Example: Genomic Testing Cooperative Solid Tumor Profile Plus

Sample report header: Anthology Diagnostics

Tumor alteration	Result	Where to find on report
ALK Rearrangement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”
BRAF V600E Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
BRAF Other Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
CUL3 Mutation	No	p.7 listed under “Genes Tested for Abnormalities in Coding Sequence” however no abnormality listed in report
EGFR Exon 19 Deletion	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
EGFR Exon 20 Insertion	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
EGFR Exon 21 L858R Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
EGFR Other Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
ERBB2 (HER2) Amplification/Copy Number Gain	No	p.3 “No evidence of ERBB2 (HER2) amplification”
ERBB2 (HER2) Mutation	No	p.7 listed under “Genes Tested for Abnormalities in Coding Sequence” however

		no abnormality listed in report
KEAP1 Mutation	No	p.7 listed under “Genes Tested for Abnormalities in Coding Sequence” however no abnormality listed in report
KRAS G12C Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
KRAS Other Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”
MET Amplification/Copy Number Gain	Unknown	p.1 “Increased MET mRNA” is an equivocal result
MET exon 14 Skipping Mutation/Splice Site Alteration	Yes	p.1 “MET splice mutation and exon 14 skipping”
MET Other Mutation	Yes, p.Leu824CysfsTer4	p.1 “MET (2 mutations)” p.6 Detailed Results, column Hgvsp
NFE2L2 Mutation	No	p.7 listed under “Genes Tested for Abnormalities in Coding Sequence” however no abnormality listed in report
NTRK1 Rearrangement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”
NTRK2 Rearrangement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”
NTRK3 Rearrangement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”
RET Rearrangement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”
ROS1 Rearragement/Fusion	No	p.1 and p.3 “No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK”

STK11 Mutation	No	p.7 listed under “Genes Tested for Abnormalities in Coding Sequence” however no abnormality listed in report
TP53 Mutation	No	p.3 “No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2”

80 James Street, Edison, NJ 08820
Tel: 732-321-7240
CLIA #: 31D0124320 CAP #: 1215701

Solid Tumor Profile Plus

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

MRN:				Indication for Testing:	C34.90 Malignant neoplasm of unspecified part of unspecified bronchus or lung
Collected Date:		Time:	02:37 PM		
Received Date:		Time:	08:22 AM		
Reported Date:		Time:	12:24 PM		

Detected Genomic Alterations

Level 1 (FDA-Approved)	Level 2 (Standard of Care)	Level 3 (Clinical Evidence)	Level 4 (Biological Evidence)	Other
MET splice mutation and exon 14 skipping	-Tumor Mutation Burden Low: 4 Mut/Mb -Homologous recombination deficiency (HRD): Negative -No evidence of microsatellite instability	BRCA1 (?Germline), MET (2 mutations), FLT4	PBRM1, KLLN (? Germline), FGF3, FAT1	Chromosomal structural analysis shows 5p+(TERT and SDHA amplification, 5q-, 9p-, 10q-, 12q +(proximal (MDM2 and FRS2 amplification), 12q-, 13q-, and 17p-.

PD-L1 testing by immunohistochemistry (IHC) as performed and reported by JFK Medical Center Department of Pathology: Clone 22C3 : Tumor proportion score (TPS): <1%.

Results Summary

- **-Somatic mutations in PBRM1, MET (2 mutations), FGF3, FLT4, and FAT1 genes**
  -Germline mutations in KLLN and BRCA1 genes, heterozygous
  -MET splice mutation and exon 14 skipping
  -No evidence of microsatellite instability
  -Tumor Mutation Burden Low: 4 Mut/Mb
  -Homologous recombination deficiency (HRD): Negative
  -No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK
  -EBV viral RNA: Not detected
  -HPV viral RNA: Not detected
  -Chromosomal structural analysis shows 5p+(TERT and SDHA amplification, 5q-, 9p-, 10q-, 12q +(proximal (MDM2 and FRS2 amplification), 12q-, 13q-, and 17p-.
  -Increased MET mRNA
  -Increased MDM2 mRNA

-PD-L1 testing by immunohistochemistry (IHC) as performed and reported by JFK Medical Center Department of Pathology: Clone 22C3 : Tumor proportion score (TPS): <1%.

