25371 Commercentre Drive, Lake Forest, CA 92630
Tel: 1-866-484-8870 | genomictestingcooperative.com
CLIA # 05D2111917 CAP # 9441574

Liquid Trace Hematology

Patient Name:		Ordering Physician:	
Date of Birth:		Physician ID:	
Gender (M/F):		Accession #:	
Client:		Specimen Type:	
		Specimen ID:	
Case #:			
Body Site:	PERIPHERAL BLOOD		

MRN:			Indication for Testing:	C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
Collected Date:		Time: 12:00 AM		
Received Date:		Time: 02:38 PM		
Reported Date:		Time: 06:23 PM		

Detected Genomic Alterations				
ATM	TCF3	BCL6	ERBB4	CREBBP
DAXX	GNAQ	PPM1D	SF3B1	ARID1A
TP53	CHEK2	DNMT3A	TERT	No detectable autosomal chromosomal structural gain or loss
B-cell clonality : Oligoclonal (IgHV 4 -80)	T-cell clonality : Not detected			

Results Summary

- **-Low-level mutations in ATM, TCF3, BCL6, ERBB4, CREBBP, DAXX, GNAQ, PPM1D, SF3B1, ARID1A, TP53, CHEK2, DNMT3A, and TERT genes**
  -No detectable autosomal chromosomal structural gain or loss
  -EBV viral RNA: Not detected
  -HPV viral RNA: Not detected
  -TTV viral RNA: Not detected
  -HLA Genotyping:
  -HLA-A: A*01:01-A*25:01
  -HLA-B: B*07:02-B*18:01
  -HLA-C: C*12:03-C*07:02
  -B-cell clonality : Oligoclonal (IgHV 4-80)
  -T-cell clonality : Not detected.

  -These findings are consistent with high-grade B-cell lymphoma.

  See additional report information at the end of the report.

Heterogeneity

There are abnormal low-level clones with ATM, TCF3, BCL6, ERBB4, CREBBP, DAXX, GNAQ, PPM1D, SF3B1, ARID1A, TP53, CHEK2, DNMT3A, and TERT mutations.

Diagnostic Implications

ATM, TCF3, BCL6, ERBB4, CREBBP, DAXX, GNAQ, PPM1D, SF3B1, ARID1A, TP53, CHEK2, DNMT3A, TERT	These findings are consistent with high-grade B-cell lymphoma

Therapeutic Implications

ATM	PARP inhibitors
ERBB4	May predict sensitivity to Lapatinib and other anti-EGF family inhibitors (Dacomitinib)
CREBBP	Bromodomain and Extra-Terminal motif (BET) inhibitors
GNAQ	MAPK pathway inhibitors
PPM1D	PPM1D inhibitors
SF3B1	Spliceosome modifiers
ARID1A	sensitivity to radiation therapy and PARP inhibitors
TP53	Aurora kinase A inhibitors, Wee1 inhibitors, Chk1 inhibitors, kevetrin, APR-246, nutlins, gene therapy
CHEK2	PARP inhibitors
DNMT3A	DNA methyltransferase inhibitors

Prognostic Implications

ATM	Poor
TCF3	Unknown
BCL6	Unknown
ERBB4	Poor
CREBBP	Poor
DAXX	Unknown
GNAQ	Unknown
PPM1D	Poor
SF3B1	Poor
ARID1A	Unknown
TP53	Poor
CHEK2	Poor
DNMT3A	Poor

TERT	Unknown

Relevant Genes with NO Alteration
No evidence of mutation in NOTCH or MYD88

Test Description:

This is a comprehensive molecular profile which uses next generation sequencing (NGS) to identify molecular abnormalities, including single nucleotide variants (SNVs), insertions/deletions (indels), copy number variants (CNVs), fusions, B- and T-cell clonality, and viruses (HPV, EBV, and TTV), in cell-free (cf) DNA of 302 genes and cfRNA in greater than 1600 genes implicated in hematologic neoplasms, including leukemia, lymphoma, myeloma, myelodysplastic syndrome, and myeloproliferative neoplasms. Whenever possible, clinical relevance and implications of detected abnormalities are described below. If a gene is not reported, then no somatic mutations were detected. This assay facilitates myelodysplastic syndrome risk assessment as it includes evaluation for mutations and significant chromosomal gains and losses in all of the genes included in the IPSS-M risk calculator: ASXL1, BCOR, BCORL1, CBL, CEBPA, DNMT3A, ETNK1, ETV6, EZH2, FLT3, GATA2, GNB1, IDH1, IDH2, KMT2A (including KMT2A(MLL)-PTD), KRAS, NF1, NPM1, NRAS, PHF6, PPM1D, PRPF8, PTPN11, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TP53, U2AF1, and WT1.

Biological relevance of detected Alterations

- ATM. The protein encoded by this gene belongs to the PI3/PI4-kinase family. This protein is an important cell cycle checkpoint kinase that phosphorylates; thus, it functions as a regulator of a wide variety of downstream proteins, including tumor suppressor proteins p53 and BRCA1, checkpoint kinase CHK2, checkpoint proteins RAD17 and RAD9, and DNA repair protein NBS1. This protein and the closely related kinase ATR are thought to be master controllers of cell cycle checkpoint signaling pathways that are required for cell response to DNA damage and for genome stability. Mutations in this gene are associated with ataxia telangiectasia, an autosomal recessive disorder. [provided by RefSeq, Aug 2010]

- TCF3. This gene encodes a member of the E protein (class I) family of helix-loop-helix transcription factors. E proteins activate transcription by binding to regulatory E-box sequences on target genes as heterodimers or homodimers, and are inhibited by heterodimerization with inhibitor of DNA-binding (class IV) helix-loop-helix proteins. E proteins play a critical role in lymphopoiesis, and the encoded protein is required for B and T lymphocyte development. Deletion of this gene or diminished activity of the encoded protein may play a role in lymphoid malignancies. This gene is also involved in several chromosomal translocations that are associated with lymphoid malignancies including pre-B-cell acute lymphoblastic leukemia (t(1;19), with PBX1), childhood leukemia (t(19;19), with TFPT) and acute leukemia (t(12;19), with ZNF384). Alternatively spliced transcript variants encoding multiple isoforms have been observed for this gene, and a pseudogene of this gene is located on the short arm of chromosome 9. [provided by RefSeq, Sep 2011]

- BCL6. The protein encoded by this gene is a zinc finger transcription factor and contains an N-terminal POZ domain. This protein acts as a sequence-specific repressor of transcription, and has been shown to modulate the transcription of STAT-dependent IL-4 responses of B cells. This protein can interact with a variety of POZ-containing proteins that function as transcription corepressors. This gene is found to be frequently translocated and hypermutated in diffuse large-cell lymphoma (DLCL), and may be involved in the pathogenesis of DLCL. Alternatively spliced transcript variants encoding different protein isoforms have been found for this gene. [provided by RefSeq, Aug 2015]

- ERBB4. This gene is a member of the Tyr protein kinase family and the epidermal growth factor receptor subfamily. It encodes a single-pass type I membrane protein with multiple cysteine rich domains, a transmembrane domain, a tyrosine kinase domain, a phosphotidylinositol-3 kinase binding site and a PDZ domain binding motif. The protein binds to and is activated by neuregulins and other factors and induces a variety of cellular responses including mitogenesis and differentiation. Multiple proteolytic events allow for the release of a cytoplasmic fragment and an extracellular fragment. Mutations in this gene have been associated with cancer. Alternatively spliced variants which encode different protein isoforms have been described; however, not all variants have been fully characterized. [provided by RefSeq, Jul 2008]

