GENOMIC TESTING COOPERATIVE®
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Tel: 1-866-484-8870 | genomictestingcooperative.com
CLIA # 05D2111917 CAP # 9441574

Solid Tumor Profile Plus

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

MRN:				Indication for Testing:	D48.5 Neoplasm of uncertain behavior of skin
Collected Date:		Time:	12:00 AM		
Received Date:		Time:	11:36 AM		
Reported Date:		Time:	11:48 AM		

Detected Genomic Alterations

Level 1 (FDA-Approved)	Level 2 (Standard of Care)	Level 3 (Clinical Evidence)	Level 4 (Biological Evidence)	Other
-t(15;15)(q21;q25)MYO5A::NTRK3 fusion mRNA -No evidence of microsatellite instability	-Homologous recombination deficiency (HRD): Negative -Tumor Mutation Burden Low: 5 Mut/Mb -No evidence of CDKN2A/B deletion -No evidence of 6p+, 8q+ -No evidence of BRAF mutation or BRAF fusion -No evidence of TERTpro mutation	POLE (?Germline), FOXP1, SMC1A, ERBB4	SLIT2, LIG4, PRKN, KEL, EXOSC6 (?Germline)	Autosomal chromosomes show no detectable chromosomoal gain or loss.

Results Summary

- **-Low-level somatic mutations in FOXP1, SMC1A, SLIT2, LIG4, ERBB4, PRKN, and KEL genes**
  -Possible germline mutations in POLE and EXOSC6 genes, heterozygous
  -t(15;15)(q21;q25)MYO5A::NTRK3 fusion mRNA
  -Homologous recombination deficiency (HRD): Negative.
  -No evidence of microsatellite instability
  -Tumor Mutation Burden Low: 5 Mut/Mb
  -No evidence of fusion mRNA involving ALK, RET, ROS1
  -No evidence of BRAF, KIT or NRAS mutations
  -EBV, HPV, TTV, and HTLV1 viral mRNA: Not detected
  -HLA Genotyping:
  -HLA-A: A*01:01-A*02:01

-HLA-B: B*08:01-B*40:02
-HLA-C: C*07:01-C*02:02
-SOX10 and MLANA expression : Markedly increased
-PRAME expression: Moderately increased.

-The MYO5A::NTRK3 fusion has been reported in Spitzoid melanoma and other types. The presence of this fusion suggests response to NTRK inhibitors (larotrectinib or entrectinib) (Tumor-agnostic).

-FOXP1 mutation suggests response to PI3k/AKT inhibitors.

-SMC1A mutation suggests response to PARP inhibitors.

-The POLE gene is detected at high level, raising the possibility of a germline abnormality. However, there is conflicting interpretation of its pathogenicity.

-The EXOSC6 mutation is detected at high level, raising the possibility of a germline mutation. This mutation leads to loss of the native start codon. However, there is no data on its clinical relevance and should be classified as of "uncertain significance" at this time.

See additional report information at the end of the report.

Tumor Heterogeneity
There are abnormal low-level clones with FOXP1, SMC1A, SLIT2, LIG4, ERBB4, PRKN, and KEL mutations. The POLE and EXOSC6 mutations are detected at high levels, possible germline abnormalities.

Expression	
SOX10 and MLANA expression : Markedly increased	PRAME: Moderately increased

Diagnostic Implications	
POLE, FOXP1, SMC1A, SLIT2, LIG4, ERBB4, PRKN, KEL, EXOSC6	-The findings are consistent with aggressive neoplasm. -The POLE and EXOSC6 mutations are likely germline variants.

Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence)	
POLE	Better response to checkpoint inhibitors
FOXP1	PI3k/AKT inhibitors
SMC1A	PARP inhibitors
ERBB4	May predict sensitivity to Lapatinib and other anti-EGF family inhibitors (Dacomitinib)

Relevant Genes with NO Alteration		
-No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA 1/2 -No specific mutation in DPYD gene, associated with enzymatic deficiency	No evidence of fusion mRNA involving ALK, RET, ROS1,	-No evidence of METex14 skipping or EGFRvIII -No evidence of ERBB2 (HER2) amplification

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, tumor mutational burden (TMB), microsatellite instability (MSI), homologous recombination deficiency (HRD), B- and T-cell clonality, and viruses (HPV, EBV, HTLV1, and TTV), in DNA of 434 genes and RNA in greater than 1600 genes implicated in solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

Biological relevance of detected Alterations

- POLE. This gene encodes the catalytic subunit of DNA polymerase epsilon. The enzyme is involved in DNA repair and chromosomal DNA replication. Mutations in this gene have been associated with colorectal cancer 12 and facial dysmorphism, immunodeficiency, livedo, and short stature. [provided by RefSeq, Sep 2013]

- FOXP1. This gene belongs to subfamily P of the forkhead box (FOX) transcription factor family. Forkhead box transcription factors play important roles in the regulation of tissue- and cell type-specific gene transcription during both development and adulthood. Forkhead box P1 protein contains both DNA-binding- and protein-protein binding-domains. This gene may act as a tumor suppressor as it is lost in several tumor types and maps to a chromosomal region (3p14.1) reported to contain a tumor suppressor gene(s). Alternative splicing results in multiple transcript variants encoding different isoforms. [provided by RefSeq, Jul 2008]

- SMC1A. Proper cohesion of sister chromatids is a prerequisite for the correct segregation of chromosomes during cell division. The cohesin multiprotein complex is required for sister chromatid cohesion. This complex is composed partly of two structural maintenance of chromosomes (SMC) proteins, SMC3 and either SMC1B or the protein encoded by this gene. Most of the cohesin complexes dissociate from the chromosomes before mitosis, although those complexes at the kinetochore remain. Therefore, the encoded protein is thought to be an important part of functional kinetochores. In addition, this protein interacts with BRCA1 and is phosphorylated by ATM, indicating a potential role for this protein in DNA repair. This gene, which belongs to the SMC gene family, is located in an area of the X-chromosome that escapes X inactivation. Mutations in this gene result in Cornelia de Lange syndrome. Alternative splicing results in multiple transcript variants encoding different isoforms. [provided by RefSeq, Jul 2013]

- SLIT2. This gene encodes a member of the slit family of secreted glycoproteins, which are ligands for the Robo family of immunoglobulin receptors. Slit proteins play highly conserved roles in axon guidance and neuronal migration and may also have functions during other cell migration processes including leukocyte migration. Members of the slit family are characterized by an N-terminal signal peptide, four leucine-rich repeats, nine epidermal growth factor repeats, and a C-terminal cysteine knot. Proteolytic processing of this protein gives rise to an N-terminal fragment that contains the four leucine-rich repeats and five epidermal growth factor repeats and a C-terminal fragment that contains four epidermal growth factor repeats and the cysteine knot. Both full length and cleaved proteins are secreted extracellularly and can function in axon repulsion as well as other specific processes. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Sep 2015]

- LIG4. The protein encoded by this gene is a DNA ligase that joins single-strand breaks in a double-stranded polydeoxynucleotide in an ATP-dependent reaction. This protein is essential for V(D)J recombination and DNA double-strand break (DSB) repair through nonhomologous end joining (NHEJ). This protein forms a complex with the X-ray repair cross complementing protein 4 (XRCC4), and further interacts with the DNA-dependent protein kinase (DNA-PK). Both XRCC4 and DNA-PK are known to be required for NHEJ. The crystal structure of the complex formed by this protein and XRCC4 has been resolved. Defects in this gene are the cause of LIG4 syndrome. Alternatively spliced transcript variants encoding the same protein have been observed. [provided by RefSeq, Jul 2008]

- 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]

- PRKN. The precise function of this gene is unknown; however, the encoded protein is a component of a multiprotein E3 ubiquitin ligase complex that mediates the targeting of substrate proteins for proteasomal degradation. Mutations in this gene are known to cause Parkinson disease and autosomal recessive juvenile Parkinson disease. Alternative splicing of this gene produces multiple transcript variants encoding distinct isoforms. Additional splice variants of this gene have been described but currently lack transcript support. [provided by RefSeq, Jul 2008]

