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Patient Name: 한기수
Gender: M
Sample ID: N25-44

Primary Tumor Site: lung
Collection Date: 2025.05.22

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	MET	None detected
BRAF	None detected	NRG1	None detected
EGFR	None detected	NTRK1	None detected
ERBB2	None detected	NTRK2	None detected
FGFR1	None detected	NTRK3	None detected
FGFR2	None detected	RET	None detected
FGFR3	None detected	ROS1	None detected
KRAS	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	***13.27 Mut/Mb measured***

Relevant Biomarkers

No biomarkers associated with relevant evidence found in this sample

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, STK11 c.921-2A>T, YAP1 amplification, UGT1A1 p.(G71R) c.211G>A, HLA-A p.(L180) c.539T>A, HLA-B deletion, EMSY amplification, ACVR1B p.(V108Cfs*21) c.322delG, CDH1 p.(R222*) c.664A>T, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	56.96%	NM_000463.3	missense
HLA-A	p.(L180*)	c.539T>A	.	chr6:29911240	16.38%	NM_001242758.1	nonsense

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ACVR1B	p.(V108Cfs*21)	c.322delG	.	chr12:52369276	15.31%	NM_020328.4	frameshift Deletion
CDH1	p.(R222*)	c.664A>T	.	chr16:68842728	9.71%	NM_004360.5	nonsense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	47.57%	NM_000903.3	missense
STK11	p.(?)	c.921-2A>T	.	chr19:1222982	13.39%	NM_000455.5	unknown
NTRK1	p.(K506N)	c.1518G>C	.	chr1:156845888	19.77%	NM_002529.3	missense
REG3G	p.(E114*)	c.340G>T	.	chr2:79254939	10.61%	NM_001008387.3	nonsense
TP63	p.(V69F)	c.205G>T	.	chr3:189456444	16.26%	NM_003722.5	missense
RNF8	p.(N458S)	c.1373A>G	.	chr6:37349062	49.25%	NM_003958.4	missense
KMT2C	p.(P3009R)	c.9026C>G	.	chr7:151873512	54.28%	NM_170606.3	missense
OR10G8	p.(S139W)	c.416C>G	.	chr11:123900745	9.81%	NM_001004464.2	missense
KMT2D	p.(M999I)	c.2997G>C	.	chr12:49444374	11.10%	NM_003482.4	missense
PARP4	p.(P1244R)	c.3731C>G	.	chr13:25009548	49.07%	NM_006437.4	missense
IGF1R	p.(G171A)	c.512G>C	.	chr15:99251208	4.85%	NM_000875.5	missense
CNTNAP4	p.(I693S)	c.2078T>G	.	chr16:76532523	9.21%	NM_138994.5	missense
KEAP1	p.(L19Q)	c.56T>A	.	chr19:10610654	58.54%	NM_203500.2	missense
SMARCA4	p.(E1056D)	c.3168G>T	.	chr19:11136184	9.95%	NM_001128849.3	missense
CIC	p.(K962N)	c.2886G>T	.	chr19:42795897	11.53%	NM_015125.5	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
HLA-B	chr6:31322252	0.88	0.67
EMSY	chr11:76157926	4.78	1.83
YAP1	chr11:101981594	5.68	2.1

Biomarker Descriptions

STK11 c.921-2A>T

serine/threonine kinase 11

Background: The STK11 gene, also known as liver kinase B1 (LKB1), encodes the serine/threonine kinase 11 protein. STK11 is a tumor suppressor with multiple substrates including AMP-activated protein kinase (AMPK) that regulates cell metabolism, growth, and tumor suppression[1]. Germline mutations in STK11 are associated with Peutz-Jeghers syndrome, an autosomal dominant disorder, characterized by gastrointestinal polyp formation and elevated risk of neoplastic development[2,3].

Alterations and prevalence: Somatic mutations in STK11 have been reported in 10% of lung cancer, 4% of cervical cancer, and up to 3% of cholangiocarcinoma and uterine cancer[4,5,6,7]. Mutations in STK11 are found to co-occur with KEAP1 and KRAS mutations in lung cancer[6,7]. Copy number deletion leads to inactivation of STK11 in cervical, ovarian, and lung cancers, among others[2,5,6,7,8].