- CREBBP. This gene is ubiquitously expressed and is involved in the transcriptional coactivation of many different transcription factors. First isolated as a nuclear protein that binds to cAMP-response element binding protein (CREB), this gene is now known to play critical roles in embryonic development, growth control, and homeostasis by coupling chromatin remodeling to transcription factor recognition. The protein encoded by this gene has intrinsic histone acetyltransferase activity and also acts as a scaffold to stabilize additional protein interactions with the transcription complex. This protein acetylates both histone and non-histone proteins. This protein shares regions of very high sequence similarity with protein p300 in its bromodomain, cysteine-histidine-rich regions, and histone acetyltransferase domain. Mutations in this gene cause Rubinstein-Taybi syndrome (RTS). Chromosomal translocations involving this gene have been associated with acute myeloid leukemia. Alternative splicing results in multiple transcript variants encoding different isoforms. [provided by RefSeq, Feb 2009]

- DAXX. This gene encodes a multifunctional protein that resides in multiple locations in the nucleus and in the cytoplasm. It interacts with a wide variety of proteins, such as apoptosis antigen Fas, centromere protein C, and transcription factor erythroblastosis virus E26 oncogene homolog 1. In the nucleus, the encoded protein functions as a potent transcription repressor that binds to sumoylated transcription factors. Its repression can be relieved by the sequestration of this protein into promyelocytic leukemia nuclear bodies or nucleoli. This protein also associates with centromeres in G2 phase. In the cytoplasm, the encoded protein may function to regulate apoptosis. The subcellular localization and function of this protein are modulated by post-translational modifications, including sumoylation, phosphorylation and polyubiquitination. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Nov 2008]

- GNAQ. This locus encodes a guanine nucleotide-binding protein. The encoded protein, an alpha subunit in the Gq class, couples a seven-transmembrane domain receptor to activation of phospolipase C-beta. Mutations at this locus have been associated with problems in platelet activation and aggregation. A related pseudogene exists on chromosome 2.[provided by RefSeq, Nov 2010]

- PPM1D. The protein encoded by this gene is a member of the PP2C family of Ser/Thr protein phosphatases. PP2C family members are known to be negative regulators of cell stress response pathways. The expression of this gene is induced in a p53-dependent manner in response to various environmental stresses. While being induced by tumor suppressor protein TP53/p53, this phosphatase negatively regulates the activity of p38 MAP kinase, MAPK/p38, through which it reduces the phosphorylation of p53, and in turn suppresses p53-mediated transcription and apoptosis. This phosphatase thus mediates a feedback regulation of p38-p53 signaling that contributes to growth inhibition and the suppression of stress induced apoptosis. This gene is located in a chromosomal region known to be amplified in breast cancer. The amplification of this gene has been detected in both breast cancer cell line and primary breast tumors, which suggests a role of this gene in cancer development. [provided by RefSeq, Jul 2008]

- SF3B1. This gene encodes subunit 1 of the splicing factor 3b protein complex. Splicing factor 3b, together with splicing factor 3a and a 12S RNA unit, forms the U2 small nuclear ribonucleoproteins complex (U2 snRNP). The splicing factor 3b/3a complex binds pre-mRNA upstream of the intron's branch site in a sequence independent manner and may anchor the U2 snRNP to the pre-mRNA. Splicing factor 3b is also a component of the minor U12-type spliceosome. The carboxy-terminal two-thirds of subunit 1 have 22 non-identical, tandem HEAT repeats that form rod-like, helical structures. Alternative splicing results in multiple transcript variants encoding different isoforms. [provided by RefSeq, Jul 2008]

- ARID1A. This gene encodes a member of the SWI/SNF family, whose members have helicase and ATPase activities and are thought to regulate transcription of certain genes by altering the chromatin structure around those genes. The encoded protein is part of the large ATP-dependent chromatin remodeling complex SNF/SWI, which is required for transcriptional activation of genes normally repressed by chromatin. It possesses at least two conserved domains that could be important for its function. First, it has a DNA-binding domain that can specifically bind an AT-rich DNA sequence known to be recognized by a SNF/SWI complex at the beta-globin locus. Second, the C-terminus of the protein can stimulate glucocorticoid receptor-dependent transcriptional activation. It is thought that the protein encoded by this gene confers specificity to the SNF/SWI complex and may recruit the complex to its targets through either protein-DNA or protein-protein interactions. Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Jul 2008]

- TP53. This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]

