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

Hematology Profile Plus

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

MRN:		Tumor Type:	Mantle cell lymphoma
Collected Date:	Time: 12:00 AM		
Received Date:	Time: 12:04 PM		
Reported Date:	Time: 06:42 PM		

Detected Genomic Alterations

ATM	ARID2	NOTCH1	SMARCB1	LRP1B
del(20)(q13q13) SLC9A8::LAMA5 fusion mRNA	Autosomal chromosomal structural analysis shows numerous abnormalities including: -1, 2p-, distal 3q+, 6q-, +7, 8p-, proximal 8q-, distal 8q+, 9p- (homoyzgous CDKN2A/B deletion), proximal 9q-, 11q- (ATM deletion), 12q-, -13, +16, 17p- (TP53 deletion), proximal 17q-, distal 17q+, 20p-, -21	B cell clonality: Detected [IGHV1-8 (99%) / IGKV3-11 (99%)]	T cell clonality: Not detected	CCND1 mRNA: Marked increase, reflecting promoter hijacking [t(11;14)]

Results Summary

- **-Mutations in ATM, ARID2, NOTCH1, SMARCB1, and LRP1B genes**
  -Autosomal chromosomal structural analysis shows numerous abnormalities including: -1, 2p-, distal 3q+, 6q-, +7, 8p-, proximal 8q-, distal 8q+, 9p- (homoyzgous CDKN2A/B deletion), proximal 9q-, 11q- (ATM deletion), 12q-, -13, +16, 17p- (TP53 deletion), proximal 17q-, distal 17q+, 20p-, -21
  -del(20)(q13q13) SLC9A8::LAMA5 fusion mRNA
  -B cell clonality: Detected [IGHV1-8 (99%) / IGKV3-11 (99%)]
  -T cell clonality: Not detected
  -B cell markers: Increased with normal pattern
  -CCND1 mRNA: Marked increase, reflecting promoter hijacking [t(11;14)]
  -KI67, CD5, SOX11 mRNA: Increased

-MYC mRNA: Moderately increased
-EBV, HPV, TTV, and HTLV1 viral mRNA: Not detected
-HLA Genotyping:
-HLA-A: A*23:01-A*31:01
-HLA-B: B*18:01-B*39:05
-HLA-C: C*07:02-C*07:797N

-The findings are consistent with aggressive mantle cell lymphoma (MCL) with monoallelic TP53 deletion and biallelic ATM abnormalities (mutation and deletion).

-See additional report information at the end of the report

Heterogeneity
There is a dominant abnormal clone with ATM, ARID2, NOTCH1, and SMARCB1 mutations. The LRP1B mutation is detected in a subclone.

Expression	
B cell markers: Increased with normal pattern	CCND1 mRNA: Marked increase, reflecting promoter hijacking [t(11;14)]
KI67, CD5, SOX11 mRNA: Increased	MYC mRNA: Moderately increased

Diagnostic Implications	
ATM, ARID2, NOTCH1, SMARCB1, LRP1B	The findings are consistent with aggressive mantle cell lymphoma (MCL)

Therapeutic Implications	
ATM	PARP inhibitors

Prognostic Implications	
ATM	Poor
LRP1B	Unknown

Relevant Genes with NO Alteration
No evidence of mutation in NOTCH, SF3B1, TP53, 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, IgVH mutation analysis, and viruses (HPV, EBV, HTLV1, and TTV), in DNA of 302 genes and RNA 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]

- ARID2. This gene encodes a member of the AT-rich interactive domain (ARID)-containing family of DNA-binding proteins. Members of the ARID family have roles in embryonic patterning, cell lineage gene regulation, cell cycle control, transcriptional regulation and chromatin structure modification. This protein functions as a subunit of the polybromo- and BRG1-associated factor or PBAF (SWI/SNF-B) chromatin remodeling complex which facilitates ligand-dependent transcriptional activation by nuclear receptors. Mutations in this gene are associated with hepatocellular carcinomas. A pseudogene of this gene is found on chromosome1. [provided by RefSeq, Dec 2016]