- KEL. This gene encodes a type II transmembrane glycoprotein that is the highly polymorphic Kell blood group antigen. The Kell glycoprotein links via a single disulfide bond to the XK membrane protein that carries the Kx antigen. The encoded protein contains sequence and structural similarity to members of the neprilysin (M13) family of zinc endopeptidases. [provided by RefSeq, Jul 2008]

- EXOSC6. This gene product constitutes one of the subunits of the multisubunit particle called exosome, which mediates mRNA degradation. The composition of human exosome is similar to its yeast counterpart. This protein is homologous to the yeast Mtr3 protein. Its exact function is not known, however, it has been shown using a cell-free RNA decay system that the exosome is required for rapid degradation of unstable mRNAs containing AU-rich elements (AREs), but not for poly(A) shortening. The exosome does not recognize ARE-containing mRNAs on its own, but requires ARE-binding proteins that could interact with the exosome and recruit it to unstable mRNAs, thereby promoting their rapid degradation. [provided by RefSeq, Jul 2008]

Drug Information

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

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)

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)

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.

Lapatinib

Lapatinib (TYKERB) is an EGFR-ErbB-2 kinase inhibitor indicated for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.

Neratinib

Neratinib is a tyrosine kinase inhibitor which exhibits antitumor action against Epidermal Growth Factor Receptor (EGFR), HER2, and Human Epidermal Growth Factor Receptor 4 (HER4) postive carcinomas. This prevents auotphoshorylation of tyrosine residues on the receptor and reduces oncogenic signalling through the mitogen-activated protein kinase and Akt pathways.

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites
https://clinicaltrials.gov/study/NCT07027488	Recruiting	An Open-Label, Phase 1 Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Antitumor Activity of AB821 in Adult Participants With Locally Advanced or Metastatic Melanoma and Other Solid Tumors	Melanoma	AB821	Yale University, New Haven, Connecticut 06510
https://clinicaltrials.gov/study/NCT06961006	Recruiting	A Phase 2, Randomized, Double-Blind, Placebo- and Active-Comparator-Controlled Clinical Study of V940 (mRNA-4157) Plus Pembrolizumab Versus Placebo Plus Pembrolizumab in Participants With First-Line Advanced Melanoma (INTerpath-012)	Melanoma	V940, Pembrolizumab, Placebo	UCSF Medical Center at Mission Bay (Site 4044), San Francisco, California 94158 Fred Hutchinson Cancer Center (Site 4041), Seattle, Washington 98109 Highlands Oncology Group (Site 4042), Springdale, Arkansas 72762
https://clinicaltrials.gov/study/NCT04464759	Recruiting	LIMIT Melanoma: (Lysosomal Inhibition + Melanoma ImmunoTherapy) A Phase 1/2 Open Label Trial of Nivolumab and Hydroxychloroquine or Nivolumab/Ipilimumab and Hydroxychloroquine in Patients With Advanced Melanoma	Melanoma	Nivolumab, Hydroxychloroquine, Ipilimumab	Abramson Cancer Center at University of Pennsylvania, Philadelphia, Pennsylvania 19104
https://clinicaltrials.gov/study/NCT06697301	Recruiting	A Multicenter, Randomized, Double-Blind, Active Comparator-Controlled, Adaptive Phase 2/3 Study to Evaluate the Safety and Efficacy of EIK1001 and Pembrolizumab Versus Placebo and Pembrolizumab as First-Line Therapy in Participants With Advanced Melanoma (TeLuRide-006)	Melanoma	EIK1001, Pembrolizumab (KEYTRUDA®)	Helios Clinical Research, Los Angeles, California 90015 Ironwood Cancer & Research Centers, Chandler, Arizona 85224 Providence Medical Foundation, Santa Rosa, California 95403

