ThermoFisher SCIENTIFIC

Connecting patients everywhere to precision oncology

Oncomine Dx Express Test (CE-IVD)

The Oncomine Dx Express Test—a true end-to-end solution, from specimen to clinical report

The Ion Torrent™ Oncomine™ Dx Express Test enables laboratories to deliver clinically relevant genomic profiling in as little as 24 hours to aid clinicians in making timely therapy decisions.

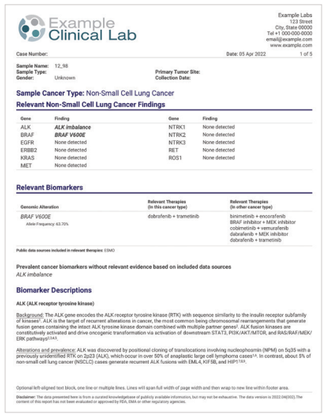
This automated, true end-to-end solution—from a single supplier, with only 20 minutes of hands-on time—can be implemented in a broad spectrum of clinical labs, even without next-generation sequencing (NGS) expertise. The Ion Torrent™ Oncomine™ Reporter Dx reporting software provides biomarker results matched to approved therapies, guidelines, clinical trials, and peer-reviewed literature to aid clinicians in therapy management of cancer patients.

The Oncomine Dx Express Test enables:

Guideline recommendations—Content covers gene targets recommended by professional guidelines for multiple solid tumors including substitutions, insertions and deletions (indels), copy number variants, and fusions and splicing variants across 46 genes, such as *EGFR, BRAF, KRAS, ERBB2, MET, ALK, ROS1, RET,* and *NTRK1/2/3*, among others.

Efficient use of samples—Requiring only 10 ng of DNA and RNA extracted from as little as two 5-micron FFPE slides, results can be generated from limited tissue and small biopsies. Plasma from liquid biopsy provides an additional sample type.

Fast results—Results can be generated in as little as 24 hours, enabling integration of molecular and IHC results into one complete report to aid clinicians in making timely therapy decisions.


Example Clinical Lab

Example Labs
123 Street
City, State 00000
Tel +1 000-000-0000
email@example.com
www.example.com

Case Number: Date: 05 Apr 2022 1 of 5

Sample Name: 12_98
Sample Type:
Gender: Unknown

Primary Tumor Site:
Collection Date:

Sample Cancer Type: Non-Small Cell Lung Cancer

Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	***ALK imbalance***	NTRK1	None detected
BRAF	***BRAF V600E***	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Relevant Biomarkers

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)
BRAF V600E Allele Frequency: 43.70%	dabrafenib + trametinib	binimetinib + encorafenib cobimetinib + BRAF inhibitor cobimetinib + vemurafenib dabrafenib + MEK inhibitor dabrafenib + trametinib

Public data sources included in relevant therapies: ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources
ALK imbalance

Biomarker Descriptions

ALK (ALK receptor tyrosine kinase)

Background: The *ALK* gene encodes the ALK receptor tyrosine kinase (RTK) with sequence similarity to the insulin receptor subfamily of kinases[1]. ALK is the target of recurrent alterations in cancer, the most common being chromosomal rearrangements that generate fusion genes containing the intact ALK tyrosine kinase domain combined with multiple partner genes[2]. *ALK* fusion kinases are oncogenic, constitutively activated and drive oncogenic transformation via activation of downstream STAT3, PI3K/AKT/MTOR, and RAS/RAF/MEK/ERK pathways[3,4,5].

Alterations and prevalence: ALK was discovered by positional cloning of translocations involving nucleophosmin (NPM) on 5q35 with a previously unidentified RTK on 2p23 (ALK), which occur in over 50% of anaplastic large cell lymphoma cases[1,6]. In contrast, about 5% of non-small-cell lung cancer (NSCLC) cases generate recurrent *ALK* fusions with EML4, KIF5B, and HIP1[7,8].

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Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2022.04(ESO).The content of this report has not been evaluated or approved by FDA, EMA or other regulatory agencies.