- NOTCH1. This gene encodes a member of the NOTCH family of proteins. Members of this Type I transmembrane protein family share structural characteristics including an extracellular domain consisting of multiple epidermal growth factor-like (EGF) repeats, and an intracellular domain consisting of multiple different domain types. Notch signaling is an evolutionarily conserved intercellular signaling pathway that regulates interactions between physically adjacent cells through binding of Notch family receptors to their cognate ligands. The encoded preproprotein is proteolytically processed in the trans-Golgi network to generate two polypeptide chains that heterodimerize to form the mature cell-surface receptor. This receptor plays a role in the development of numerous cell and tissue types. Mutations in this gene are associated with aortic valve disease, Adams-Oliver syndrome, T-cell acute lymphoblastic leukemia, chronic lymphocytic leukemia, and head and neck squamous cell carcinoma. [provided by RefSeq, Jan 2016]

- SMARCB1. The protein encoded by this gene is part of a complex that relieves repressive chromatin structures, allowing the transcriptional machinery to access its targets more effectively. The encoded nuclear protein may also bind to and enhance the DNA joining activity of HIV-1 integrase. This gene has been found to be a tumor suppressor, and mutations in it have been associated with malignant rhabdoid tumors. Alternatively spliced transcript variants have been found for this gene. [provided by RefSeq, Dec 2015]

- LRP1B. This gene encodes a member of the low density lipoprotein (LDL) receptor family. These receptors play a wide variety of roles in normal cell function and development due to their interactions with multiple ligands. Disruption of this gene has been reported in several types of cancer. [provided by RefSeq, Jun 2016]

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)

A BCL-2 inhibitor indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy. Venetoclax induces rapid and potent onset apoptosis of CLL cells, powerful enough to act within 24h and to lead to tumor lysis syndrome. Selective targeting of BCL2 with venetoclax has demonstrated a manageable safety profile and has been shown to induce significant response in patients with relapsed CLL (chronic lymphocytic leukemia) or SLL (small lymphocytic leukemia), including patients with poor prognostic features.

Olaparib

Olaparib (LYNPARZA) is an antineoplastic agent, Poly(ADP-ribose) Polymerase1;2;3 inhibitor. (PARP 1;2;3 inhibitor).

Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated(gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. (1.1, 2.2)

Talazoparib

Talazoparib is a poly(ADP-ribose) Polymerase 1, 2 (PARP 1;2 inhibitor). Talazoparib was approved by the FDA for use in germline BRCA mutated, HER2 negative, locally advanced or metastatic breast cancer on October 16, 2018 under the trade name Talzenna. Talazoparib prevents PARP-mediated repair of DNA damage in cancer cells, allowing accumulation of damage and PARP-DNA complexes. Repair related errors by error prone secondary repair pathways may also contribute to the cytotoxicity of Talazoparib. Talazoparib is indicated for the treatment of deleterious or suspected deleterious germline BRCA mutated, HER2 negative locally advanced or metastatic breast cancer in adults

Niraparib

Niraparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) with potential antineoplastic activity. PARP Inhibitor MK4827 inhibits PARP activity, enhancing the accumulation of DNA strand breaks and promoting genomic instability and apoptosis. The PARP family of proteins detect and repair single strand DNA breaks by the base-excision repair (BER) pathway. The specific PARP family member target for PARP inhibitor MK4827 is unknown. (NCI Thesaurus)

ZEJULA is a poly(ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Rucaparib

Rucaparib is a potent mammalian poly(ADP-ribose) polymerase 1, 2 and 3 inhibitor with anticancer properties (PARP 1;2;3 inhibitor).

Rucaparib is an inhibitor of PARP-1, PARP-2, and PARP-3. Via an inhibitory effect on the PARP enzymatic activity, rucaparib decreases the formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. It is proposed that PARP inhibition specifically targets tumor cells with preexisting HRD, such as those cells possessing mutations in the BRCA1 or BRCA2 genes.