Biomarker Descriptions (continued)

Potential relevance: Currently, no therapies are approved for STK11 aberrations. However, in 2023, the FDA granted fast track designation to a first-in-class inhibitor of the CoREST complex (Co-repressor of Repressor Element-1 Silencing Transcription), TNG-260[9] in combination with an anti-PD-1 antibody, for advanced non-small cell lung cancer harboring STK11-mutations. The presence of STK11 mutations may be a mechanism of resistance to immunotherapies. Mutations in STK11 are associated with reduced expression of PD-L1, which may contribute to the ineffectiveness of anti-PD-1 immunotherapy in STK11 mutant tumors[10]. In a phase III clinical trial of nivolumab in lung adenocarcinoma, patients with KRAS and STK11 co-mutations demonstrated a worse (0/6) objective response rate (ORR) in comparison to patients with KRAS and TP53 co-mutations (4/7) or KRAS mutations only (2/11) (ORR= 0% vs 57.1% vs 18.25%, respectively)[11].

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[12]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[13]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[14]. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self[15,16,17]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B[18].

Alterations and prevalence: Somatic mutations in HLA-B are observed in 10% of diffuse large B-cell lymphoma (DLBCL), 5% of cervical squamous cell carcinoma and stomach adenocarcinoma, 4% of head and neck squamous cell carcinoma and colorectal adenocarcinoma, 3% of uterine cancer, and 2% of esophageal adenocarcinoma and skin cutaneous melanoma[6,7]. Biallelic loss of HLA-B is observed in 5% of DLBCL[6,7].

Potential relevance: Currently, no therapies are approved for HLA-B aberrations.

HLA-A p.(L180*) c.539T>A

major histocompatibility complex, class I, A

Background: The HLA-A gene encodes the major histocompatibility complex, class I, A[12]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[13]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[14]. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self[15,16,17]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-A[18].

Alterations and prevalence: Somatic mutations in HLA-A are observed in 7% of diffuse large B-cell lymphoma (DLBCL), 4% of cervical squamous cell carcinoma and head and neck squamous cell carcinoma, 3% of colorectal adenocarcinoma, and 2% of uterine corpus endometrial carcinoma and stomach adenocarcinoma[6,7]. Biallelic loss of HLA-A is observed in 4% of DLBCL[6,7].

Potential relevance: Currently, no therapies are approved for HLA-A aberrations.

CDH1 p.(R222*) c.664A>T

cadherin 1

Background: The CDH1 gene encodes epithelial cadherin or E-cadherin, a member of the cadherin superfamily that includes the classical cadherins: neural cadherin (N-cadherin), retinal cadherin (R-cadherin), and placental cadherin (P-cadherin)[12,19]. E-cadherin proteins, composed of 5 extracellular cadherin repeats, a single transmembrane domain, and conserved cytoplasmic tail, are calcium-dependent transmembrane glycoproteins expressed in epithelial cells[12]. Extracellular E-cadherin monomers form homodimers with those on adjacent cells to form adherens junctions. Adherens junctions are reinforced by intracellular complexes formed between the cytoplasmic tail of E-cadherin and catenins, proteins which directly anchor cadherins to actin filaments[20]. E-cadherin is a critical tumor suppressor and when lost, results in epithelial-mesenchymal transition (EMT), anchorage-independent cell growth, loss of cell polarity, and tumor metastasis[21,22]. Germline mutations in CDH1 are enriched in a rare autosomal-dominant genetic malignancies such as hereditary diffuse gastric cancer, lobular breast cancer, and colorectal cancer[23].

Alterations and prevalence: Mutations in CDH1 are predominantly missense or truncating and have been observed to result in loss of function[6,7,24,25]. In cancer, somatic mutation of CDH1 is observed in 12% of invasive breast carcinoma, 10% of stomach adenocarcinoma, 7% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma and skin cutaneous melanoma, 3% of bladder urothelial carcinomas, and 2% of lung squamous cell and liver hepatocelluar carcinomas[6,7]. Biallelic deletion of CDH1 is

Biomarker Descriptions (continued)

observed in 3% of prostate adenocarcinoma and ovarian serous cystadenocarcinoma, and 2% of esophageal adenocarcinoma, diffuse large B-cell lymphoma, and breast invasive carcinoma[6,7].

Potential relevance: Currently, no therapies are approved for CDH1 aberrations.

YAP1 amplification

Yes associated protein 1

Background: The YAP1 gene encodes the Yes1 associated transcriptional regulator[12]. YAP1 functions as a transcriptional coactivator for TEAD transcription factors and is an important effector of the Hippo signaling pathway[26]. The Hippo pathway is considered a tumor suppressor pathway due to its involvement in various cellular processes including cell proliferation, apoptosis, stem cell expansion, and negative regulation of YAP1[26,27]. Aberrations in YAP1, including upregulation, have been associated with tumorigenesis and shorter survival[27,28]. Germline mutations, specifically R331W, have been associated with an increased risk for lung adenocarcinoma[29].