-MET exon 14 skipping and MET mutation suggest response to MET inhibitors (tepotinib, capmatinib..).

-MDM2 amplification can be targeted by MDM2 inhibitor Alrizomadlin (APG-115).

-The BRCA1 mutation is detected at high level raising the possibility of a germline abnormality. This mutation has been reported as a germline pathogenic abnormality associated with predisposition to cancer. The presence of this mutation suggests response to PARP inhibitors.

-FLT4 mutation suggests response to mTOR and angiogenic and KDR inhibitors.

-FAT1 abnormality can be targeted by Verteporfin to suppress metastasis.

-The KLLN mutation is detected at high level, most suggestive of a germline mutation. This mutation leads to early termination (loss of function). However, there is no data on its clinical relevance and should be classified as of “uncertain significance” at this time.

Tumor Heterogeneity
There is a dominant abnormal clone with PBRM1 mutation. The MET (2 mutations), FGF3, FLT4, and FAT1 mutations are detected in subclones. The KLLN and BRCA1 mutations are detected at high level, possible germline abnormalities.

Expression	
Increased MET mRNA	Increased MDM2 mRNA

Diagnostic Implications	
PBRM1, KLLN, BRCA1, MET (2 mutations), FGF3, FLT4, FAT1	These findings are consistent with aggressive neoplasm. The KLLN and BRCA1 mutations are likely germline variants.

FDA-Approved Therapeutics	
MET exon 14 skipping	Capmatinib, Tepotinib..

FDA-Approved Therapeutics in Other Tumor Types	
BRCA1	Rucaparib, Niraparib, Talazoparib, Olaparib + Bevacizumab, Olaparib

Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence)	
MET	ALK/MET inhibitors
FLT4	mTOR, angiogenic, KDR inhibitors

MET exon 14 skipping	MET inhibitors

Relevant Genes with NO Alteration		
-No evidence of mutation in KRAS, NRAS, EGFR, BRAF, TP53, or BRCA2 -No specific mutation in DPYD gene, associated with enzymatic deficiency	No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK	-No evidence of EGFR Viii -No evidence of ERBB2 (HER2) amplification

Test Description:

This is a comprehensive molecular profile which uses next generation sequencing (NGS), fragment length analysis and Sanger Sequencing testing to identify molecular abnormalities (including SNVs, INDELS, CNVs, Fusions, TMB, MSI, HRD, EBV, and HPV) in DNA of 434 genes and RNA in 1600 genes implicated in solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

Biological relevance of detected Alterations

- PBRM1. This locus encodes a subunit of ATP-dependent chromatin-remodeling complexes. The encoded protein has been identified as in integral component of complexes necessary for ligand-dependent transcriptional activation by nuclear hormone receptors. Mutations at this locus have been associated with primary clear cell renal cell carcinoma. [provided by RefSeq, Feb 2012]

- KLLN. The protein encoded by this intronless gene is found in the nucleus, where it can inhibit DNA synthesis and promote S phase arrest coupled to apoptosis. The expression of this DNA binding protein is upregulated by transcription factor p53. [provided by RefSeq, Dec 2012]