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites
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	Mantle-cell Lymphoma	SGR-1505	Medical College of Wisconsin, Milwaukee, Wisconsin 53226
https://clinicaltrials.gov/study/NCT05006716	Recruiting	A Phase 1/2, Open-Label, Dose-Escalation and -Expansion Study of the Bruton Tyrosine Kinase Targeted Protein Degrader BGB-16673 in Patients With B-Cell Malignancies	Mantle-cell Lymphoma	BGB-16673	Midwestern Regional Medical Center, Zion, Illinois 60099-2676
https://clinicaltrials.gov/study/NCT06564038	Recruiting	A Phase I/II Open-Label Multi-Centre Master Protocol to Evaluate the Safety and Efficacy of AZD0486 Monotherapy or in Combination With Other Anticancer Agents in Participants With Mature B-Cell Malignancies	Mantle-cell Lymphoma	AZD0486, Prednisone (or equivalent), Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, Acalabrutinib	Research Site, Columbus, Ohio 43210
https://clinicaltrials.gov/study/NCT06022029	Recruiting	A Phase 1 Dose-Escalation and Expansion Study of Intratumorally Administered ONM-501 Alone and in Combination With Cemiplimab in Patients With Advanced Solid Tumors and Lymphomas	Mantle-cell Lymphoma	ONM-501, Cemiplimab	Ohio State University, Columbus, Ohio 43210

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.Arg250Ter	NM_000051.3:c.748C>T	R/*	Cga/Tga	stop_gained	66.5	197	0
ARID2	NP_689854.2:p.Pro955GlnfsTer8	NM_152641.2:c.2864del	P/X	Cca/ca	frameshift_variant	43.46	1169	0
NOTCH1	NP_060087.3:p.Gln2440Ter	NM_017617.3:c.7318C>T	Q/*	Cag/Tag	stop_gained	40.71	452	0
SMARCB1	NP_001007469.1:p.Gln359Ter	NM_001007468.1:c.1075C>T	Q/*	Cag/Tag	stop_gained	40.32	506	0

LRP1B	NP_061027.2:p.Ser65Phe	NM_018557.2:c.194C>T	S/F	tCt/tTt	missense_variant	4.17	336	deleterious

Methodology and Test Background

This is a next generation sequencing (NGS) test that involves separate analysis of DNA and RNA panels for abnormalities that are reported in various types of hematologic neoplasms. The DNA panel is composed of 302 genes and the RNA panel is composed of >1600 genes. The DNA and RNA components of this assay were developed, validated, and set up as separate workflows, with independent extraction, library preparation, sequencing, and analysis pipelines. The NGS assay also detects several viruses that are important in oncology, including EBV, HPV, HTLV 1, 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 fresh cells, peripheral blood cells, bone marrow, body fluid, or paraffin-embedded tissue. For optimal results, neoplastic cells should be >30% of the analyzed cells. For fresh bone marrow specimens with the clinical indication of myeloma, enrichment for CD138-positive cells may be performed using immunomagnetic positive selection and both the CD138-positive and CD138-negative cell fractions extracted for NGS testing and the findings integrated within the final report. 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 DNA sequencing method has a sensitivity of 1% for detecting single nucleotide variants (SNVs) and small (<60 bp) insertions/ deletions (indels). Significant gene amplification and deletion (copy number variants) are also reported. In addition, fragment length analysis is performed for CALR, FLT3, and NPM1 to enhance the detection of large indels and has a sensitivity of 2%-5% for detecting CALR, FLT3-ITD, and NPM1 indels in wildtype background. For cases with indication of acute myeloid leukemia, preliminary FLT3-ITD results based on fragment analysis will be 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), human T-lymphotropic virus type-1 (HTLV1), and torque teno virus (TTV) viral RNA are also analyzed and reported. In cases of suspected chronic lymphocytic leukemia (CLL), IgVH mutation rate will also be reported. The sensitivity of this assay for detecting fusion mRNA is between 5% and 10%. This test specifically detects 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 proper normal expression control. Since the clinical relevance of the RNA expression level of most of the genes is not well-characterized at this time, only a small subset of the genes may be described based on the suspected disease, including but not limited to MYC, BCL2, CD274, CD19, CD22, CD34, and CD138. CRLF2 mRNA levels are reported in acute lymphoblastic leukemia. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. Performance of the assay may vary dependent on the quantity and quality of nucleic acid, sample preparation, and sample age. Decalcified specimens have not been validated. Decalcification with strong acids is not recommended and may lead to poor nucleic acid quality and suboptimal results.