Oncomine Reporter Dx

Oncomine Reporter Dx is a reporting software that matches genomic variant information with relevant therapies, guidelines, clinical trials, and peer-reviewed literature. It is an intuitive software that produces a clear and concise biomarker report without requiring specialized bioinformatics expertise.

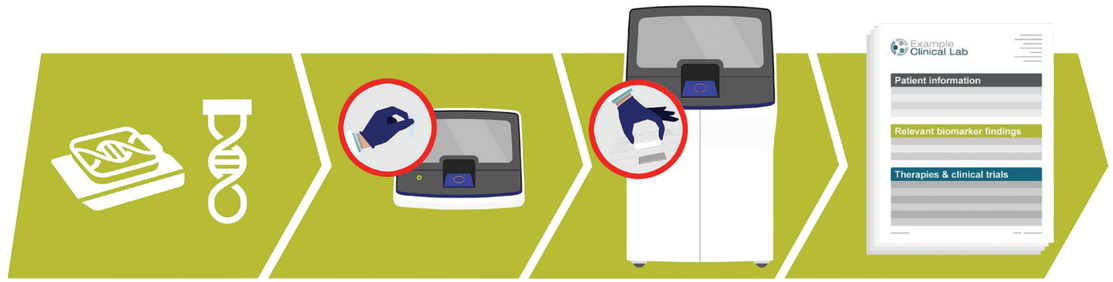
A true end-to-end solution from one supplier

The Ion Torrent™ Genexus™ Dx System automates the NGS workflow, from the patient sample to report, and delivers results in as little as 24 hours with just two user touch points.*

With automated library preparation, sequencing, and analysis involving 20 minutes of hands-on time, the Oncomine Dx Express Test on the Genexus Dx System helps reduce laboratory staff burden and the potential for human errors.

The intuitive *in vitro* diagnostic (IVD) software facilitates tracking sample information through the workflow. On-instrument analysis and local reporting alleviate the need for specialized bioinformatics expertise.

* Timing varies by number of samples and sample type.



Patient sample | **Nucleic acid extraction** | **Library preparation, sequencing, and analysis** | **Report**

Table 1. Oncomine Dx Express Test gene list

Deletions, insertions, and substitutions			Copy number alterations	Fusions and splicing variants
AKT1	*ESR1*	*MAP2K2*	***AR***	*ALK*
AKT2	*FGFR1*	*MET*	***EGFR***	***AR***
AKT3	*FRFR2*	*NRAS*	***ERBB2***	***BRAF***
ALK	*FRFR3*	*NTRK1*	***ERBB3***	***ESR1***
AR	*FGFR4*	*NTRK2*	***FRFR1***	***FGFR1***
ARAF	*FLT3*	*NTRK3*	***FGFR2***	***FGFR2***
BRAF	*GNAS*	*PDGFRA*	***FGFR3***	***FGFR3***
CDK4	*HRAS*	*PIK3CA*	***KRAS***	*MET*
CHEK2	*IDH1*	*PTEN*	***MET***	***NRG1***
CTNNB1	*IDH2*	*RAF1*	***PIK3CA***	*NTRK1*
EGFR	*KEAP1*	*RET*		*NTRK2*
ERBB2	*KIT*	*ROS1*		*NTRK3*
ERBB3	*KRAS*	*STK11*		***NUTM1***
ERBB4	*MAP2K1*	*TP53*		*RET*
				ROS1
				RSPO2
				RSPO3

Genes in bold are only available for FFPE.

Oncomine Dx Express Test performance—FFPE samples

Extensive performance studies were conducted to establish performance characteristics of the Oncomine Dx Express Test for FFPE samples. For complete studies and results, refer to the Oncomine Dx Express Test User Guide.