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
POLE	NP_006222.2:p.Asp90GlufsTer59	NM_006231.2:c.270del	D/X	gaC/ga	frameshift_variant	46.31	542	0
FOXP1	NP_001012523.1:p.Pro113Leu	NM_001012505.1:c.338C>T	P/L	cCa/cTa	missense_variant	7.14	630	0
SMC1A	NP_001268392.1:p.Arg474Cys	NM_001281463.1:c.1420C>T	R/C	Cgc/Tgc	missense_variant	6.57	350	deleterious
SLIT2	NP_004778.1:p.Thr805Ile	NM_004787.1:c.2414_2415CC>TT	T/I	aCC/aTT	missense_variant	5.93	1096	deleterious
LIG4	NP_002303.2:p.Pro534Leu	NM_002312.3:c.1601C>T	P/L	cCa/cTa	missense_variant	2.69	1750	tolerated
ERBB4	NP_005226.1:p.Arg711Cys	NM_005235.2:c.2131C>T	R/C	Cgt/Tgt	missense_variant	2.54	1499	deleterious
PRKN	NP_054642.2:p.Val216Leu	NM_013987.2:c.646G>C	V/L	Gtc/Ctc	missense_variant	1.9	1580	deleterious
KEL	NP_000411.1:p.Arg675Gln	NM_000420.2:c.2024G>A	R/Q	cGa/cAa	missense_variant	1.7	529	tolerated
EXOSC6 (RNA)	NP_478126.1:p.?	NM_058219.2:c.3G>A	M/I	atG/atA	start_lost	59.4	133	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 to be altered in various types of solid tumors. The DNA panel is composed of 434 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 paraffin-embedded tissue. For optimal results neoplastic cells should be greater than 30% of the analyzed cells. H&E-sections are reviewed by a pathologist and tumor-enrichment is performed by macrodissection when possible. 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 3% for detecting hotspot mutations and 5% for detecting single nucleotide variants (SNVs) and small (<60 bp) insertions/ deletions (indels). MSI status is inferred by interrogating all available genomic microsatellites covered. Borderline MSI results by NGS are confirmed by fragment analysis. Tumor mutational burden (TMB) is measured by counting all nonsynonymous variants and filter settings as follows: (A) Pass all filters; (B) inside genes; (C) had a mutant allele frequency >5%; (D) not found in the dbSNP (to exclude germline variations). The median for TMB is 10 mutations/Mb based on lung carcinoma analysis. The cut off for other types of tumors is not well-established at this time. 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, 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. B- and T-cell clonality will be reported, if clonal or clinically relevant. 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. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. This assay is not designed to detect minimal residual disease and should be used for diagnosis. Performance of the assays 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 <100X 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. ASXL1 NM_001164603 20:30946620- 30946635, ATM NM_000051 11:108186550-108186638, BAP1 NM_004656 3:52443858-52443894, BCR NM_004327 22:23652510-23652620, BRD4 NM_058243 19:15353808-15354193,5355041-15355411, CCNE1 NM_001238 19:30303463-30303485, CD274 NM_001267706 9:5456109-5456165, CD79A NM_001783 19:42384736-42384805, CSF3R NM_000760 1:36937667-36937740, DDX11 NM_001257144 12:31240872-31240917, ERBB3 NM_001982 12:56492284-56492359, FANCI NM_001113378 15:89835919-89836052, FLT3 NM_004119 13:28674605-28674652, FLT4 NM_002020 5:180035281-180035284, GEN1 NM_001130009 2:17954486-17954525, H3-3A NM_002107 1:226259140-226259180, IRS2 NM_003749 13:110437126-110437363, 110437805-110437899, 110438359- 110438400, JAK1 NM_002227 1:65309747-65309771, MAGI2 NM_012301 7:77648719-77649044, MITF NM_000248 3:70005606-70005681, MYCL NM_001033081 1:40367518-40367565, NF1 NM_000267 17:29664837-29664898, NOTCH2 NM_001200001 1:120572528-120572610, PBRM1 NM_018313 3:52677264-52677322, PIK3R2 NM_005027 19:18272089-18272305, PMS2 NM_000535 7:6013024-6013173, RANBP2 NM_006267 2:109363166-109363254, 109367779-109367838, 109367984-109368069, 109369453-109369497, 109378578-109378651, .RHEB NM_005614 7:151216546-151216597, SUFU NM_001178133 10:104263911-104264039, TNFRSF14 NM_003820 1:2494304- 2494335.