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/gtc-hematology-profile-plus/ *(click the DNA tab)*

The table below contains a partial list of the tested RNA genes (Fusions/Expression). For a complete list, please go to: https://genomictestingcooperative.com/genomic-tests/gtc-hematology-profile-plus/ *(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

Reference

1. Mantle Cell Lymphoma: Optimal Treatment With Bruton Tyrosine Kinase-Targeted Approaches. Eyre TA, Cheah CY, Sarkozy C, Kumar A, Le Gouill S. J Clin Oncol. 2025 Jul 10;43(20):2300-2310. doi: 10.1200/JCO-25-00146. Epub 2025 May 29. PMID: 40440566.

2. Frontline management of mantle cell lymphoma. Ryan CE, Armand P, LaCasce AS. Blood. 2025 Feb 13;145(7):663-672. doi: 10.1182/blood.2023022352. PMID: 38498174.

3. Mantle cell lymphoma-Update on molecular biology, prognostication and treatment approaches. Silkenstedt E, Dreyling M. Hematol Oncol. 2023 Jun;41 Suppl 1:36-42. doi: 10.1002/hon.3149. PMID: 37294961.

4. CAR T-Cell therapy for the management of mantle cell lymphoma. Huang Z, Chavda VP, Bezbaruah R, Dhamne H, Yang DH, Zhao HB. Mol Cancer. 2023 Mar 31;22(1):67. doi: 10.1186/s12943-023-01755-5. PMID: 37004047.

Electronic Signature

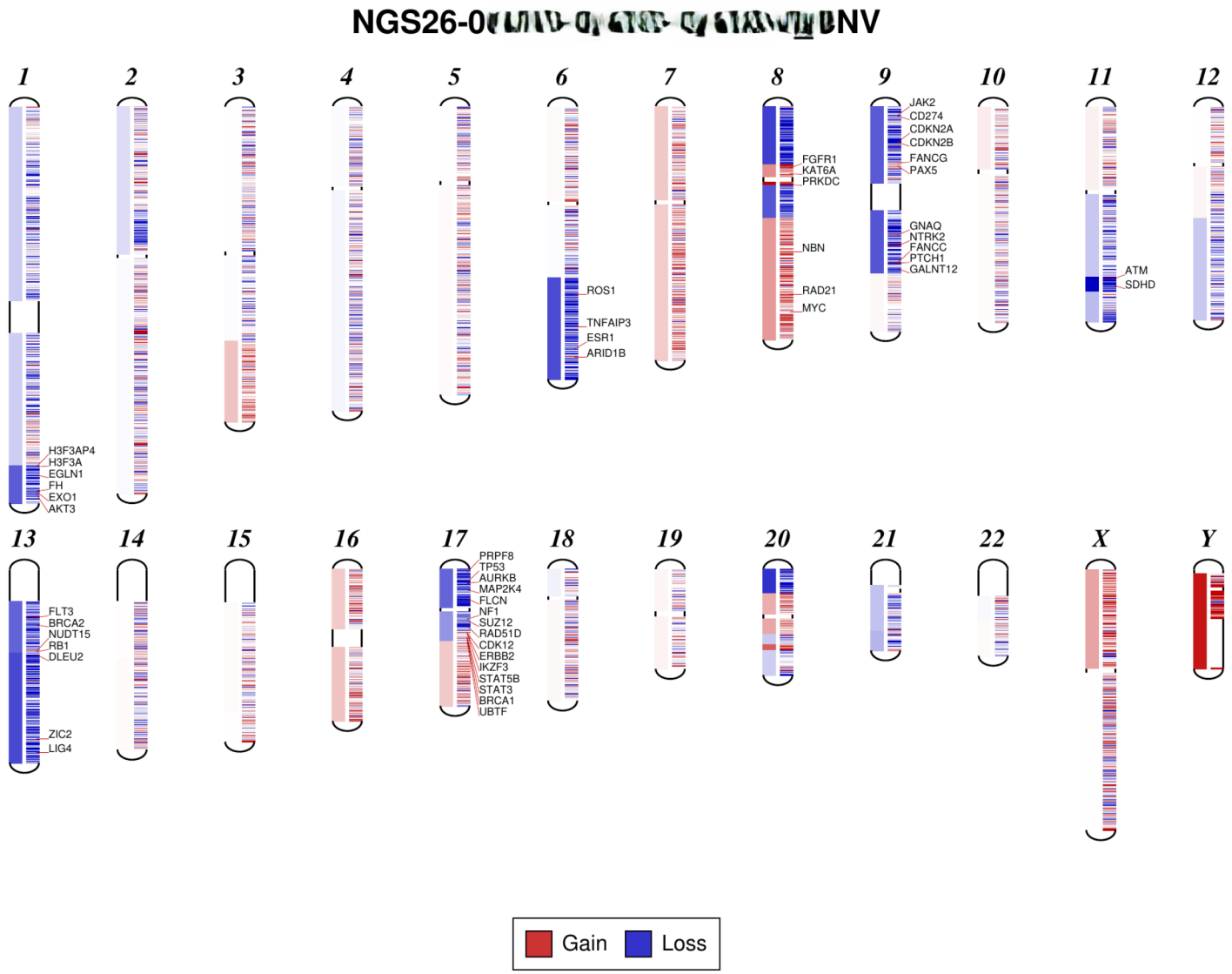
Maher Albitar, M.D.