Analytical accuracy study

The analytical accuracy was evaluated with 151 clinical FFPE samples from 6 cancer types (breast cancer, colorectal cancer (CRC), glioma, melanoma, non-small cell lung cancer (NSCLC), and thyroid cancer). The variants evaluated included single nucleotide variants (SNVs), insertions and deletions (indels), copy number variants (CNVs), and fusions (Table 2). The concordance evaluation study included:

- **75 variant-negative and 76 variant-positive specimens**
- **2 sites**
- **2 NGS-based orthogonal reference assays: Reference Assay 1 and Reference Assay 2**

The positive percent agreement (PPA) and negative percent agreement (NPA) were defined as the proportion of variant-positive and variant-negative specimens, respectively, as determined by the reference methods that were also determined by the Oncomine Dx Express Test.

Analytical accuracy results are summarized in Table 3.

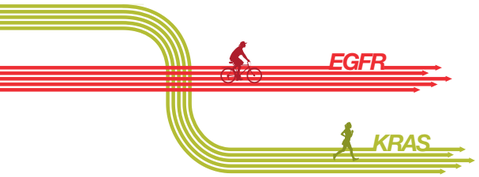


Table 2. Variant description for FFPE sample

Indication	Gene	Variant	Variant type
Breast	*PIK3CA*	E545 or H1047	SNV
	PIK3CA	Amplification	CNV
	ERBB2	Amplification	CNV
	NTRK	*NTRK3*	Fusion
CRC	*KRAS*	G12C	SNV
	BRAF	V600K or V600E	SNV
	NTRK	*NTRK1*	Fusion
NSCLC	*EGFR*	L858R	SNV
	EGFR	T790M	SNV
	BRAF	V600E	SNV
	KRAS	G12C	SNV
	EGFR	Exon 19 deletion	Indel
	EGFR	Exon 20 insertion	Indel
	ERBB2	Exon 20 insertion	Indel
	ALK	Fusion	Fusion
	ROS1	Fusion	Fusion
	RET	Fusion	Fusion
	MET	MET Exon 14 skipping	Alt splice form
	MET	Amplification	CNV
Melanoma	*BRAF*	V600K or V600E	SNV
	NTRK	*NTRK1*	Fusion
Thyroid	*BRAF*	V600K or V600E	SNV
	RET	Mutations	SNV
	RET	Fusion	Fusion
	NTRK	*NTRK1* and *NTRK3*	Fusion
Glioma	*IDH1*	R132	SNV
	IDH2	R172	SNV

Table 3. Oncomine Dx Express Test—concordance

	Variant type	Reference assay	Percent agreement (%)	95% CI
PPA	SNVs and indels	1	93.44% (57/61)	(84.05%, 98.18%)
NPA	SNVs and indels	1	99.99% (43,026/43,029)	(99.98%, 100.00%)
PPA	CNVs	2	100.00% (27/27)	(87.23%, 100.00%)
NPA	CNVs	2	99.30% (283/285)	(97.49%, 99.91%)
PPA	Fusions	1	91.67% (11/12)	(61.52%, 99.79%)
NPA	Fusions	1	99.98% (11,642/11,644)	(99.94%, 100.00%)

Limit of blank study

The limit of blank was established by profiling 30 clinical FFPE samples confirmed to be variant-negative by a reference method. The study included:

- **2 replicates per sample**
- **2 reagent lots**
- **11 tissue types: bladder, brain, breast, bile duct, colon, endometrium, lung, pancreas, prostate, skin, and thyroid**

For all 30 samples, the false-positive rate of the test was determined to be 0.75% for SNVs, 0% for indels, 0% for CNVs, and 0% for fusions. By definition of the Clinical and Laboratory Standards Institute (CLSI) EP17-A2, the limit of blank is zero.

Limit of detection (LoD) study

The LoD was evaluated with 20 representative SNVs, indels, CNVs, and RNA fusions detected by the Oncomine Dx Express Test in clinical FFPE samples. The LoD is defined as the lowest variant level that can be detected at least 95% of the time.