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/solid-tumor-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/solid-tumor-profile-plus/ *(click the RNA tab)*

Tested genes

Genes Tested for Abnormalities in Coding Sequence															
ABCB7	ATRX	BTK	CDKN2B	DKC1	FANCA	FLI1	GREM1	INPP4B	LIG4	MSH2	NSD2 (WHSC1)	POLE	RAF1	SDHD	STAG2	TP53
ABL1	AURKA	CALR	CDKN2C	DNM2	FANCB	FLT1	GRIN2A	IRF2	LMO1	MSH6	NTRK1	POT1	RANBP2	SEC23B	STAT3	TRAF3
ABL2	AURKB	CARD11	CEBPA	DNMT3A	FANCC	FLT3	GRM3	IRF4	LPIN2	MTOR	NTRK2	PPM1D	RARA	SETBP1	STAT4	TSC1
ABRAXAS1	AURKC	CBFB	CHD2	DOT1L	FANCD2	FLT4	GSK3B	IRS2	LRP1B	MUTYH	NTRK3	PPP2R1A	RB1	SETD2	STAT6	TSC2
ACD	AXIN1	CBL	CHD4	EED	FANCE	FOXL2	GSKIP	JAGN1	LYN	MVK	NUP93	PRDM1	RBBP6	SF3B1	STK11	TSHR
ACVR1B	AXIN2	CBLB	CHEK1	EGFR	FANCF	FOXP1	H3-3A (H3F3A)	JAK1	LYST	MYC	PAK3	PREX2	RBM10	SLIT2	SUFU	U2AF1
ADA	AXL	CBLC	CHEK2	EGLN1	FANCG	FRS2	H3C2	JAK2	LZTR1	MYCL	PALB2	PRKAR1A	RBM8A	SLX4	SUZ12	U2AF2
ADGRA2	B2M	CCN6 (WISP3)	CIC	ELANE	FANCI	FUBP1	HAX1	JAK3	MAGI2	MYCN	PAX5	PRKCI	REEP5	SMAD2	SYK	VEGFA
AK2	BAP1	CCND1	CREBBP	EMSY	FANCL	G6PC3	HGF	JUN	MAP2K1	MYD88	PBRM1	PRKDC	RET	SMAD3	TAF1	VHL
AKT1	BARD1	CCND2	CRKL	EP300	FANCM	GABRA6	HNF1A	KAT6A	MAP2K2	NBN	PDCD1LG2	PRKN (PARK2)	RHEB	SMAD4	TAL1	WAS
AKT2	BCL2	CCND3	CRLF2	EPAS1	FAS	GALNT12	HOXA11	KDM5A	MAP2K4	NF1	PDGFRA	PRSS1	RHOA	SMAD9	TBX3	WT1

