

## Hematology Profile Plus

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

Ethnicity:		Family History:	
MRN:		Indication for Testing:	
Collected Date:	Time :	Reason for Referral:	Malignant Neoplasm of Lung
Received Date:	Time :	Tumor Type:	Lung
Reported Date:	Time :	Stage:	T2B

### Test Description:

This is a next generation sequencing (NGS) test to identify molecular abnormalities in DNA of 275 genes and RNA expression in 1408 genes implicated in hematologic neoplasms, including leukemia, lymphoma and MDS. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

#### Detected Genomic Alterations

FIP1L1	JAK2	CHD2	KDM6A	Expression of fusion mRNA: PAX5-ZCCHC7
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#### Heterogeneity

There is a dominant clone with JAK2 and KDM6A mutations. The FIP1L1 and CHD2 mutations are detected in subclones.

#### Expression

High expression of B-cell Markers (CD19, CD22, CD79A, CD79B)	Expression of fusion PAX5-ZCCHC7 mRNA resulting from interstitial deletion at 9p13
High (40 fold) expression of CRLF2 mRNA	CD19 exon 2 skipping in 2% of CD19 mRNA

#### Diagnostic Implications

These findings are consistent with the diagnosis of Philadelphia-like acute lymphoblastic leukemia (Ph-Like-ALL).

#### Prognostic Implications

JAK2 Mutation	Poor
High CRLF2	Poor
PAX5 fusion	Poor
FIP1L1	Unknown

KDM6A	unknown
CDH2	Unknown

### Relevant Genes with No Alteration

ABL1, EPOR, TP53

## Results Summary

- **Mutations in JAK2, FIP1L1, KDM6A, and CDH2.**
- **Expression of a fusion mRNA PAX5-ZCCHC7 resulting from interstitial deletion at 9p13.2**
- **RNA expression profile consistent with B-cell with significantly high expression level of CRLF2 mRNA**
  - These findings are consistent with Ph-like acute lymphoblastic leukemia.
  - The presence of JAK2 mutation and high CRLF2 suggests possible response to JAK2 inhibitors.

## Biological Relevance of Detected Alterations

- JAK2 is a kinase that is misregulated or mutated in a number of myeloproliferative diseases and cancers. The mutation V617F is the most clinically relevant variant, and is seen in around half of myeloproliferative disorders. The variant is a known activating mutation, and activated JAK2 is sufficient to drive myeloproliferative disorders in mouse models. V617F, while most recurrent, is not the only mechanism by which JAK2 can be activated in patients. JAK2 is now one of the first diagnostic markers tested upon diagnosis with a myeloproliferative disorder. JAK2, an intracellular kinase, is frequently altered by mutation or chromosomal rearrangement in hematologic malignancies. JAK2 is a non-receptor tyrosine kinase that regulates cytokine signaling and requires a cognate receptor to respond to extracellular cytokine signaling (PMID: 25057888, 1848670). Activated JAK2 signaling is necessary for the normal production of blood cells such as erythrocytes and thrombocytes (PMID: 9590173). Activation of JAK2 leads to the recruitment and phosphorylation of downstream effectors, such as STAT3/5 and MAPK, enabling the translocation of these signaling molecules to the nucleus to activate transcription (PMID: 25057888). Gain-of-function mutations in JAK2 have been identified in patients with myeloproliferative disorders, including 95% of polycythemia vera and 50% of essential thrombocytopenia and myelofibrosis malignancies (PMID: 1583762, 23009934, 25629741), suggesting that JAK2 functions predominantly as an oncogene. JAK2 fusions and activating mutations have also been identified in various leukemias and lymphomas (PMID: 9360930, 18270328). The most commonly identified mutation is JAK2 V617F, an alteration that activates kinase activity by impairing the autoinhibitory domain of the kinase, leading to constitutive activation of the JAK/STAT signaling pathway (PMID: 17721432). Murine models engineered to express the JAK2 V617F mutation develop a myeloproliferative disorder (PMID: 28640953). While JAK2 mutations are rare in solid tumors, activation of the JAK2/STAT pathway has been found to be oncogenic in many tumor types (PMID: 26151455). The JAK2 kinase inhibitor ruxolitinib has been FDA-approved for the treatment of patients with high-risk myelofibrosis and polycythemia vera (PMID: 20843246). However, resistance to JAK2 inhibition has been found to occur via the formation of drug-resistant JAK1/JAK2 heterodimers (PMID: 22820254). Additional JAK2 inhibitors are currently being tested in preclinical and clinical trials to improve drug efficacy and reduce off-target effects (PMID: 28673391). JAK2/STAT inhibitors are currently available in clinical trials for the treatment of certain types of cancer.
- FIP1L1 (Factor Interacting With PAPOLA And CPSF1) gene is located at 4q12 and encodes for a subunit of the CPSF (cleavage and polyadenylation specificity factor) complex that polyadenylates the 3' end of mRNA precursors. This gene, the homolog of yeast Fip1 (factor interacting with PAP), binds to U-rich sequences of pre-mRNA and stimulates poly(A) polymerase activity. Its N-terminus contains a PAP-binding site and its C-terminus an RNA-binding domain. An interstitial chromosomal deletion on 4q12 creates an in-frame fusion of human genes FIP1L1 and PDGFRA (platelet-derived growth factor receptor, alpha). The FIP1L1-PDGFRA fusion gene encodes a constitutively activated tyrosine kinase that joins the first 233 amino acids of FIP1L1 to the last 523 amino acids of PDGFRA. This gene fusion and chromosomal deletion is the cause