- BRCA1 mutations in the germline have become a hallmark for hereditary breast and ovarian cancers. Variants that have been demonstrated to reduce the function of the protein have been shown to increase the risk for these cancers, as well as prostate and pancreatic cancer. These findings have been the impetus for the increased popularity of genetic testing of healthy individuals to assess risk. Recent studies in ovarian cancer have also demonstrated that BRCA mutation status can predict treatment response. A number of trials assessing BRCA mutation status have shown an improved response to platinum agents, and more recently has led to the FDA-approval of PARP inhibitors for BRCA-positive ovarian cancers. These studies have resulted in the Society of Gynecologic Oncology to recommend germline BRCA testing in all patients with a diagnosis of ovarian cancer.This gene encodes a 190 kD nuclear phosphoprotein that plays a role in maintaining genomic stability, and it also acts as a tumor suppressor. The BRCA1 gene contains 22 exons spanning about 110 kb of DNA. The encoded protein combines with other tumor suppressors, DNA damage sensors, and signal transducers to form a large multi-subunit protein complex known as the BRCA1-associated genome surveillance complex (BASC). This gene product associates with RNA polymerase II, and through the C-terminal domain, also interacts with histone deacetylase complexes. This protein thus plays a role in transcription, DNA repair of double-stranded breaks, and recombination. Mutations in this gene are responsible for approximately 40% of inherited breast cancers and more than 80% of inherited breast and ovarian cancers. Alternative splicing plays a role in modulating the subcellular localization and physiological function of this gene. Many alternatively spliced transcript variants, some of which are disease-associated mutations, have been described for this gene, but the full-length natures of only some of these variants has been described. A related pseudogene, which is also located on chromosome 17, has been identified. [provided by RefSeq, May 2020]

- MET. Mesenchymal Epithelial Transition MET is a prototypical receptor tyrosine kinase. Its ligand is Hepatocyte Growth Factor (HGF). MET alterations are drivers of human cancer. Amplification and resulting overexpression has been reported in several cancers, and make the receptor's activity independent of HGF. Gene fusions also decouple kinase activity from the cell membrane and render it constitutively active. Finally, exclusion of the juxtamembrane (JM) domain of the kinase by "skipping" of exon 14 activates the kinase.This gene encodes a member of the receptor tyrosine kinase family of proteins and the product of the proto-oncogene MET. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that are linked via disulfide bonds to form the mature receptor. Further processing of the beta subunit results in the formation of the M10 peptide, which has been shown to reduce lung fibrosis. Binding of its ligand, hepatocyte growth factor, induces dimerization and activation of the receptor, which plays a role in cellular survival, embryogenesis, and cellular migration and invasion. Mutations in this gene are associated with papillary renal cell carcinoma, hepatocellular carcinoma, and various head and neck cancers. Amplification and overexpression of this gene are also associated with multiple human cancers. [provided by RefSeq, May 2016]

- FGF3. The protein encoded by this gene is a member of the fibroblast growth factor (FGF) family. FGF family members possess broad mitogenic and cell survival activities and are involved in a variety of biological processes including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion. This gene was identified by its similarity with mouse fgf3/int-2, a proto-oncogene activated in virally induced mammary tumors in the mouse. Frequent amplification of this gene has been found in human tumors, which may be important for neoplastic transformation and tumor progression. Studies of the similar genes in mouse and chicken suggested the role in

inner ear formation. [provided by RefSeq, Jul 2008]

- MET. Mesenchymal Epithelial Transition MET is a prototypical receptor tyrosine kinase. Its ligand is Hepatocyte Growth Factor (HGF). MET alterations are drivers of human cancer. Amplification and resulting overexpression has been reported in several cancers, and make the receptor's activity independent of HGF. Gene fusions also decouple kinase activity from the cell membrane and render it constitutively active. Finally, exclusion of the juxtamembrane (JM) domain of the kinase by "skipping" of exon 14 activates the kinase.This gene encodes a member of the receptor tyrosine kinase family of proteins and the product of the proto-oncogene MET. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that are linked via disulfide bonds to form the mature receptor. Further processing of the beta subunit results in the formation of the M10 peptide, which has been shown to reduce lung fibrosis. Binding of its ligand, hepatocyte growth factor, induces dimerization and activation of the receptor, which plays a role in cellular survival, embryogenesis, and cellular migration and invasion. Mutations in this gene are associated with papillary renal cell carcinoma, hepatocellular carcinoma, and various head and neck cancers. Amplification and overexpression of this gene are also associated with multiple human cancers. [provided by RefSeq, May 2016]