The test (sample processing, sequencing and data generation) was performed at Genomic Testing Cooperative, LCA, 25371 Commercentre Drive Lake Forest, CA 92630. 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. (CLIA #: 05D2111917 CAP #: 9441574). The signing pathologist is fully responsible for the accuracy and interpretation of results and the release of this report.

The test was developed and its performance characteristics have been determined by Genomic Testing Cooperative, LCA. 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

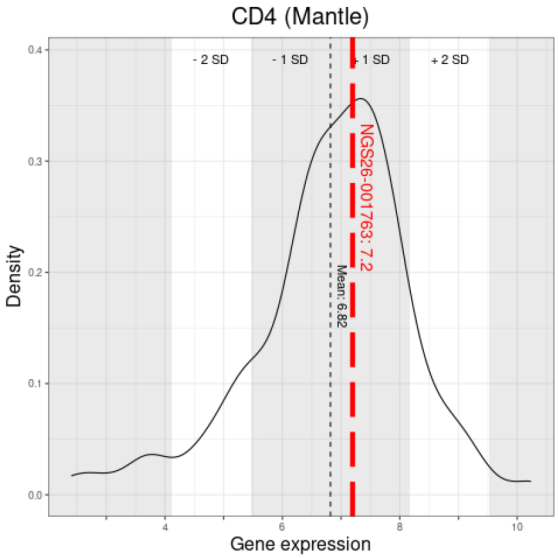
Chromosomal Abnormality Graph

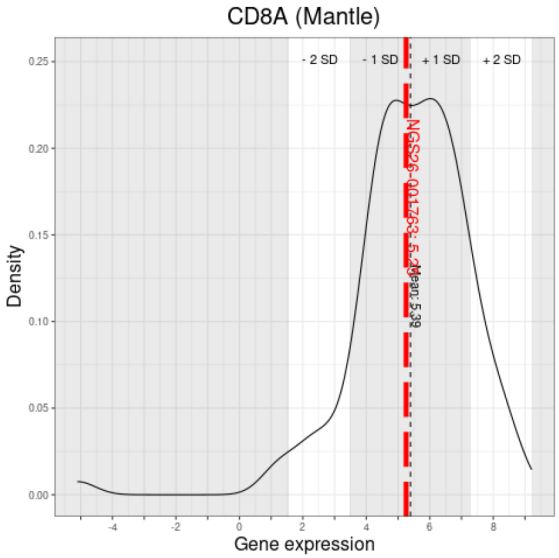


