding exons	NM_005089			

※ The test has been developed by GC Genome (Laboratory - developted Test, LDT) and it has been deemed suitable for clinical testing through appropriate evaluation. This report contains the results of the genetic analysis.

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