- FLT4. This gene encodes a tyrosine kinase receptor for vascular endothelial growth factors C and D. The protein is thought to be involved in lymphangiogenesis and maintenance of the lymphatic endothelium. Mutations in this gene cause hereditary lymphedema type IA. [provided by RefSeq, Jul 2008]

- FAT1. This gene is an ortholog of the Drosophila fat gene, which encodes a tumor suppressor essential for controlling cell proliferation during Drosophila development. The gene product is a member of the cadherin superfamily, a group of integral membrane proteins characterized by the presence of cadherin-type repeats. In addition to containing 34 tandem cadherin-type repeats, the gene product has five epidermal growth factor (EGF)-like repeats and one laminin A-G domain. This gene is expressed at high levels in a number of fetal epithelia. Its product probably functions as an adhesion molecule and/or signaling receptor, and is likely to be important in developmental processes and cell communication. Transcript variants derived from alternative splicing and/or alternative promoter usage exist, but they have not been fully described. [provided by RefSeq, Jul 2008]

Drug Information

Cabozantinib

Cabozantinib inhibits specific receptor tyrosine kinases such as VEGFR-1, -2 and -3, KIT, TRKB, FLT3, AXL, RET, MET, and TIE2. Cabozantinib suppresses metastasis, angiogenesis, and oncognesis by inhibiting receptor tyrosine kinases. Cabozantinib is indicated for the treatment of metastatic medullary thyroid cancer and for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

Capmatinib

Capmatinib is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.

Crizotinib

Crizotinib an inhibitor of receptor tyrosine kinase for the treatment of non-small cell lung cancer (NSCLC). Crizotinib is a tyrosine kinase receptor inhibitor. More specifically, it inhibits anaplastic lymphoma kinase (ALK), hepatocyte growth factor receptor (HGFR, c-MET), and Recepteur d'Origine Nantais (RON). Abnormalities in the ALK gene caused by mutations or translocations may lead to expression of oncogenic fusion proteins. In patients with NSCLC, they have the EML4-ALK gene. Crizotinib inhibits ALK tyrosine kinase which ultimately results in decreased proliferation of cells that carry the genetic mutation and tumour survivability.

Tepotinib

Tepotinib, in its hydrochloride salt form, is an orally bioavailable inhibitor of MET tyrosine kinase with potential antineoplastic activity. Upon oral administration, tepotinib selectively binds to MET tyrosine kinase and disrupts MET signal transduction pathways, which may induce apoptosis in tumor cells overexpressing this kinase. The receptor tyrosine kinase MET (also known as hepatocyte growth factor receptor or HGFR), is the product of the proto-oncogene c-Met and is overexpressed or mutated in many tumor cell types; this protein plays key roles in tumor cell proliferation, survival, invasion, and metastasis, and tumor angiogenesis.

Olaparib

Olaparib (LYNPARZA) is an antineoplastic agent, Poly(ADP-ribose) Polymerase1;2;3 inhibitor. (PARP1;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)

Rucaparib

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

PPAR is an enzyme that plays an essential role in DNA repair by activating response pathways and facilitating repair, and defects in these repair mechanisms have been demonstrated in various malignancies, including cancer. Regulation of repair pathways is critical in promoting necessary cell death. BRCA genes are tumor suppressor genes mediate several cellular processes including DNA replication, transcription regulation, cell cycle checkpoints, apoptosis, chromatin structuring and homologous recombination (HR). Homologous recombination deficiency (HRD), along with PPAR inhibition, is a vulnerability that enhances the cell death pathway when the single mutations alone would permit viability. Ovarian cancer commonly possesses defects in DNA repair pathways such as HRD due to BRCA mutations or otherwise. Rucaparib has shown to induce cytotoxicity in tumor cell lines with deficiencies in BRCA1/2 and other DNA repair genes. Of all the BRCA1/2 mutations in ovarian cancer, most are due to germline mutations (18%), and approximately 7% represent somatic mutations acquired within the tumor.

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.

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.