Alterations and prevalence: Somatic mutations in YAP1 are observed in 3% of uterine corpus endometrial carcinoma, 2% of skin cutaneous melanoma, esophageal adenocarcinoma, kidney chromophobe, and 1% of uveal melanoma, kidney renal papillary cell carcinoma, lung squamous cell carcinoma, cervical squamous cell carcinoma, and colorectal adenocarcinoma[6,7]. Amplification of YAP1 is observed in 10% of cervical squamous cell carcinoma, 5% of head and neck squamous cell carcinoma and ovarian cystadenocarcinoma, and 3% of bladder urothelial carcinoma, sarcoma, and esophageal adenocarcinoma[6,7]. YAP1 fusions are observed in 1% of sarcoma, esophageal adenocarcinoma, cervical squamous cell carcinoma, skin cutaneous melanoma, and head and neck squamous cell carcinoma[6,7].

Potential relevance: Currently, no therapies are approved for YAP1 aberrations. YAP1::TFE3 fusion is considered an ancillary diagnostic marker for epithelioid hemangioendothelioma[30]. Overexpression of YAP1 is a poor prognostic marker in hepatocellular carcinoma, gastric cancer, colorectal cancer, non-small cell lung cancer, and small cell lung cancer[26].

ACVR1B p.(V108Cfs*21) c.322delG

activin A receptor type 1B

Background: The ACVR1B gene encodes the activin A type 1B receptor protein, a transmembrane serine-threonine kinase receptor and member of the bone morphogenic protein (BMP)/transforming growth factor-beta (TGFβ) receptor family[12,31]. ACVR1B is a type I receptor that forms a heterotetrametric complex with at least two type I receptors (including ACVR1) and two type II receptors (including BMPR2, ACVR2A, and ACVR2B)[31,32]. When ligands, such as activin A or BMPs, dimerize and bind to the heterotetrametric complex, type II receptors transphosphorylate and activate type I receptors leading to phosphorylation of SMAD proteins and downstream signaling[31,32]. Loss of function mutations and homozygous deletion in ACVR1B has been observed in pancreatic cancer and is associated with increased cell growth, colony formation, and tumorigenicity[33,34].

Alterations and prevalence: Somatic mutations of ACVR1B are observed in 5% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma, 3% of stomach adenocarcinoma, 2% of lung adenocarcinoma, skin cutaneous melanoma, lung squamous cell carcinoma, uterine carcinosarcoma, esophageal adenocarcinoma, and kidney chromophobe, and 1% of head and neck squamous cell carcinoma, kidney renal clear cell carcinoma, breast invasive carcinoma, brain lower grade glioma, ovarian serous cystadenocarcinoma, pancreatic adenocarcinoma, liver hepatocellular carcinoma, and acute myeloid leukemia[6,7]. Biallelic deletion of ACRV1B is observed in 1% of stomach adenocarcinoma, brain lower grade glioma, and pancreatic adenocarcinoma[6,7].

Potential relevance: Currently, no therapies are approved for ACVR1B aberrations.

EMSY amplification

EMSY transcriptional repressor, BRCA2 interacting

Background: The EMSY gene encodes the EMSY transcriptional repressor, BRCA2 interacting[12]. EMSY is a nuclear protein that interacts with the transactivation domain of BRCA2, resulting in the suppression of BRCA2 transcriptional activity.[35,36]. EMSY colocalizes with γ-H2AX at DNA damage sites, regulates chromatin remodeling, and suppresses interferon-stimulated genes in a BRCA2 dependent manner[35,37]. Overexpression of EMSY inactivates BRCA2 leading to chromosomal instability and tumorigenesis[35,37].

Alterations and prevalence: Somatic mutations in EMSY are observed in 7% of uterine corpus endometrial carcinoma, 6% of skin cutaneous melanoma, 3% of bladder urothelial carcinoma, lung squamous cell carcinoma, colorectal adenocarcinoma, and 2% of lung adenocarcinoma, uterine carcinosarcoma, and stomach adenocarcinoma[6,7]. Amplification of EMSY is observed in 8% of ovarian serous cystadenocarcinoma, 6% of breast invasive carcinoma and esophageal adenocarcinoma, and 4% of head and neck squamous cell carcinoma and skin cutaneous melanoma[6,7].