of some forms of idiopathic hypereosinophilic syndrome (HES). This syndrome, recently reclassified as chronic eosinophilic leukemia (CEL), is responsive to treatment with tyrosine kinase inhibitors.

- CDH2 (Cadherin 2) gene is located at 18q12.1 and encodes for a classical cadherin and member of the cadherin superfamily. Alternative splicing results in multiple transcript variants, at least one of which encodes a preproprotein is proteolytically processed to generate a calcium-dependent cell adhesion molecule and glycoprotein. This protein plays a role in the establishment of left-right asymmetry, development of the nervous system and the formation of cartilage and bone.
- KDM6A: (LYSINE (K)-SPECIFIC DEMETHYLASE 6A) gene is located on the X chromosome and encodes a tetratricopeptide repeat (TPR) protein. This protein catalyzes the demethylation of tri/dimethylated histone H3 and involved in chromatin remodeling. This gene belong to a family of genes *that* were found to be mutated in both solid and liquid tumors, including AML, chronic myelogenous leukemia (CML), T-all, MM, Hodgkin's lymphoma (HL), TCC, breast, prostate, colon, esophageal, pancreas, endometrial, GBM, small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC), and RCC. *KDM6A* mutations in bladder carcinoma are quite common (20%–29%). Patients with activating mutation in *KDM6A* might be good candidate for therapy with KDM inhibitors.

## Drug Information

### RUXOLITINIB

Ruxolitinib phosphate/ The phosphate salt form of ruxolitinib, an orally bioavailable Janus-associated kinase (JAK) inhibitor with potential antineoplastic and immunomodulating activities. Ruxolitinib specifically binds to and inhibits protein tyrosine kinases JAK 1 and 2, which may lead to a reduction in inflammation and an inhibition of cellular proliferation. The JAK-STAT (signal transducer and activator of transcription) pathway plays a key role in the signaling of many cytokines and growth factors and is involved in cellular proliferation, growth, hematopoiesis, and the immune response; JAK kinases may be upregulated in inflammatory diseases, myeloproliferative disorders, and various malignancies. (NCI Thesaurus)

Jakafi is a kinase inhibitor indicated for treatment of: intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis in adults. (1.1) polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea. (1.2) steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older (1.3)

### FEDRATINIB

Fedratinib A selective small-molecule inhibitor of JAK2. INREBIC® is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

INREBIC is a kinase inhibitor indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF) (1).

## Potential Clinical Trials

Title	Drugs	Status	Locations	URL
CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory CD19/CD22-expressing B Cell Malignancies	CD19/CD22 CAR T-Cells Fludarabine Cyclophosphamide	Recruiting	National Institutes of Health Clinical Center, Bethesda, Maryland, United States	<a href="https://clinicaltrials.gov/ct2/show/NCT03448393">https://clinicaltrials.gov/ct2/show/NCT03448393</a>
Administration of Donor MultiTAA-Specific T Cells for ALL	MultiTAA-specific T cells	Recruiting	Houston Methodist Hospital, Houston, Texas, United States Texas Children's Hospital, Houston, Texas, United States	<a href="https://clinicaltrials.gov/ct2/show/NCT02475707">https://clinicaltrials.gov/ct2/show/NCT02475707</a>
Venetoclax and Chemotherapy as Frontline Therapy in Older Patients and Patients With	Venetoclax Standard Chemotherapy	Recruiting	Dana Farber Cancer Institute, Boston, Massachusetts, United States MD Anderson Cancer Center, Houston, Texas, United States	<a href="https://clinicaltrials.gov/ct2/show/NCT03319901">https://clinicaltrials.gov/ct2/show/NCT03319901</a>