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

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites
https://classic.clinicaltrials.gov/show/NCT04467723	Recruiting	Combination of Atezolizumab and Pirfenidone in Second-line and Beyond NSCLC	Non-small Cell Lung Cancer	Atezolizumab	The University of Kansas Cancer Center (KUCC), Fairway, Kansas, United States The University of Kansas Cancer Center, Westwood Campus, Kansas City, Kansas, United States
https://classic.clinicaltrials.gov/show/NCT04317534	Recruiting	Adjuvant Pembrolizumab vs Observation Following Curative Resection for Stage I Non-small Cell Lung Cancer (NSCLC) With Primary Tumors Between 1-4 cm	Non-small Cell Lung Cancer	Pembrolizumab	Moffit Cancer Center, Tampa, Florida, United States University of Illinois Cancer Center, Chicago, Illinois, United States University of Minnesota, Minneapolis, Minnesota, United States

https://classic.clinicaltrials.gov/show/NCT04681131	Recruiting	CAB-AXL-ADC Safety and Efficacy Study in Adults With NSCLC	Non-small Cell Lung Cancer	CAB-AXL-ADC PD-1 inhibitor	City of Hope - Duarte, Duarte, California, United States California Research Institute, Los Angeles, California, United States USC Norris, Los Angeles, California, United States

Detailed Results

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

Gene name	Hgvsp	Hgvsc	Aminoacids	Codons	Consequence	Allele frequency	Read depth	Predicted effect on protein
PBRM1	NP_060783.3:p.Tyr420His	NM_018313.4:c.1258T>C	Y/H	Tat/Cat	missense_variant	54.15	253	deleterious (0)
KLLN	NP_001119521.1:p.Ala115SerfsTer58	NM_001126049.1:c.339_340delAG	TG/TX	acAGgg/acgg	frameshift_variant	53.14	271	0
BRCA1	NP_009231.2:p.Gln1777ProfsTer74	NM_007300.3:c.5329dupC	Q/PX	cag/cCag	frameshift_variant	45.24	126	0
MET	NP_001120972.1:p.Leu824CysfsTer4	NM_001127500.1:c.2470delC	S/X	tCc/tc	frameshift_variant	23.29	249	0
FGF3	NP_005238.1:p.Asp218Asn	NM_005247.2:c.652G>A	D/N	Gat/Aat	missense_variant	20.7	285	tolerated - low confidence (0.44)
MET	NP_001120972.1:p.Asp1028His	NM_001127500.1:c.3082G>C	D/H	Gat/Cat	"missense_variant,splice_region_variant"	14.0	493	deleterious (0.01)
FLT4	NP_891555.2:p.Val791Ile	NM_182925.4:c.2371G>A	V/I	Gtc/Atc	missense_variant	11.4	193	tolerated (0.5)
FAT1	NP_005236.2:p.Arg1099Cys	NM_005245.3:c.3295C>T	R/C	Cgt/Tgt	missense_variant	5.16	213	0

Methodology and Test Background

This is a next generation sequencing (NGS) test that analyzes DNA for abnormalities in 434 genes that are reported to be altered in various types of tumors. Nucleic acid is isolated from 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. Our sequencing method has a typical sensitivity of 3% for detecting common specific mutations and 5% for other mutations. MSI status is inferred by interrogating all available genomic microsatellites covered. Tumor mutational burden (TMB) is measured by counting all non-synonymous 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 based on lung carcinoma analysis. The cut off for other types of tumors is not well established at this time. 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 is performed. This is a next generation sequencing (NGS) test that analyzes targeted RNA on 1,501 genes implicated in solid tumors. 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. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. 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. 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. For optimal results neoplastic cells should be >30% of the analyzed cells. The Universal Human Reference (UHR) RNA is used as control.