Biomarker Descriptions (continued)

Potential relevance: Currently, no therapies are approved for EMSY aberrations.

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome[38]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[39,40]. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2[41]. Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250[42]. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)[42]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[43,44,45,46,47]. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes[40]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[39,40,44,48].

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma[39,40,49,50]. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers[49,50].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[51] (2014) and nivolumab[52] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[51] is also approved as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication[51]. Dostarlimab[53] (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer[45,54]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[55] (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location[45,56,57]. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients[57]. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors[58,59]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[58,59].

UGT1A1 p.(G71R) c.211G>A

UDP glucuronosyltransferase family 1 member A1

Background: The UGT1A1 gene encodes UDP glucuronosyltransferase family 1 member A1, a member of the UDP-glucuronosyltransferase 1A (UGT1A) subfamily of the UGT protein superfamily[12,60]. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites[60,61]. UGTs play an important role in drug metabolism, detoxification, and metabolite homeostasis. Differential expression of UGTs can promote cancer development, disease progression, as well as drug resistance[62]. Specifically, elevated expression of UGT1As are associated with resistance to many anti-cancer drugs due to drug inactivation and lower active drug concentrations. However, reduced expression and downregulation of UGT1As are implicated in bladder and hepatocellular tumorigenesis and progression due to toxin accumulation[62,63,64,65]. Furthermore, UGT1A1 polymorphisms, such as UGT1A1*28, UGT1A1*93, and UGT1A1*6, confer an increased risk of severe toxicity to irinotecan-based chemotherapy treatment of solid tumors, due to reduced glucuronidation of the irinotecan metabolite, SN-38[66].

Alterations and prevalence: Biallelic deletion of UGT1A1 has been observed in 6% of sarcoma, 3% of brain lower grade glioma and uveal melanoma, and 2% of thymoma, cervical squamous cell carcinoma, bladder urothelial carcinoma, head and neck squamous cell carcinoma, and esophageal adenocarcinoma[6,7].

Potential relevance: Currently, no therapies are approved for UGT1A1 aberrations.

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLCO1B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, ZNF217, ZNF429

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4, ERRFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBFB, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRFI1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFBR2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFHX3, ZMYM3, ZRSR2

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	***0.0%***
Not Detected	***Not Applicable***

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.0.2 data version 2025.04(004)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-03-19. NCCN information was sourced from www.nccn.org and is current as of 2025-03-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-03-19. ESMO information was sourced from www.esmo.org and is current as of 2025-03-03. Clinical Trials information is current as of 2025-03-03. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