- CHEK2. In response to DNA damage and replication blocks, cell cycle progression is halted through the control of critical cell cycle regulators. The protein encoded by this gene is a cell cycle checkpoint regulator and putative tumor suppressor. It contains a forkhead-associated protein interaction domain essential for activation in response to DNA damage and is rapidly phosphorylated in response to replication blocks and DNA damage. When activated, the encoded protein is known to inhibit CDC25C phosphatase, preventing entry into mitosis, and has been shown to stabilize the tumor suppressor protein p53, leading to cell cycle arrest in G1. In addition, this protein interacts with and phosphorylates BRCA1, allowing BRCA1 to restore survival after DNA damage. Mutations in this gene have been linked with Li-Fraumeni syndrome, a highly penetrant familial cancer phenotype usually associated with inherited mutations in TP53. Also, mutations in this gene are thought to confer a predisposition to sarcomas, breast cancer, and brain tumors. This nuclear protein is a member of the CDS1 subfamily of serine/threonine protein kinases. Several transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Apr 2012]

- DNMT3A. CpG methylation is an epigenetic modification that is important for embryonic development, imprinting, and X-chromosome inactivation. Studies in mice have demonstrated that DNA methylation is required for mammalian development. This gene encodes a DNA methyltransferase that is thought to function in de novo methylation, rather than maintenance methylation. The protein localizes to the cytoplasm and nucleus and its expression is developmentally regulated. [provided by RefSeq, Mar 2016]

- TERT. Telomerase is a ribonucleoprotein polymerase that maintains telomere ends by addition of the telomere repeat TTAGGG. The enzyme consists of a protein component with reverse transcriptase activity, encoded by this gene, and an RNA component which serves as a template for the telomere repeat. Telomerase expression plays a role in cellular senescence, as it is normally repressed in postnatal somatic cells resulting in progressive shortening of telomeres. Deregulation of telomerase expression in somatic cells may be involved in oncogenesis. Studies in mouse suggest that telomerase also participates in chromosomal repair, since de novo synthesis of telomere repeats may occur at double-stranded breaks. Alternatively spliced variants encoding different isoforms of telomerase reverse transcriptase have been identified; the full-length sequence of some variants has not been determined. Alternative splicing at this locus is thought to be one mechanism of

regulation of telomerase activity. [provided by RefSeq, Jul 2008] In addition, recurring somatic mutations at multiple spots in the proximal promoter (particularly at 124bp and 146bp upstream of the translation start site) are found in tumors of many tissue origins. These mutations are thought to affect binding of Ets family proteins and nuclear factor kappa B and alter secondary structure and long-range interactions, leading to increased promoter activity. [provided by RefSeq, May 2023]

Drug Information

Rituximab (Rituxan)

Rituximab is a monoclonal antibody that targets the CD20 antigen, which is expressed on the surface of pre-B and mature B-lymphocytes. After binding to CD20, rituximab mediates B-cell lysis (or breakdown). The possible mechanisms of cell lysis include complement dependent cytotoxicity (CDC) and antibody dependent cell-mediated cytotoxicity (ADCC).

Rituximab is indicated in the following conditions:
-Non-Hodgkin Lymphoma (NHL)
-Chronic Lymphocytic Leukemia (CLL)
-Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely-active RA
-Granulomatosis with Polyangiitis (GPA) (Wegener Granulomatosis) and Microscopic Polyangiitis (MPA)
-Moderate to severe Pemphigus Vulgaris (PV) in adult patients

Ibrutinib (Imbruvica)

Ibrutinib is a small molecule that acts as an irreversible potent inhibitor of Bruton tyrosine kinase (BTK). It is designated as a targeted covalent drug and it presents a very promising activity in B cell malignancies. Ibrutinib forms a covalent bond with a cysteine residue in the active site of BTK (Cys481), leading to its inhibition. The inhibition of BTK plays a role in the B-cell receptor signaling and thus, the presence of ibrutinib prevents the phosphorylation of downstream substrates such as PLC-gamma.