Relapsed/Refractory ALL				
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## Detailed Results

Single Nucleotide Variant (SNV)								
Gene name	Hgvsp	Hgvsc	Aminoacids	Codons	Consequence	Allele frequency	Read depth	Predicted effect on protein
FIP1L1	NP_112179.2:p.Ser568IlefsTer2	NM_030917.3:c.1701dupA			frameshift_variant, feature_elongation	10.43	165	
JAK2	<b>NP_004963.1:p.Thr875Asn (somatic, 0.95)</b>	NM_004972.3:c.2624C>A	T/N	aCt/aAt	missense_variant	35.71	28	deleterious(0)
CHD2	NP_001262.3:p.Val175SerfsTer18	NM_001271.3:c.522dupA			frameshift_variant, feature_elongation	14.96	380	
KDM6A	NP_066963.2:p.Arg612Ter	NM_021140.2:c.1834C>T	R/*	Cga/Tga	stop_gained	32.26	31	

## Methodology and Test Background

This is a next generation sequencing (NGS) test that analyzes DNA for abnormalities in 250 genes that are reported to be altered in various types of hematologic neoplasms. Nucleic acid is isolated from plasma, fresh cells peripheral blood cells or bone marrow or body fluid), or paraffin-embedded tissue. 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 50 nucleotides at the 5' and 3' ends of each coding exon. Fragment length analysis is also performed on CALR, FLT3, and NPM1 to enhance the detection of insertion/deletion mutations in these genes. Our sequencing method has a typical sensitivity of 3% for detecting common specific mutations and 5% for other mutations. Known hot spots in specific genes such as IDH1/2, NRAS, and KRAS are reported at levels of 1% and higher. The FLT3-ITD fragment analysis assay has a sensitivity of 2%-5% for detecting FLT3-ITD in wildtype background. The CALR fragment analysis test has a sensitivity of 2%-5% for detecting heterozygous insertion/deletions in the wild-type background. Performance of the assay may vary dependent on the quantity and quality of nucleic acid, sample preparation and sample age. The assay is designed to detect significant gene amplification and deletion in addition to various single nucleotide variations (SNV) and indels.

In addition to DNA analysis, targeted RNA NGS analysis was performed. This analyzes targeted RNA with a focus on 68 genes. It is based on hybrid capture of targeted RNA. Duplicates are excluded for levels measurements. While the major focus of the analysis is the detection of fusion mRNA, mutations in the expressed RNA of the analyzed genes are also analyzed and reported. mRNA expression levels are evaluated, and only significant high expression of specific genes are relatively reported, mainly to distinguish B-cell neoplasms from myeloid. CRLF2 mRNA levels are reported in acute lymphoblastic leukemia. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. If requested, detailed expression levels will be provided as a research data and not for clinical use. All detect fusion transcripts are reported. 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 expression level of most of these genes is not characterized at this time, only few specific genes (MYC, BCL2, CD274, CD19, CD22, CD79A, CD79B) will be commented on. The sensitivity of this assay in detecting fusion mRNA is between 1% and 5%. This assay is not designed to detect minimal residual disease and should be used for diagnosis when neoplastic cells are >10% of the analyzed cells. The Universal Human Reference (UHR) RNA is used as control.

### Tested genes

Genes Tested for DNA Abnormalities in Coding Sequence												
ABL1	BCL2	CBL	CDKN2C	DICER1	FAS	IDH2	KMT2A	MPL	PAX5	PTCH1	SMAD2	TGFB2
AKT1	BCL2L1	CBLB	CEBPA	DNMT3A	FBXW7	IGF1R	KMT2B	MRE11A	PBRM1	PTEN	SMAD4	TP53
AKT2	BCL6	CBLC	CHEK1	EP300	FLT3	IKZF1	KMT2C	MTOR	PDGFRA	PTPN11	SMARCA4	TSC1