References

1. Li et al. Role of the LKB1/AMPK pathway in tumor invasion and metastasis of cancer cells (Review). Oncol. Rep. 2015 Dec;34(6):2821-6. PMID: 26398719
2. Zhou et al. LKB1 Tumor Suppressor: Therapeutic Opportunities Knock when LKB1 Is Inactivated. Genes Dis. 2014 Sep 1;1(1):64-74. PMID: 25679014
3. Hemminki et al. A serine/threonine kinase gene defective in Peutz-Jeghers syndrome. Nature. 1998 Jan 8;391(6663):184-7. PMID: 9428765
4. Campbell et al. Distinct patterns of somatic genome alterations in lung adenocarcinomas and squamous cell carcinomas. Nat. Genet. 2016 Jun;48(6):607-16. PMID: 27158780
5. Cancer Genome Atlas Research Network. Comprehensive molecular profiling of lung adenocarcinoma. Nature. 2014 Jul 31;511(7511):543-50. doi: 10.1038/nature13385. Epub 2014 Jul 9. PMID: 25079552
6. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
7. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov. 2012 May;2(5):401-4. PMID: 22588877
8. Sanchez-Cespedes et al. Inactivation of LKB1/STK11 is a common event in adenocarcinomas of the lung. Cancer Res. 2002 Jul 1;62(13):3659-62. PMID: 12097271
9. https://ir.tangotx.com//news-releases/news-release-details/tango-therapeutics-announces-first-patient-dosed-tng260-phase-12
10. Koyama et al. STK11/LKB1 Deficiency Promotes Neutrophil Recruitment and Proinflammatory Cytokine Production to Suppress T-cell Activity in the Lung Tumor Microenvironment. Cancer Res. 2016 Mar 1;76(5):999-1008. PMID: 26833127
11. Skoulidis et al. STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Lung Adenocarcinoma. Cancer Discov. 2018 Jul;8(7):822-835. PMID: 29773717
12. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. Nucleic Acids Res. 2016 Jan 4;44(D1):D733-45. PMID: 26553804
13. Hulpke et al. The MHC I loading complex: a multitasking machinery in adaptive immunity. Trends Biochem Sci. PMID: 23849087
14. Adams et al. The adaptable major histocompatibility complex (MHC) fold: structure and function of nonclassical and MHC class I-like molecules. Annu Rev Immunol. 2013;31:529-61. PMID: 23298204
15. Rossjohn et al. T cell antigen receptor recognition of antigen-presenting molecules. Annu Rev Immunol. 2015;33:169-200. PMID: 25493333
16. Parham. MHC class I molecules and KIRs in human history, health and survival. Nat Rev Immunol. 2005 Mar;5(3):201-14. PMID: 15719024
17. Sidney et al. HLA class I supertypes: a revised and updated classification. BMC Immunol. 2008 Jan 22;9:1. PMID: 18211710
18. Cornel et al. MHC Class I Downregulation in Cancer: Underlying Mechanisms and Potential Targets for Cancer Immunotherapy. Cancers (Basel). 2020 Jul 2;12(7). PMID: 32630675
19. Halbleib et al. Cadherins in development: cell adhesion, sorting, and tissue morphogenesis. Genes Dev. 2006 Dec 1;20(23):3199-214. PMID: 17158740
20. Pećina-Slaus. Tumor suppressor gene E-cadherin and its role in normal and malignant cells. Cancer Cell Int. 2003 Oct 14;3(1):17. PMID: 14613514
21. Hirohashi. Inactivation of the E-cadherin-mediated cell adhesion system in human cancers. Am J Pathol. 1998 Aug;153(2):333-9. PMID: 9708792
22. Bruner et al. Loss of E-Cadherin-Dependent Cell-Cell Adhesion and the Development and Progression of Cancer. Cold Spring Harb Perspect Biol. 2018 Mar 1;10(3). PMID: 28507022
23. Adib et al. CDH1 germline variants are enriched in patients with colorectal cancer, gastric cancer, and breast cancer. Br J Cancer. 2022 Mar;126(5):797-803. PMID: 34949788
24. Al-Ahmadie et al. Frequent somatic CDH1 loss-of-function mutations in plasmacytoid variant bladder cancer. Nat Genet. 2016 Apr;48(4):356-8. PMID: 26901067
25. Kim et al. Loss of CDH1 (E-cadherin) expression is associated with infiltrative tumour growth and lymph node metastasis. Br J Cancer. 2016 Jan 19;114(2):199-206. PMID: 26742007
26. Shibata et al. A time for YAP1: Tumorigenesis, immunosuppression and targeted therapy. Int J Cancer. 2018 Nov 1;143(9):2133-2144. PMID: 29696628
27. Fernandez-L et al. YAP1 is amplified and up-regulated in hedgehog-associated medulloblastomas and mediates Sonic hedgehog-driven neural precursor proliferation. Genes Dev. 2009 Dec 1;23(23):2729-41. PMID: 19952108

References (continued)