AKT3	BCL2L1	CCNE1	CSF1R	EPCAM	FAT1	GATA1	HOXB13	KDM5C	MAP3K1	NF2	PDGFRB	PRSS8	RICTOR	SMARCA4	TCF3	XPO1
ALK	BCL2L2	CD274	CSF3R	EPHA3	FBXW7	GATA2	HRAS	KDM6A	MAP3K14	NFE2L2	PDK1	PSTPIP1	RIT1	SMARCB1	TCIRG1	XRCC2
AMER1	BCL6	CD79A	CTC1	EPHA5	FGF10	GATA3	HSD3B1	KDR	MAPK1	NFKBIA	PHF6	PTCH1	RNF168	SMC1A	TENT5C (FAM46C)	XRCC3
ANKRD26	BCOR	CD79B	CTCF	EPHA7	FGF14	GATA4	HSP90AA1	KEAP1	MCL1	NHP2	PIK3C2B	PTEN	RNF43	SMC3	TERC	ZBTB2
APC	BCORL1	CDAN1	CTNNA1	EPHB1	FGF19	GATA6	ID3	KEL	MDM2	NKX2-1	PIK3CA	PTPN11	ROS1	SMO	TERF1	ZNF217
AR	BCR	CDC73	CTNNB1	ERBB2	FGF23	GEN1	IDH1	KIF23	MDM4	NLRP3	PIK3CB	QKI	RPTOR	SNCAIP	TERF2	ZNF703
ARAF	BIRC3	CDH1	CUL3	ERBB3	FGF3	GFI1	IDH2	KIT	MED12	NME1	PIK3CG	RAB27A	RTEL1	SOCS1	TERF2IP	ZRSR2
ARFRP1	BLM	CDIN1 (C15orf41)	CUX1	ERBB4	FGF4	GFI1B	IGF1R	KLF1	MEF2B	NOP10	PIK3R1	RAC1	RUNX1	SOX10	TERT	-
ARID1A	BMPR1A	CDK12	CXCR4	ERCC4	FGF6	GID4	IGF2	KLHL6	MEFV	NOTCH1	PIK3R2	RAD21	RUNX1T1	SOX2	TET2	-
ARID1B	BRAF	CDK4	CYLD	ERG	FGFR1	GLI1	IKBKE	KLLN	MEN1	NOTCH2	PIM1	RAD50	SAMD9L	SOX9	TGFBR2	-
ARID2	BRCA1	CDK6	DAXX	ERRFI1	FGFR2	GLI2	IKZF1	KMT2A	MET	NOTCH3	PLCG1	RAD51	SBDS	SPEN	TNFAIP3	-
ASXL1	BRCA2	CDK8	DDR2	ESR1	FGFR3	GNA11	IKZF3	KMT2B	MITF	NPM1	PLCG2	RAD51B	SBF2	SPOP	TNFRSF14	-
ATG2B	BRD4	CDKN1A	DDX11	ETV6	FGFR4	GNA13	IL2RG	KMT2C	MLH1	NR0B1	PMS1	RAD51C	SDHA	SPTA1	TNFRSF1A	-
ATM	BRIP1	CDKN1B	DDX41	EXO1	FH	GNAQ	IL7R	KMT2D	MPL	NRAS	PMS2	RAD51D	SDHB	SRC	TOP1	-
ATR	BTG1	CDKN2A	DICER1	EZH2	FLCN	GNAS	INHBA	KRAS	MRE11	NSD1	POLD1	RAD54L	SDHC	SRSF2	TOP2A	-

RNA Fusions/Expression

Fusion/Expression													
ABL1	BCL6	CD274 (PD-L1)	EGFR	EWSR1	FLI1	IKZF3	MAP3K1	NRG1	NUP98	PML	RET	SS18	THADA
AKT3	BRAF	CIC	ERG	FGFR1	FOXO1	JAK2	MECOM	NTRK1	PAX8	PPARG	RHOA	STAT6	TMPRSS2
ALK	CAMTA1	CREB1	ETS1	FGFR2	FUS	KIAA1549	MYB	NTRK2	PDGFRA	PRKACA	ROS1	TAL1	YAP1
AR	CBFB	CREBBP	ETV1	FGFR3	GLI1	KMT2A	MYC	NTRK3	PDGFRB	RAF1	RUNX1	TCF3	YWHAE
BCL2	CCND1	ERBB2	ETV6	FIP1L1	HMGA2	MAML2	NOTCH1	NUP214	PICALM	RARA	RUNX1T1	TFG	ZFTA

Reference

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Electronic Signature

Maher Albitar, M.D.