AKT3	BCOR	CCND1	CHEK2	ERG	GATA1	IKZF3	KMT2D	MUTYH	PDGFRB	RAD21	SMARCB1	TSC2
ALK	BCORL1	CCND3	CIC	ETV6	GATA2	IRF4	KRAS	MYC	PHF6	RAD50	SMC1A	TSHR
AMER1	BCR	CD274	CREBBP	EZH2	GATA3	JAK1	MAP2K1	MYD88	PIK3CA	RAD51	SMO	WT1
APC	BIRC3	CD79A	CRLF2	FAM175A	GEN1	JAK2	MAP2K2	NFKBIA	PIK3R1	RB1	SOCS1	ZNF217
ARID1A	BLM	CD79B	CSF1R	FAM46C	GNAQ	JAK3	MAP2K4	NOTCH1	PIK3R2	RHOA	SRC	ZRSR2
ARID1B	BRAF	CDH1	CSF3R	FANCA	GNAS	KAT6A	MAP3K1	NOTCH2	PIM1	RNF43	SRSF2	MEF2B
ARID2	BRCA1	CDK12	CTNNA1	FANCC	H3F3A	KDM5C	MAP3K14	NOTCH3	PLCG1	RUNX1	STAG2	
ASXL1	BRCA2	CDK4	CTNNB1	FANCD2	HNF1A	KDM6A	MAPK1	NPM1	POLD1	SDHB	STAT3	
ATM	BTK	CDK6	CUX1	FANCE	HOXB13	KDR	MCL1	NRAS	POLE	SETBP1	STK11	
ATRX	CALR	CDKN2A	CXCR4	FANCF	HSP90AA1	KEAP1	MDM2	NSD1	PPM1D	SETD2	TERT	
B2M	CARD11	CDKN2B	DDR2	FANCG	IDH1	KIT	MDM4	PALB2	PPP2R1A	SF3B1	TET2	