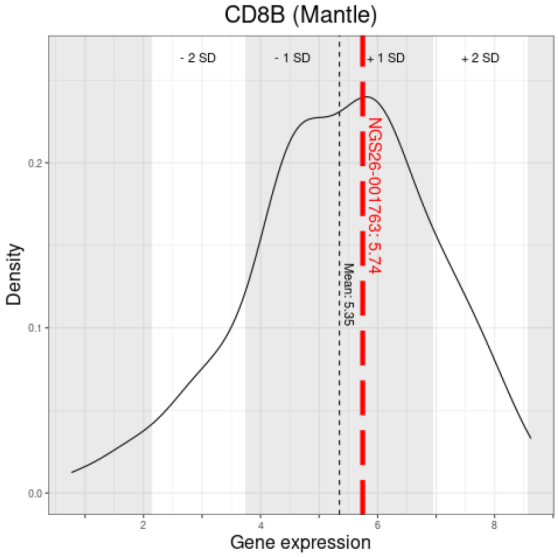
Additional Report Information

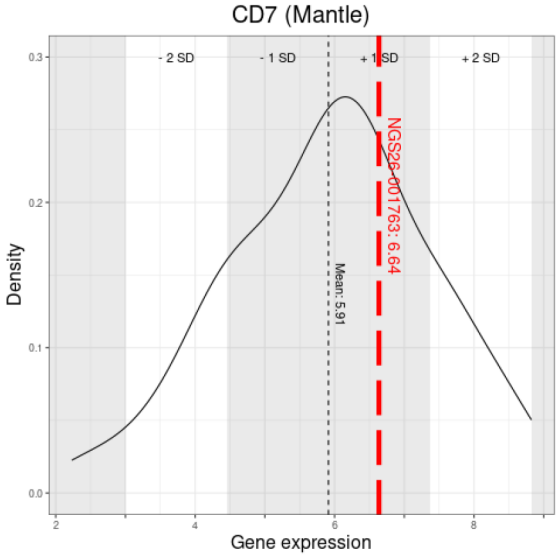
RNA Expression Plots

These plots represent the distribution of the expression in log2 transformed TPM (transcript per million) for each gene across GTC's history for the specified disease. The mean for each distribution is denoted by the black dotted line, while the alternating shaded areas depict the standard deviation. The expression for the current patient is marked by the red dotted line.









Additional Report Information

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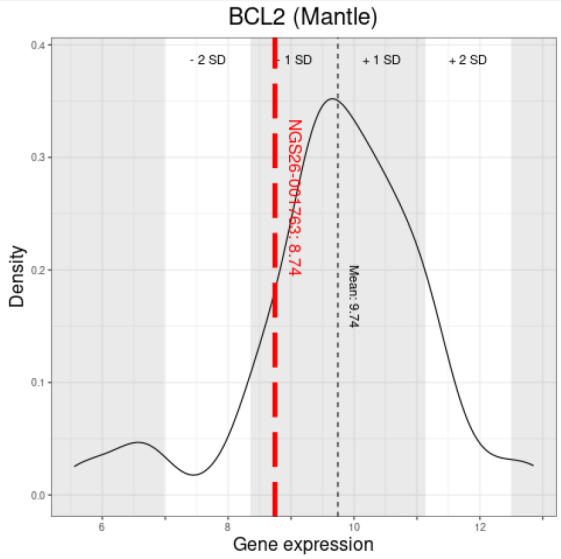