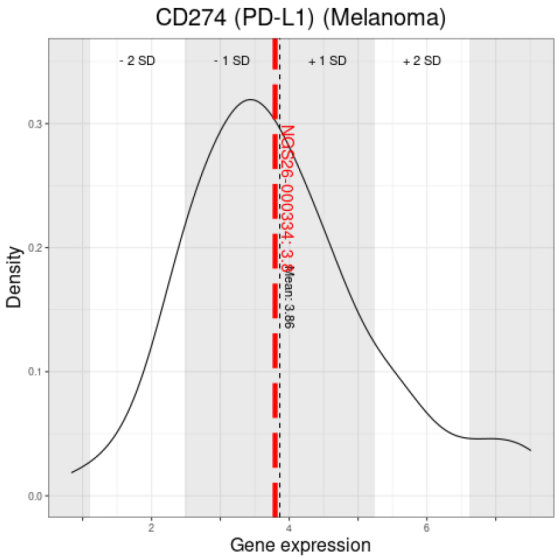
The test (sample processing, sequencing and data generation) was performed at Genomic Testing Cooperative, LCA, 25371 Commercentre Drive Lake Forest, CA 92630. Medical Director Maher Albitar, M.D. Analysis of the data was performed by Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, 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.

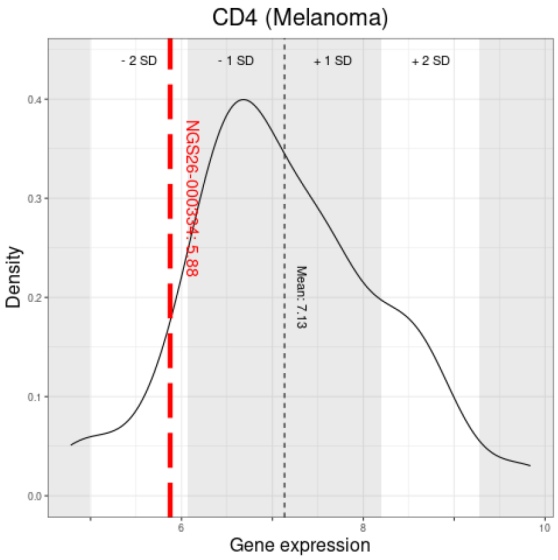
The test was developed and its performance characteristics have been determined by Genomic Testing Cooperative, LCA. This test has not been approved by the FDA. The FDA has determined such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity clinical testing.

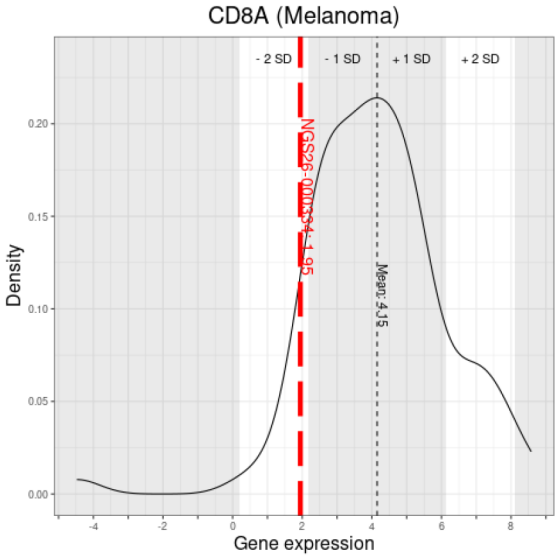
Additional Report Information

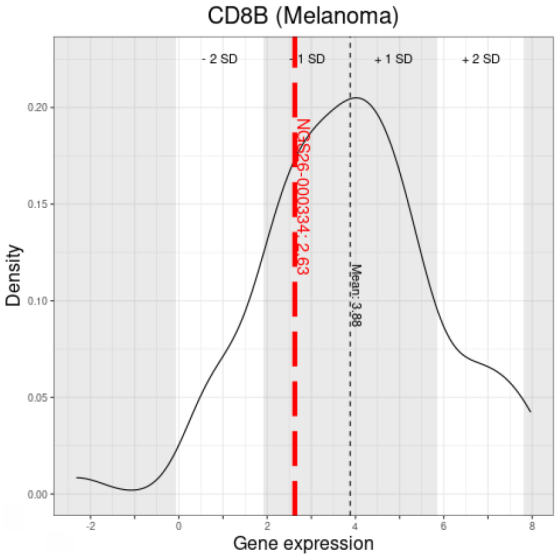
RNA Expression Plots

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.