## Genes Tested for Abnormalities in RNA

ABCC3	BAP1	CCND3	COX6C	EDIL3	FCRL4	GOT1	IDH1	LAMA5	MET	NOTCH1	PLCB4	RAD50	SGK1	SUV39H2	TRPS1
ABI1	BARD1	CCNE1	CPNE1	EDNRB	FEN1	GPC3	IDH2	LAMP2	METT L18	NOTCH2	PLCG1	RAD51	SGPP2	SUZ12	TSC1
ABL1	BAX	CCNG1	CPS1	EED	FEV	GPHN	IFNG	LASP1	METT L7B	NOTCH3	PLCG2	RAD51B	SH2D5	SYK	TSC2
ABL2	BAZ2A	CCT6B	CPSF6	EEFS EC	FGF1	GPR124	IFRD1	LCK	MFNG	NOTCH4	PLEKH M2	RAD51C	SH3BP1	SYP	TSHR
ABLIM1	BCAS3	CD19	CRADD	EGF	FGF10	GPR128	IGF1	LCP1	MGEA5	NPM1	PML	RAD51D	SH3D19	TACC1	TTK
ACACA	BCAS4	CD22	CREB1	EGFR	FGF13	GPR34	IGF1R	LEF1	MGMT	NPM2	PMS1	RAD52	SH3GL1	TACC2	TTL
ACE	BCL10	CD274	CREB3L1	EGR1	FGF14	GRB10	IGFBP2	LEFTY2	MI6	NR3C1	PMS2	RAF1	SH3GL2	TACC3	TUSC3
ACER1	BCL11A	CD28	CREB3L2	EGR2	FGF19	GRB2	IGFBP3	LFNG	MIPO L1	NR4A3	POFUT1	RALGDS	SHC1	TAF1	TYK2
ACKR3	BCL11B	CD36	CREBBP	EGR3	FGF2	GRHRP	IKKBK	LGALS3	MITF	NR6A1	POLD1	RANBP17	SHC2	TAF15	TYMS
ACSBG1	BCL2	CD44	CRKL	EGR4	FGF23	GRID1	IKBKE	LGR5	MKI67	NRAS	POLD4	RANBP2	SIK3	TAL1	U2AF1
ACSL3	BCL2A1	CD58	CRLF2	EIF4A2	FGF3	GRIN2A	IKZF1	LHFP	MKL1	NSD1	POLR2H	RAP1GDS1	SIN3A	TAL2	U2AF2
ACSL6	BCL2L1	CD70	CRTC1	EIF4E	FGF4	GRIN2B	IKZF2	LHX2	MKL2	NT5C2	POM121	RARA	SIRT1	TAOK1	UBE2B
ACVR1B	BCL2L2	CD74	CRTC3	ELF4	FGF6	GRM1	IKZF3	LHX4	MLF1	NTF3	POMGNT1	RASAL1	SKP2	TBL1XR1	UBE2C
ACVR1C	BCL3	CD79A	CSF1	ELK4	FGF8	GRM3	IL12RB2	LIFR	MLH1	NTF4	POSTN	RASGEF1A	SLC1A2	TBX15	UFC1
ACVR2A	BCL6	CD79B	CSF1R	ELL	FGF9	GSK3B	IL13	LINC00598	MLLT1	NTRK1	POT1	RASGRF1	SLC34A2	TCEA1	UFM1
ADD3	BCL7A	CD8A	CSF3	ELN	FGFR1	GSN	IL13RA2	LINC00982	MLLT10	NTRK2	POU2AF1	RASGRF2	SLC45A3	TCF12	USP16
ADM	BCL9	CDC14A	CSF3R	ELOVL2	FGFR1OP	GSTT1	IL15	LINGO2	MLLT11	NTRK3	POU5F1	RASGRP1	SLC7A5	TCF3	USP42
AFF1	BCOR	CDC14B	CSNK1G2	ELP2	FGFR1OP2	GTF2I	IL1B	LMBRD1	MLLT3	NUMA1	PPAP2B	RB1	SLCO1B3	TCF7L2	USP5
AFF3	BCORL1	CDC25A	CSNK2A1	EML1	FGFR2	GTSE1	IL1R1	LMO1	MLLT4	NUP107	PPARG	RBM15	SLX4	TCL1A	USP6
AFF4	BCR	CDC25C	CTCF	EML4	FGFR3	H2AFX	IL1RAP	LMO2	MLLT6	NUP214	PPARGC1A	RBM6	SMAD2	TCL6	USP7
AGR3	BDNF	CDC42	CTDSP2	ENPP2	FGFR4	H3F3A	IL2	LMO7	MMP7	NUP93	PPFIA2	RCHY1	SMAD3	TCTA	VCAM1
AHCYL1	BHLHE22	CDC73	CTLA4	EP300	FH	HAS2	IL21R	LNP1	MMP9	NUP98	PPFIP1	RCOR1	SMAD4	TEAD1	VEGFA
AH11	BICC1	CDH1	CTNNA1	EP400	FHIT	HDAC1	IL2RA	LOX	MN1	NUTM1	PPM1D	RCSD1	SMAD6	TEAD2	VEGFC
AHR	BIN1	CDH11	CTNNB1	EPC1	FHL2	HDAC2	IL3	LPAR1	MNA T1	NUTM2A	PPP1CB	RECQL4	SMAP1	TEAD3	VGLL3
AHRR	BIRC3	CDK1	CTNND2	EPCAM	FIGF	HDAC3	IL6	LPP	MNX1	NUTM2B	PPP1R13B	REEP3	SMARCA1	TEAD4	VHL
AIP	BIRC6	CDK12	CTRB1	EPHA10	FIP1L1	HDAC4	IL7R	LPXN	MPL	OFD1	PPP1R13L	RELA	SMARCA4	TEC	VTI1A
AK2	BLM	CDK2	CTSA	EPHA2	FLCN	HDAC5	INHBA	LRRG3	MRE11A	OLIG1	PPP2CB	RELN	SMARCA5	TENM1	WASF2
AK5	BMP4	CDK4	CUX1	EPHA3	FLI1	HDAC6	INPP4A	LRMP	MSH2	OLIG2	PPP2R1A	RERG	SMARCB1	TERF1	WDFY3
AKAP12	BMPR1A	CDK5RAP2	CXCL8	EPHA5	FLNA	HDAC7	INPP4B	LRP1B	MSH3	OLR1	PPP2R1B	RET	SMC1A	TERF2	WDR1
AKAP6	BRAF	CDK6	CXCR4	EPHA7	FLNC	HECW1	INPP5A	LRP5	MSH6	OMD	PPP2R2B	RGS7	SMC3	TERT	WDR18
AKAP9	BRCA1	CDK7	CXXC4	EPHB1	FLT1	HEPH	INPP5D	LRPPRC	MSI2	P2RY8	PPP2R4	RHBD F2	SMO	TET1	WDR70
AKR1C3	BRCA2	CDK8	CYFIP2	EPHB6	FLT3	HERPUD1	IQCG	LRRRC37B	MSN	PAFAH1B2	PPP3CA	RHOA	SNAPC3	TET2	WDR90