Ibrutinib was developed by Pharmacyclics Inc and in November 2013 was FDA-approved for the treatment of mantle cell lymphoma. Later, in February 2014, ibrutinib was approved for the treatment of chronic lymphocytic leukemia and it is also indicated for the treatment of patients with Waldenstrom Macroglobulinemia. Ibrutinib has also been approved by the EMA for the treatment of chronic lymphocytic leukemia and mantle cell lymphoma. Ibrutinib was approved for use in chronic graft versus host disease in August 2017.

Ibrutinib is indicated for:
-treatment of mantle cell lymphoma who have received at least one prior therapy.
-treatment of chronic lymphocytic leukemia (CLL) who have at least one prior therapy.
-treatment of chronic lymphocytic leukemia (CLL) with 17p deletion.
-treatment of patients with Waldenstrom Macroglobulinemia (WM).

Venetoclax (Venclexta)

Venetoclax is a selective inhibitor of both BCL-2 and BCL-2-like 1 (BCL-X(L)), which has demonstrated clinical efficacy in some BCL-2-dependent hematological cancers. Selective inhibition of BCL-2 by venetoclax, sparing BCL-xL enables therapeutic induction of apoptosis without the negative effect of thrombocytopenia. Venetoclax helps restore the process of apoptosis by binding directly to the BCL-2 protein, displacing pro-apoptotic proteins, leading to mitochondrial outer membrane permeabilization and the activation of caspase enzymes. In nonclinical studies, venetoclax has shown cytotoxic activity in tumor cells that overexpress BCL-2

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites

https://clinicaltrials.gov/study/NCT05512390	Recruiting	A First In Human Multicenter, Open-Label Study to Determine the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of ABBV-319 in B-cell Malignancies	B-cell Lymphoma	ABBV-319	Memorial Sloan Kettering Cancer Center-Koch Center /ID# 249246, New York, New York 10065-6007 University Health Network_Princess Margaret Cancer Centre /ID# 243936, Toronto, Ontario M5G 2M9 Novant Health Presbyterian Medical Center /ID# 246719, Charlotte, North Carolina 28204
https://clinicaltrials.gov/study/NCT05544019	Recruiting	A Phase 1, Open-Label, Multicenter, Dose Escalation Study of SGR-1505 as Monotherapy in Subjects With Mature B-Cell Malignancies	B-cell Lymphoma	SGR-1505	Regional Cancer Care Associates, Hackensack, New Jersey 07601 Montefiore Medical Center, Bronx, New York 10467 Weill Cornell, New York, New York 10065
https://clinicaltrials.gov/study/NCT05618028	Recruiting	A First-in-Human Study of ABBV-525 (MALT1 Inhibitor) in B-Cell Malignancies	B-cell Lymphoma	ABBV-525	Memorial Sloan Kettering Cancer Center-Koch Center /ID# 245459, New York, New York 10065-6007 Yale University School of Medicine /ID# 259081, New Haven, Connecticut 06510 Levine Cancer Institute /ID# 246363, Charlotte, North Carolina 28204
https://clinicaltrials.gov/study/NCT05828589	Recruiting	A Phase 1/1b Open-Label Dose-Escalation and Dose-Optimization Study of Bcl-2 Inhibitor BGB-21447 in Patients With Mature B-Cell Malignancies	B-cell Lymphoma	BGB-21447	Laura and Isaac Perlmutter Cancer Center At Nyu Langone Health, New York, New York 10016-2708 Thomas Jefferson University, Philadelphia, Pennsylvania 19107-4216 Sidney Kimmel Comprehensive Cancer At Johns Hopkins, Baltimore, Maryland 21287

Detailed Results

Single Nucleotide Variant (SNV) and Insertions-Deletions (INDELS)

Gene name	Hgvsp	Hgvsc	Amino acids	Codons	Consequence	Allele frequency	Read depth	Predicted effect on protein