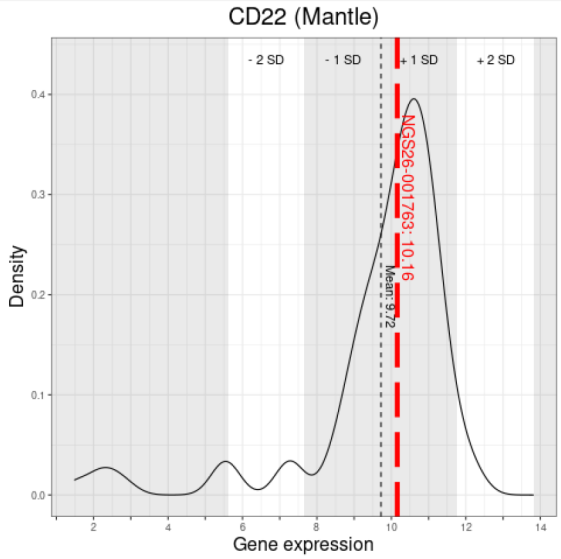

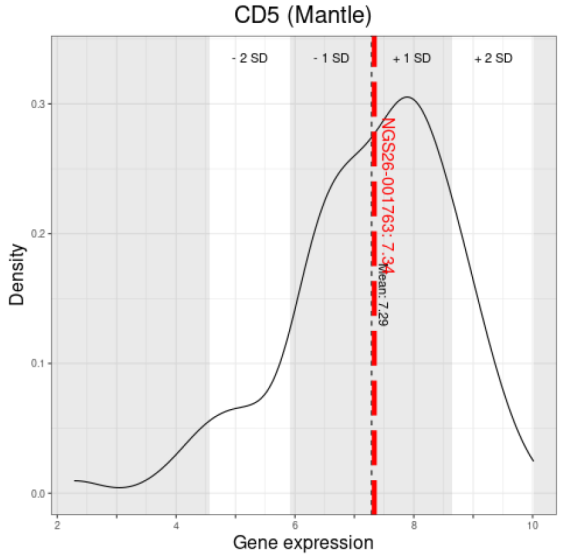

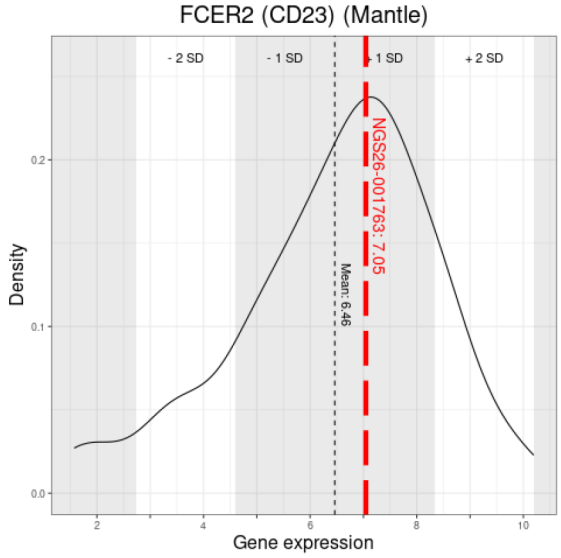

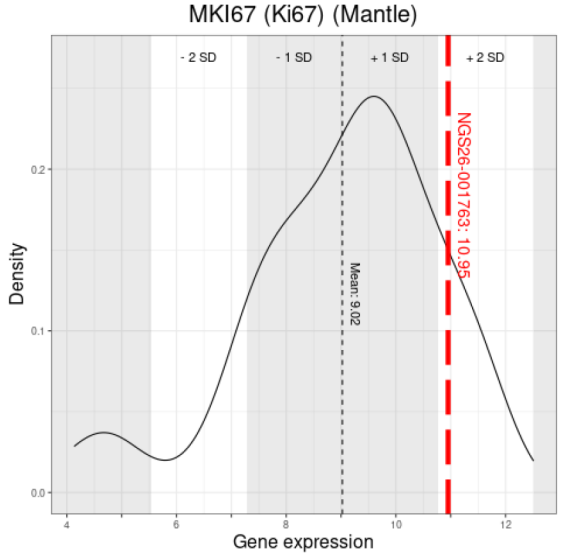

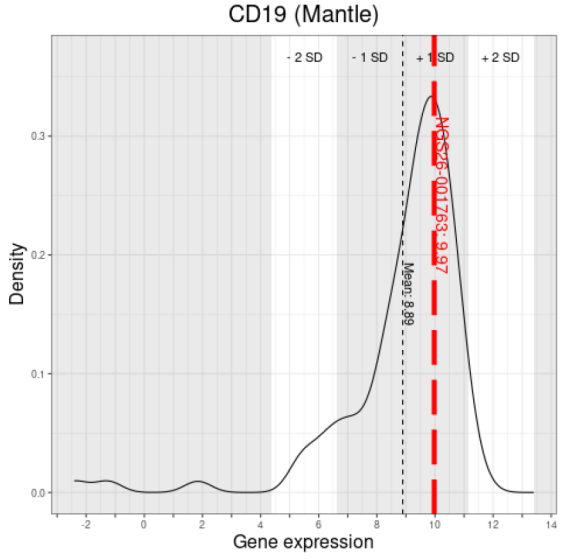

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