AKT1	BRD1	CDK9	CYLD	EPO	FLT3L G	HES1	IRF1	LRRCS 9	MTC P1	PAG1	PPP3C B	RHOD	SNCG	TFAP2 A	WEE1
AKT2	BRD3	CDKL5	CYP1 B1	EPOR	FLT4	HES5	IRF2B P2	LRRCS7	MTOR	PAK1	PPP3C C	RHOH	SNHG 5	TFDP1	WHSC 1
AKT3	BRD4	CDKN 1A	CYP2 C19	EPS1 5	FLYW CH1	HEY1	IRF4	LRRK2	MTUS 2	PAK3	PPP3R 1	RICTO R	SNW1	TFE3	WHSC 1L1
ALDH1 A1	BRIP1	CDKN 1B	DAB2 IP	ERBB 2	FBNP 1	HGF	IRF8	LTBP1	MUC1	PAK6	PPP3R 2	RLTPR	SNX2 9	TFEB	WIF1
ALDH2	BRSK1	CDKN 1C	DACH 1	ERBB 3	FOS	HHEX	IRS1	LYL1	MUTY H	PAK7	PPP4C	RMI2	SNX9	TFG	WISP 3
ALDO C	BRWD 3	CDKN 2A	DACH 2	ERBB 4	FOSB	HIF1A	IRS2	LYN	MYB	PALB2	PQLC3	RNF21 3	SOCS 1	TFPT	WNT1 0A
ALK	BTBD1 8	CDKN 2B	DAXX	ERC1	FOSL1	HIP1	IRS4	MACR OD1	MYBL 1	PAPP A	PRCC	RNF43	SOCS 2	TFRC	WNT1 0B
AMER 1	BTG1	CDKN 2C	DCLK 2	ERCC 1	FOXL2	HIPK1	ITGA5	MAD2 L1	MYC	PASK	PRDM 1	ROBO 1	SOCS 3	TGFB2	WNT1 1
AMH	BTG2	CDKN 2D	DCN	ERCC 2	FOXO 1	HIPK2	ITGA7	MADD	MYCL	PATZ1	PRDM 16	ROBO 2	SOD2	TGFB3	WNT1 6
ANGP T1	BTK	CDX1	DDB2	ERCC 3	FOXO 3	HIST1H 1C	ITGA8	MAF	MYC N	PAX3	PRDM 7	ROS1	SORB S2	TGFB1	WNT2 B
ANKR D28	BTLA	CDX2	DDIT 3	ERCC 4	FOXO 4	HIST1H 1D	ITGA V	MAFB	MYD8 8	PAX5	PRF1	RPA3	SORT 1	TGFB2	WNT3
ANLN	BUB1B	CEBP A	DDR2	ERCC 5	FOXP 1	HIST1H 1E	ITGB3	MAGE D1	MYH 11	PAX7	PRG2	RPL22	SOS1	TGFB3	WNT4
APC	C11orf 1	CEBPB	DDX1 0	ERCC 6	FRK	HIST1H 2AC	ITK	MAGE E1	MYH 9	PAX8	PRICK LE1	RPN1	SOX1 0	THADA	WNT5 B
APH1 A	C11orf 30	CEBP D	DDX2 0	ERG	FRMP D4	HIST1H 2AG	ITPKA	MALA T1	MYO1 8A	PBRM 1	PRKA CA	RPN2	SOX1 1	THBS1	WNT6
APLP2	C11orf 54	CEBP E	DDX3 9B	ERLIN 2	FRS2	HIST1H 2AL	JAG2	MALT 1	MYO1 F	PBX1	PRKA CG	RPS21	SOX2	THRAP 3	WNT7 B
APOD	C11orf 95	CENPF	DDX3 X	ESR1	FRYL	HIST1H 2AM	JAK1	MAML 1	NAB2	PC	PRKAR 1A	RPS6K A1	SP1	TIAM1	WNT8 B
AR	C2CD2 L	CENP U	DDX5	ETS1	FSTL3	HIST1H 2BC	JAK2	MAML 2	NACA	PCBP 1	PRKC A	RPS6K A2	SP3	TIRAP	WRN
ARAF	C2orf4 4	CEP17 0B	DDX6	ETS2	FUS	HIST1H 2BJ	JAK3	MAP2	NAPA	PCLO	PRKCB	RPS6K A3	SPEC C1	TLL2	WSB1
ARFRP 1	C3orf2 7	CEP57	DEK	ETV1	FUT1	HIST1H 2BK	JARID 2	MAP2 K1	NAV3	PCM1	PRKCD	RPTO R	SPEN	TLR4	WT1
ARHG AP20	CACN A1F	CEP85 L	DGKB	ETV4	FZD10	HIST1H 2B0	JAZF 1	MAP2 K2	NBEA P1	PCNA	PRKC G	RREB1	SPOP	TLX1	WWO X
ARHG AP26	CACN A1G	CHCH D7	DGKI	ETV5	FZD2	HIST1H 3B	JUN	MAP2 K3	NBN	PCSK7	PRKDC	RRM1	SPP1	TLX3	WWT R1