28. Liu et al. Clinical significance of yes-associated protein overexpression in cervical carcinoma: the differential effects based on histotypes. Int J Gynecol Cancer. 2013 May;23(4):735-42. PMID: 23502453
29. Chen et al. R331W Missense Mutation of Oncogene YAP1 Is a Germline Risk Allele for Lung Adenocarcinoma With Medical Actionability. J Clin Oncol. 2015 Jul 10;33(20):2303-10. PMID: 26056182
30. NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 4.2024]
31. Valer et al. ACVR1 Function in Health and Disease. Cells. 2019 Oct 31;8(11). PMID: 31683698
32. Haupt et al. Variable signaling activity by FOP ACVR1 mutations. Bone. 2018 Apr;109:232-240. PMID: 29097342
33. Su et al. ACVR1B (ALK4, activin receptor type 1B) gene mutations in pancreatic carcinoma. Proc Natl Acad Sci U S A. 2001 Mar 13;98(6):3254-7. PMID: 11248065
34. Togashi et al. Homozygous deletion of the activin A receptor, type IB gene is associated with an aggressive cancer phenotype in pancreatic cancer. Mol Cancer. 2014 May 27;13:126. PMID: 24886203
35. Dansonka-Mieszkowska et al. Clinical importance of the EMSY gene expression and polymorphisms in ovarian cancer. Oncotarget. 2018 Apr 3;9(25):17735-17755. PMID: 29707144
36. Hughes-Davies et al. EMSY links the BRCA2 pathway to sporadic breast and ovarian cancer. Cell. 2003 Nov 26;115(5):523-35. PMID: 14651845
37. Kondrashova et al. Clarifying the role of EMSY in DNA repair in ovarian cancer. Cancer. 2019 Aug 15;125(16):2720-2724. PMID: 31154666
38. Lander et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. PMID: 11237011
39. Baudrin et al. Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. Front Oncol. 2018 Dec 12;8:621. doi: 10.3389/fonc.2018.00621. eCollection 2018. PMID: 30631754
40. Nojadeh et al. Microsatellite instability in colorectal cancer. EXCLI J. 2018;17:159-168. PMID: 29743854
41. Saeed et al. Microsatellites in Pursuit of Microbial Genome Evolution. Front Microbiol. 2016 Jan 5;6:1462. doi: 10.3389/fmicb.2015.01462. eCollection 2015. PMID: 26779133
42. Boland et al. A National Cancer Institute Workshop on Microsatellite Instability for cancer detection and familial predisposition: development of international criteria for the determination of microsatellite instability in colorectal cancer. Cancer Res. 1998 Nov 15;58(22):5248-57. PMID: 9823339
43. Halford et al. Low-level microsatellite instability occurs in most colorectal cancers and is a nonrandomly distributed quantitative trait. Cancer Res. 2002 Jan 1;62(1):53-7. PMID: 11782358
44. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. Carcinogenesis. 2008 Apr;29(4):673-80. PMID: 17942460
45. NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2025]
46. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. Dis. Markers. 2004;20(4-5):199-206. PMID: 15528785
47. Lee et al. Low-Level Microsatellite Instability as a Potential Prognostic Factor in Sporadic Colorectal Cancer. Medicine (Baltimore). 2015 Dec;94(50):e2260. PMID: 26683947
48. Latham et al. Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. J. Clin. Oncol. 2019 Feb 1;37(4):286-295. PMID: 30376427
49. Cortes-Ciriano et al. A molecular portrait of microsatellite instability across multiple cancers. Nat Commun. 2017 Jun 6;8:15180. doi: 10.1038/ncomms15180. PMID: 28585546
50. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. JCO Precis Oncol. 2017;2017. PMID: 29850653
51. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s172lbl.pdf
52. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125554s127lbl.pdf
53. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
54. NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2025]
55. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s132lbl.pdf
56. Ribic et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. N. Engl. J. Med. 2003 Jul 17;349(3):247-57. PMID: 12867608
57. Klingbiel et al. Prognosis of stage II and III colon cancer treated with adjuvant 5-fluorouracil or FOLFIRI in relation to microsatellite status: results of the PETACC-3 trial. Ann. Oncol. 2015 Jan;26(1):126-32. PMID: 25361982
58. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. J Pers Med. 2019 Jan 16;9(1). PMID: 30654522

References (continued)

59. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. Cancer Treat. Rev. 2019 Jun;76:22-32. PMID: 31079031
60. Ouzzine et al. The UDP-glucuronosyltransferases of the blood-brain barrier: their role in drug metabolism and detoxication. Front Cell Neurosci. 2014;8:349. PMID: 25389387
61. Nagar et al. Uridine diphosphoglucuronosyltransferase pharmacogenetics and cancer. Oncogene. 2006 Mar 13;25(11):1659-72. PMID: 16550166
62. Allain et al. Emerging roles for UDP-glucuronosyltransferases in drug resistance and cancer progression. Br J Cancer. 2020 Apr;122(9):1277-1287. PMID: 32047295
63. Izumi et al. Expression of UDP-glucuronosyltransferase 1A in bladder cancer: association with prognosis and regulation by estrogen. Mol Carcinog. 2014 Apr;53(4):314-24. PMID: 23143693
64. Sundararaghavan et al. Glucuronidation and UGT isozymes in bladder: new targets for the treatment of uroepithelial carcinomas?. Oncotarget. 2017 Jan 10;8(2):3640-3648. PMID: 27690298
65. Lu et al. Drug-Metabolizing Activity, Protein and Gene Expression of UDP-Glucuronosyltransferases Are Significantly Altered in Hepatocellular Carcinoma Patients. PLoS One. 2015;10(5):e0127524. PMID: 26010150
66. Karas et al. JCO Oncol Pract. 2021 Dec 3:OP2100624. PMID: 34860573