ATM	NP_000042.3:p.Ala2415Pro	NM_000051.3:c.7243G>C	A/P	Gct/Cct	missense_variant	3.52	2669	deleterious
TCF3	0	NM_003200.3:c.1823-2A>G	0	0	splice_acceptor_variant	3.36	1818	0
BCL6	NP_001124317.1:p.Ala587Asp	NM_001130845.1:c.1760C>A	A/D	gCc/gAc	missense_variant	3.09	1454	deleterious
ERBB4	NP_005226.1:p.Cys577Ser	NM_005235.2:c.1729T>A	C/S	Tgt/Agt	missense_variant	2.88	1043	deleterious
CREBBP	NP_004371.2:p.Ala557GlyfsTer14	NM_004380.2:c.1669dup	A/GX	gcc/gGcc	frameshift_variant	2.67	1685	0
DAXX	NP_001135442.1:p.Ile539Leu	NM_001141970.1:c.1615A>T	I/L	Ata/Tta	missense_variant	2.34	1925	0
GNAQ	NP_002063.2:p.Met227Ile	NM_002072.3:c.681G>A	M/I	atG/atA	missense_variant	1.44	1044	tolerated
PPM1D	NP_003611.1:p.Gln524Ter	NM_003620.3:c.1570C>T	Q/*	Caa/Taa	stop_gained	1.39	3015	0
SF3B1	NP_036565.2:p.Lys666Asn	NM_012433.3:c.1998G>C	K/N	aaG/aaC	missense_variant	0.76	1966	deleterious
ARID1A	NP_006006.3:p.Cys1968Ter	NM_006015.4:c.5904T>A	C/*	tgT/tgA	stop_gained	0.74	2570	0
TP53	NP_000537.3:p.Ile251dup	NM_000546.5:c.751_753dup	-/I	-/ATC	inframe_insertion	0.41	2439	0
CHEK2	NP_001005735.1:p.Arg474Ser	NM_001005735.1:c.1422G>T	R/S	agG/agT	missense_variant	0.41	2211	tolerated
DNMT3A	NP_783328.1:p.Gly746GlufsTer33	NM_175629.2:c.2237delG	G/X	gGa/ga	frameshift_variant	0.3	5006	0
TERT	0	NM_198253.2:c.-124C>T	0	0	upstream_gene_variant	0.23	3539	0

Methodology and Test Background

This is a next generation sequencing (NGS) test that analyzes cfDNA for abnormalities in 302 genes and cfRNA of >1600 genes for abnormalities that are reported in various types of hematologic neoplasms. The assay also detects several viruses that are important in oncology, including EBV, HPV and TTV. TTV (torque teno virus) was first discovered in a patient with non-A-E hepatitis and is now regarded as a part of the human virome. In general, TTV does not cause pathology in immunocompetent individuals. TTV is considered as a marker of immune competence in patients with immunological impairment and inflammatory disorders. High TTV load is associated with increased risk of infection. In patients with organ transplant, low TTV load is associated with an increased risk of rejection.

Nucleic acid is isolated from peripheral blood plasma or CSF. When CSF sample is submitted, RNA sequencing is performed on the CSF cell pellet instead of cfRNA due to degradation. Performance of the assays may vary depending on the quantity and quality of nucleic acid, sample preparation and sample age. Testing is performed using massive parallel sequencing of the coding DNA of the listed genes. This includes sequencing of all the exons as well as approximately 50 nucleotides at the 5' and 3' ends of each coding exon to detect splice site abnormalities. The TERT promoter region, including the hotspots at -124 and -146 bp, is also covered. Our cfDNA sequencing method has a sensitivity of 0.1% for detecting hot spot mutations, 0.5% for detecting single nucleotide variants (SNVs) and 1% for small (<60 bp) insertions/ deletions (indels). Known hot spots in specific genes such as IDH1/2, NRAS, and KRAS are reported at levels of 0.01% and higher when both cfRNA and cfDNA results are combined. Significant gene amplification and deletion (copy number variants) are also reported. Targeted RNA NGS is performed by hybrid capture and duplicates are excluded for levels measurements. The Universal Human Reference (UHR) RNA is used as control. All detected fusion transcripts are reported. While the major focus of the RNA analysis is the detection of fusion mRNA, mutations in the expressed RNA of the analyzed genes, B- and T-cell clonality, HLA class I genotyping, and Epstein-Barr virus (EBV), human papillomavirus (HPV) and torque teno virus (TTV) viral RNA are also analyzed and