ARHG EF12	CACN A2D3	CHD2	DGKZ	ETV6	FZD3	HIST1H 4I	KALR N	MAP2 K4	NBR1	PDCD 1	PRKG2	RRM2 B	SPRY 2	TMEM 127	XBP1
ARHG EF7	CAD	CHD6	DICE R1	EWSR 1	FZD6	HLF	KANK 1	MAP2 K5	NCA M1	PDCD 11	PRMT 1	RTEL1	SPRY 4	TMEM 230	XIAP
ARID1 A	CALR	CHEK 1	DIRA S3	EXOS C6	FZD7	HMGA1	KAT2 B	MAP2 K6	NCK1 PSD	PDCD 1LG2	PRMT 8	RTN3	SPTA N1	TMEM 30A	XKR3
ARID2	CAMK 2A	CHEK 2	DIS3L 2	EXT1	FZD8	HMGA2	KAT6 A	MAP2 K7	NCOA 1	PDE4D IP	PROM 1	RUNX 1	SPTB N1	TMPRSS 2	XPA
ARIH2	CAMK 2B	CHIC2	DKK1	EXT2	GAB1	HMGB1	KAT6 B	MAP3 K1	NCOA 2	PDGF A	PRRX1	RUNX 1T1	SQST M1	TNC	XPC
ARNT	CAMK 2G	CHL1	DKK2	EYA1	GABR G2	HMGN2 P46	KCNB 1	MAP3 K14	NCOA 3	PDGF B	PRRX2	RUNX 2	SRC	TNF	XP01
ARRD C4	CAMT A1	CHMP 2B	DKK4	EYA2	GADD 45B	HNF1A	KDM1 A	MAP3 K6	NCOA 4	PDGF D	PRSS8	RYR3	SRF	TNFAI P3	XRCC 6
ASMT L	CANT1	CHN1	DLEC 1	EZH2	GANA B	HNRNP A2B1	KDM2 B	MAP3 K7	NCOR 2	PDGF RA	PSD3	S1PR2	SRGA P3	TNFRS F10B	YAP1
ASPH	CAPRI N1	CHST 11	DLL1	EZR	GAS1	HOOK3	KDM4 C	MAPK 1	NCST N	PDGF RB	PSEN1	SARN P	SRRM 3	TNFRS F10D	YPEL 5
ASPSC R1	CAPZB	CHUK	DLL3	FAF1	GAS5	HOXA1 0	KDM5 A	MAPK 3	NDC8 0	PDK1	PSIP1	SBDS	SRSF 2	TNFRS F11A	YTHD F2
ASTN2	CARD1 1	CIC	DLL4	FAM1 27C	GAS7	HOXA1 1	KDM5 C	MAPK 8	NDE1	PEG3	PSMD 2	SCN8 A	SRSF 3	TNFRS F14	YWHA E
ASXL1	CARM 1	CIITA	DMR T1	FAM1 9A2	GATA 1	HOXA1 3	KDM6 A	MAPK 8IP2	NDRG 1	PER1	PTBP1	SDC4	SS18	TNFRS F17	YY1A P1
ATF1	CARS	CIRH1 A	DMR TA2	FAM1 9A5	GATA 2	HOXA3	KDR	MAPK 9	NDUF AF1	PFDN5	PTCH1	SDHA	SS18L 1	TNFRS F6B	ZBTB 16
ATF3	CASC5	CIT	DNAJ B1	FAM4 6C	GATA 3	HOXA9	KDSR	MAPR E1	NEDD 4	PHB	PTCRA	SDHA F2	SSBP 2	TOP1	ZC3H 7A
ATG13	CASP3	CKB	DNM 1	FAM6 4A	GATA 6	HOXC1 1	KEAP 1	MATK	NEUR L1	PHF1	PTEN	SDHB	SSX1	TOP2A	ZC3H 7B
ATG5	CASP7	CKS1B	DNM 2	FANC A	GBP2	HOXC1 3	KIAA0 232	MAX	NF1	PHF23	PTGS2	SDHC	SSX2	TOP2B	ZFP6 4
ATIC	CASP8	CLP1	DNM 3	FANC B	GDF6	HOXD1 1	KIAA1 524	MB21 D2	NF2	PHF6	PTK2	SDHD	SSX4	TP53	ZFPM 2
ATL1	CAV1	CLTA	DNM T1	FANC C	GFAP	HOXD1 3	KIAA1 549	MBNL 1	NFAT C1	PHOX 2B	PTK2B	SEC31 A	ST6G AL1	TP53B P1	ZFYV E19
ATM	CBFA2 T3	CLTC	DNM T3A	FANC D2	GHR	HOXD9	KIAA1 598	MBTD 1	NFAT C2	PI4KA	PTK7	SEPT2	STAG 2	TP63	ZIC2
ATP1B 4	CBFB	CLTCL 1	DOCK 1	FANC E	GID4	HRAS	KIF5B	MCL1	NFE2 L2	PICAL M	PTPN1 1	SEPT5	STAT 1	TP73	ZMIZ 1
ATP8A 2	CBL	CMKL R1	DOT1 L	FANC F	GIT2	HSP90 AA1	KIT	MDC1	NFIB	PIK3C A	PTPN2	SEPT6	STAT 3	TPD52 L2	ZMY M2