Based on our validation study, the following regions of the genes listed below are not covered appropriately (<100 X coverage) and sequencing by NGS may not be reliable in these regions. This poor coverage is due to high GC content with inherited problem in obtaining adequate coverage. CSF3R, 36937661, 36937745, R343-K357, 1. RANBP2, 109378551, 109378656, V868-k899, 2. PBRM1, 52677258, 52677364, R300-R332, 3. BAP1, 52443852, 52443899, M1-G13, 3. FLT4, 180035275, 180035289, R1298 (Last AA), 5. RHEB, 151216540, 151216602, M1-G18, 7. RHEB, 151195169, 151195198, Intronic region, 7. ANKRD26, 27368955, 27369112, Intonic region, 10. ERBB3, 56492278, 56492364, T873-G898, 12. DDX11, 31240866, 31240922, R186-K202, 12. IRS2, 110437064, 110437332, S357-A441, 13. FLT3, 28674599, 28674652, M1-V15, 13. CCNE1, 30303457, 30303490, M1-R8, 19. MED12, 70361074, 70361225, Q2090-2136, X

The table below contains 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	AURKB	C15ORF41	CEBPA	DNMT3A	FANCC	FLT3	GRIN2A	IRF2	LMO1	MSH6	NTRK2	POT1	RARA	SF3B1	STAT6	TSHR
ABL1	AURKC	CALR	CHD2	DOT1L	FANCD2	FLT4	GRM3	IRF4	LPIN2	MTOR	NTRK3	PPM1D	RB1	SLIT2	STK11	U2AF1
ABL2	AXIN1	CARD11	CHD4	EED	FANCE	FOXL2	GSK3B	IRS2	LRP1B	MUTYH	NUP93	PPP2R1A	RBBP6	SLX4	SUFU	U2AF2
ACD	AXIN2	CBFB	CHEK1	EGFR	FANCF	FOXP1	GSKIP	JAGN1	LYN	MVK	PAK3	PRDM1	RBM10	SMAD2	SUZ12	VEGFA
ACVR1B	AXL	CBL	CHEK2	EGLN1	FANCG	FRS2	H3F3A	JAK1	LYST	MYC	PALB2	PREX2	RBM8A	SMAD3	SYK	VHL
ADA	B2M	CBLB	CIC	ELANE	FANCI	FUBP1	HAX1	JAK2	LZTR1	MYCL	PARK2	PRKAR1A	RET	SMAD4	TAF1	WAS
AK2	BAP1	CBLC	CREBBP	EP300	FANCL	G6PC3	HGF	JAK3	MAGI2	MYCN	PAX5	PRKCI	RHEB	SMAD9	TAL1	WHSC1
AKT1	BARD1	CCND1	CRKL	EPAS1	FANCM	GABRA6	HIST1H3B	JUN	MAP2K1	MYD88	PBRM1	PRKDC	RHOA	SMAD9L	TBX3	WISP3
AKT2	BCL2	CCND2	CRLF2	EPCAM	FAS	GALNT12	HNF1A	KAT6A	MAP2K2	NBN	PDCD1LG2	PRSS1	RICTOR	SMARCA4	TCF3	WT1
AKT3	BCL2L1	CCND3	CSF1R	EPHA3	FAT1	GATA1	HOXA11	KDM5A	MAP2K4	NF1	PDGFRA	PRSS8	RIT1	SMARCB1	TCIRG1	XPO1
ALK	BCL2L2	CCNE1	CSF3R	EPHA5	FBXW7	GATA2	HOXB13	KDM5C	MAP3K1	NF2	PDGFRB	PSTPIP1	RNF168	SMC1A	TERC	XRCC2
AMER1	BCL6	CD274	CTC1	EPHA7	FGF10	GATA3	HRAS	KDM6A	MAP3K14	NFE2L2	PDK1	PTCH1	RNF43	SMC3	TERF1	XRCC3
ANKRD26	BCOR	CD79A	CTCF	EPHB1	FGF14	GATA4	HSD3B1	KDR	MAPK1	NFKBIA	PHF6	PTEN	ROS1	SMO	TERF2	ZBTB2
APC	BCORL1	CD79B	CTNNA1	ERBB2	FGF19	GATA6	HSP90AA1	KEAP1	MCL1	NHP2	PIK3C2B	PTPN11	RPTOR	SNCAIP	TERF2IP	ZNF217
AR	BCR	CDAN1	CTNNB1	ERBB3	FGF23	GEN1	ID3	KEL	MDM2	NKX2-1	PIK3CA	QKI	RTEL1	SOCS1	TERT	ZNF703
ARAF	BIRC3	CDC73	CUL3	ERBB4	FGF3	GFI1	IDH1	KIF23	MDM4	NLRP3	PIK3CB	RAB27A	RUNX1	SOX10	TET2	ZRSR2
ARFRP1	BLM	CDH1	CUX1	ERCC4	FGF4	GFI1B	IDH2	KIT	MED12	NME1	PIK3CG	RAC1	RUNX1T1	SOX2	TGFBR2	-
ARID1A	BMPR1A	CDK12	CXCR4	ERG	FGF6	GID4	IGF1R	KLF1	MEF2B	NOP10	PIK3R1	RAD21	SBDS	SOX9	TNFAIP3	-
ARID1B	BRAF	CDK4	CYLD	ERRFI1	FGFR1	GLI1	IGF2	KLHL6	MEFV	NOTCH1	PIK3R2	RAD50	SBF2	SPEN	TNFRSF14	-
ARID2	BRCA1	CDK6	DAXX	ESR1	FGFR2	GLI2	IKBKE	KLLN	MEN1	NOTCH2	PIM1	RAD51	SDHA	SPOP	TNFRSF1A	-
ASXL1	BRCA2	CDK8	DDR2	ETV6	FGFR3	GNA11	IKZF1	KMT2A	MET	NOTCH3	PLCG1	RAD51B	SDHB	SPTA1	TOP1	-
ATG2B	BRD4	CDKN1A	DDX11	EXO1	FGFR4	GNA13	IKZF3	KMT2B	MITF	NPM1	PLCG2	RAD51C	SDHC	SRC	TOP2A	-
ATM	BRIP1	CDKN1B	DDX41	EZH2	FH	GNAQ	IL2RG	KMT2C	MLH1	NRAS	PMS1	RAD51D	SDHD	SRSF2	TP53	-
ATR	BTG1	CDKN2A	DICER1	FAM175A	FLCN	GNAS	IL7R	KMT2D	MPL	NROB1	PMS2	RAD54L	SEC23B	STAG2	TRAF3	-
ATRX	BTK	CDKN2B	DKC1	FAM46C	FLI1	GPR124	INHBA	KRAS	MRE11A	NSD1	POLD1	RAF1	SETBP1	STAT3	TSC1	-