reported. The sensitivity of this assay in detecting fusion mRNA is between 5% and 10%. This test specifically covers translocations that lead to the expression of fusion RNA. Translocations that lead to deregulation of expression can be addressed by this test if compared to the expression proper normal control. Since the clinical relevance of the RNA expression level of most of the genes is not characterized at this time, only a few specific genes will be commented on when abnormalities are detected.

Based on our validation study, the following exonic regions of the genes listed below are not covered appropriately <100 X coverage and sequencing by NGS may not be reliable in these regions. The poor coverage is primarily due to the inherent difficulty in obtaining adequate sequencing coverage in regions with high GC content. No well-characterized hotspots are present in these regions. RAD51 NM_133487 chr15:40994004-40994124, BRCA1 NM_007300 chr17:41231351-41231416, FUBP1 NM_003902 chr1:78435609-78435699, CBLB NM_170662 chr3:105420938-105421303, TERT NM_198253 chr5:1295183-1295250, ARID1B NM_017519 chr6:157098715-157100605, CUX1 NM_001202543 chr7:101740644-101740781, KMT2C NM_170606 chr7:151891314-151891346 and 151935792-151935911, GALNT12 NM_024642 chr9:101569952-101570351, ATM NM_000051 chr11:108164040-108164204, CDK17 NM_001170464 chr12:96679880-96679926, RB1 NM_000321 chr13:48954189-48954220, SETBP1 NM_015559 chr18:42643044-42643692, KMT2B NM_014727 chr19:36208921-36209283, AR NM_000044 chrX:66764889-66766604, STAG2 NM_001042749 chrX:123200025-123200112.

The table below may contain a partial list of the tested DNA genes. For a complete list, please go to:
https://genomictestingcooperative.com/genomic-tests/liquid-trace-hematologic-malignancies/ (click the DNA tab)

For a complete list of tested RNA genes (Fusions/Expression), please go to:
https://genomictestingcooperative.com/genomic-tests/liquid-trace-hematologic-malignancies/ (click the RNA tab)