ATR	CBLB	CNBP	DPM1	FANC G	GLI1	HSP90 AB1	KLF4	MDH1	NFKB 1	PIK3C B	PTPN6	SEPT9	STAT 4	TPM3	ZMY M3
ATRNL 1	CBLC	CNOT 2	DPYD	FANC I	GLI3	HSPA1 A	KLHL 6	MDM2	NFKB 2	PIK3C D	PTPRA	SERP2	STAT 5A	TPM4	ZMYN D11
ATRX	CCAR2	CNTN 1	DST	FANC L	GMPS	HSPA2	KLK2	MDM4	NFKB IA	PIK3C G	PTPRK	SERPI NE1	STAT 5B	TPO	ZNF2 07
AURK A	CCDC2 8A	CNTR L	DTX1	FANC M	GNA1 1	HSPA4	KLK7	MDS2	NGF	PIK3R 1	PTPRO	SERPI NF1	STAT 6	TPR	ZNF2 17
AURK B	CCDC6	COG5	DTX4	FAS	GNA1 2	HSPA5	KMT2 A	MEAF 6	NGFR	PIK3R 2	PTPRR	SET	STIL	TRAF2	ZNF2 4
AUTS2	CCDC8 8C	COL11 A1	DUSP 2	FASL G	GNA1 3	HTRA1	KMT2 B	MEO M	NIN	PIM1	PTTG1	SETBP 1	STK1 1	TRAF3	ZNF3 31
AXIN1	CCK	COL1A 1	DUSP 22	FBN2	GNAI1	HUWE1	KMT2 C	MED1 2	NIPB L	PKM	PVT1	SETD2	STL	TRAF5	ZNF3 84
AXL	CCL2	COL1A 2	DUSP 26	FBXO 11	GNAQ	IBSP	KMT2 D	MEF2 B	NKX2 -1	PLA2G 2A	RABEP 1	SETD7	STRN	TRHDE	ZNF4 44
BACH 1	CCNA 2	COL3A 1	DUSP 9	FBXO 31	GNAS	ICAM1	KPNB 1	MEF2 C	NKX2 -5	PLA2G 5	RAC1	SF3B1	STX5	TRIM2 4	ZNF5 21
BACH 2	CCNB 1IP1	COL6A 3	DUX4	FBXW 7	GNM4	ICK	KRAS	MEF2 D	NOD1	PLAG1	RAC2	SFPQ	STYK 1	TRIM2 7	ZNF5 85B
BAG4	CCNB 3	COL9A 3	E2F1	FCGP	GOLG A5	ID1	KSR1	MELK	NODAL	PLAT	RAC3	SFRP2	SUFU	TRIM3 3	ZNF6 87
BAIAP 2L1	CCND 1	COMM D1	EBF1	FCGR 2B	GOPC	ID3	KTN1	MEN1	NON O	PLAU	RAD21	SFRP4	SUGP 2	TRIP11	ZNF7 03
	CCND 2		ECT2 L		GOSR 1	ID4	LAMA 1		NOS3	PLCB1			SULF 1		ZRSR 2

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## Electronic Signature

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The Technical Component Processing, Analysis and Professional Component of this test was completed at GTC Laboratories, 21 Technology Dr. #100, Irvine, CA / 92618/  
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The performance characteristics of this test have been determined by GTC Laboratories. 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.