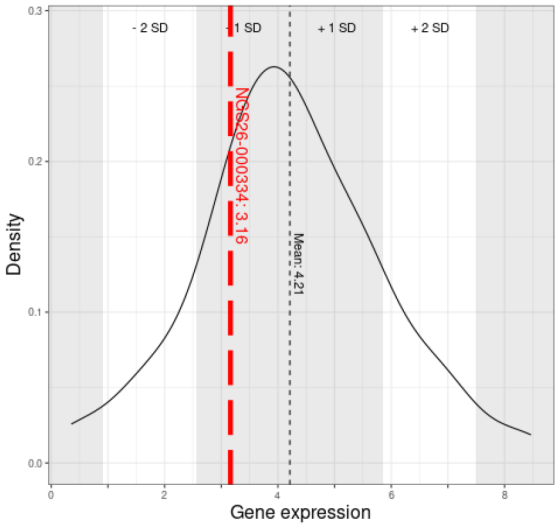




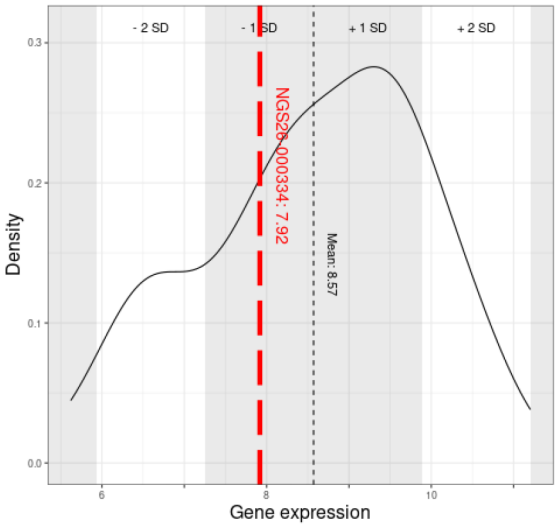
Additional Report Information

RNA Expression Plots

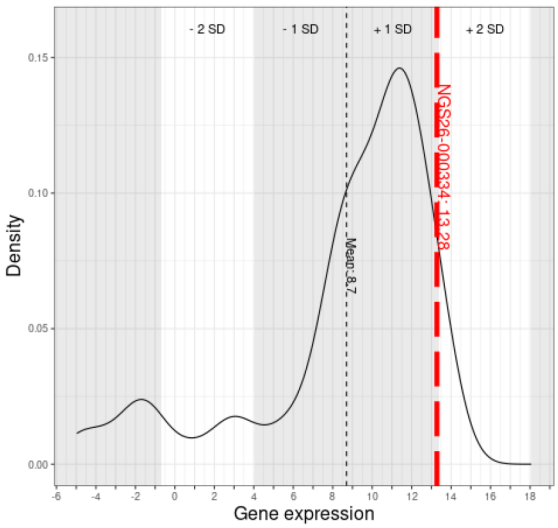
CTLA4 (Melanoma)



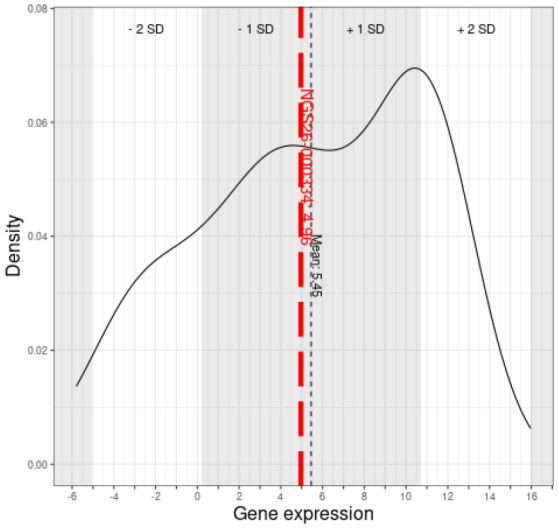
MKI67 (Ki67) (Melanoma)



MLANA (Melanoma)



PRAME (Melanoma)



SOX10 (Melanoma)