Tested genes

Genes Tested for Abnormalities in Coding Sequence												
ABL1	B2M	CCNE1	CUX1	ETNK1	GALNT12	IL7R	MCL1	NFE2L2	PIM1	RB1	SMO	TRAF3
ABRAXAS1	BAP1	CD274	CXCR4	ETV6	GATA1	INHBA	MDM2	NFKBIA	PLCG1	RET	SOCS1	TSC1
ACVR1B	BARD1	CD79A	CYLD	EXO1	GATA2	IRF4	MDM4	NKX2-1	PMS1	RHEB	SOX2	TSC2
AKT1	BCL2	CD79B	DAXX	EZH2	GATA3	JAK1	MED12	NOTCH1	PMS2	RHOA	SOX9	TSHR
AKT2	BCL2L1	CDC73	DDR2	FANCA	GEN1	JAK2	MEF2B	NOTCH2	POLD1	RIT1	SPOP	U2AF1
AKT3	BCL6	CDH1	DDX41	FANCC	GNA11	JAK3	MEN1	NOTCH3	POLE	RNF43	SRC	U2AF2
ALK	BCOR	CDK12	DICER1	FANCD2	GNAQ	KAT6A	MET	NPM1	POT1	ROS1	SRSF2	UBA1
AMER1	BCORL1	CDK4	DNM2	FANCE	GNAS	KDM5C	MITF	NRAS	PPM1D	RUNX1	STAG2	VHL
ANKRD26	BCR	CDK6	DNMT3A	FANCF	GNB1	KDM6A	MLH1	NSD1	PPP2R1A	SAMD9	STAT3	WT1
APC	BIRC3	CDKN1B	DOT1L	FANCG	GREM1	KDR	MPL	NSD2 (WHSC1)	PRDM1	SAMD9L	STAT5B	XPO1
AR	BLM	CDKN2A	EED	FAS	GRIN2A	KEAP1	MRE11	NTHL1	PRKAR1A	SDHA	STK11	XRCC2
ARAF	BMPR1A	CDKN2B	EGFR	FBXW7	H3-3A (H3F3A)	KIT	MSH2	NTRK1	PRKDC	SDHAF2	SUFU	XRCC3
ARID1A	BRAF	CDKN2C	EGLN1	FGF4	H3C2 (HIST1H3B)	KMT2A	MSH3	NTRK2	PRPF8	SDHB	SUZ12	ZNF217
ARID1B	BRCA1	CEBPA	ELANE	FGF6	HGF	KMT2B	MSH6	NTRK3	PRSS1	SDHC	TAL1	ZRSR2
ARID2	BRCA2	CHEK1	EP300	FGFR1	HNF1A	KMT2C	MTOR	PAK3	PTCH1	SDHD	TCF3	-
ASXL1	BRIP1	CHEK2	EPAS1	FGFR2	HOXB13	KMT2D	MUTYH	PALB2	PTEN	SETBP1	TENT5C (FAM46C)	-
ATM	BTK	CIC	EPCAM	FGFR3	HRAS	KRAS	MYC	PAX5	PTPN11	SETD2	TERC	-
ATR	CALR	CREBBP	EPHA3	FGFR4	HSP90AA1	LRP1B	MYCL	PBRM1	RAC1	SF3B1	TERT	-
ATRX	CARD11	CRLF2	EPHA5	FH	ID3	MAP2K1	MYCN	PDGFRA	RAD21	SMAD2	TET2	-
AURKA	CBL	CSF1R	ERBB2	FLCN	IDH1	MAP2K2	MYD88	PDGFRB	RAD50	SMAD4	TGFBR2	-
AURKB	CBLB	CSF3R	ERBB3	FLT3	IDH2	MAP2K4	NBN	PHF6	RAD51	SMARCA4	TMEM127	-
AURKC	CBLC	CTCF	ERBB4	FLT4	IGF1R	MAP3K1	NF1	PIK3CA	RAD51C	SMARCB1	TNFAIP3	-
AXIN1	CCND1	CTNNA1	ERG	FOXL2	IKZF1	MAP3K14	NF2	PIK3R1	RAD51D	SMC1A	TNFRSF14	-
AXIN2	CCND3	CTNNB1	ESR1	FUBP1	IKZF3	MAPK1	NFE2	PIK3R2	RAF1	SMC3	TP53	-

RNA Fusions/Expression

Fusion/Expression															
ABL1	BCL2	CCND1	CREBBP	EGFR	ETV4	FGFR2	FOXO1	IKZF3	MAP3K1	MYH9	NTRK3	PAX5	PDGFRB	PTK2B	ROS1	TAL1
ABL2	BCL6	CD274 (PD-L1)	CRLF2	EPOR	ETV5	FGFR3	FUS	JAK2	MECOM	NOTCH1	NUP214	PBX1	PICALM	RARA	RUNX1	TCF3
AKT3	BRAF	CBL	CSF1R	ERG	ETV6	FIP1L1	GLI1	KMT2A	MRTFA	NTRK1	NUP98	PCM1	PIGA	RET	RUNX1T1	TFG
ALK	CBFB	CIC	DUSP22	ETV1	FGFR1	FLT3	HLF	LYN	MYC	NTRK2	P2RY8	PDGFRA	PML	RHOA	STAT6	TYK2

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Electronic Signature

Maher Albitar, M.D.

The test (sample processing, sequencing and data generation) was performed at Regional Cancer Care Associates Laboratory, Key Genomics 92 Second Street Hackensack, NJ 07601. Medical Director Maher Albitar, M.D. Analysis of the data was performed by Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D.

The test was developed and its performance characteristics have been determined by Regional Cancer Care Associates Laboratory. This test has not been approved by the FDA. The FDA has determined such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity clinical testing.

Additional Report Information

Mutations Load (mol/mL)