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AURKA	C11orf40	CDKN2C	DNM2	FANCA	FLT1	GREM1	INPP4B	LIG4	MSH2	NTRK1	POLE	RANBP2	SETD2	STAT4	TSC2	-

RNA Fusions/Expression

Fusion/Expression													
ABL1	BCL2	CBFB	ERG	FGFR2	FOXO1	IKZF3	MAP3K1	NTRK1	NUP98	PICALM	RHOA	SS18	TCF3
AKT3	BCL6	CIC	ETV6	FGFR3	FUS	JAK2	MECOM	NTRK2	PDGFRA	PML	ROS2	STAT6	TFG
ALK	BRAF	CREBBP	EWSR1	FIP1L1	GLI1	KIAA1549	MYC	NTRK3	PDGFRB	RARA	RUNX1	TAFG	YWHAE
BCL1	CAMTA1	EGFR	FGFR1	FLAG1	HMGA2	KMT2A	NOTCH1	NUP214	PD-L1	RET	RUNX1T1	TAL1	

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Electronic Signature

Maher Albitar, M.D.

The test (sample processing, sequencing and data generation) was performed at Anthology Diagnostics-JFK Medical Center Lab, 80 James Street, Edison, NJ 08820. Medical Director Clinton Ewing, M.D. Analysis of the data was performed by Genomic Testing Cooperative, LCA, 175 Technology Drive, Suite 100, Irvine, CA 92618. Medical Director: Maher Albitar, M.D.

The test was developed and its performance characteristics have been determined by Anthology Diagnostics-JFK Medical Center Lab. 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.