Clinical specimens representing 6 cancer types (breast cancer, colorectal cancer, glioma, NSCLC, melanoma, and thyroid cancer) were used as the source of DNA and RNA. Variant-containing specimens were blended with wild-type samples, and the study included:

- **6 titration levels**
- **2 reagent lots**
- **10 replicates per sample blend**

Based on a representative approach, the LoDs ranged from:

- **3.07% to 6.48% allelic frequencies for SNVs and indels (mean = 4.29% allelic frequency)**
- **4.91 to 5.32 copies for CNVs**
- **5.27 to 12.35 molecular counts (median = 8.85 molecular counts) and 7.87 to 207.5 reads for fusions**

Precision study

The repeatability and reproducibility were evaluated using 20 representative DNA variants and RNA fusions in FFPE samples from 6 cancer types: breast cancer, colorectal cancer, glioma, melanoma, NSCLC, and thyroid cancer.

Three sites, with 2 operators and instruments per site, were used for the study. DNA and RNA was extracted from clinical FFPE samples, then blended with wild-type DNA or RNA into 7 DNA blends and 7 RNA blends. Two levels per blend were generated and distributed to sites and operators for testing.

The mean call rates excluding no-calls were 99.23%, 100%, and, 99.69% for variant-positive SNVs/indels, CNVs, and fusions, respectively. The mean call rates excluding no-calls was 100% for wild-type DNA (negative-calls) and wild-type RNA.

For details, see the Oncomine Dx Express Test User Guide.

Oncomine Dx Express Test performance—plasma samples

Extensive performance studies were conducted to establish performance characteristics of the Oncomine Dx Express Test for cell-free total nucleic acid (cfTNA). For complete studies and results, refer to the Oncomine Dx Express Test User Guide.

Analytical accuracy study

The analytical accuracy of the Oncomine Dx Express Test for plasma was evaluated with 80 plasma samples from NSCLC comprising 40 variant-positive and 40 variant-negative samples (Table 4). The concordance study was performed at two sites that received an identical set of samples. One site used the Oncomine Dx Express Test, and the second site used an NGS-based reference assay.

The PPA and NPA were defined as the proportion of variant-positive and variant-negative specimens, respectively, as determined by the reference method and the Oncomine Dx Express Test.

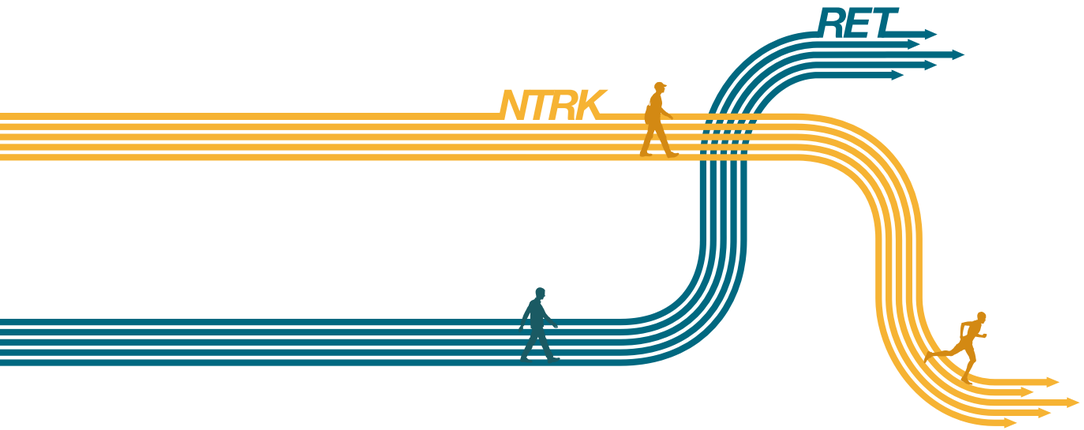
Analytical accuracy results are summarized in Table 5.

Table 4. Variant description for plasma samples

Gene	Variant	Variant type
ERBB2	SNV	SNV
EGFR	L858R	SNV
EGFR	T790M	SNV
BRAF	V600E	SNV
KRAS	G12C	SNV
EGFR	Exon 19 deletion	Indel
EGFR	Exon 20 insertion	Indel
ERBB2	Exon 20 insertion	Indel
ALK	Fusion	Fusion
ROS1	Fusion	Fusion
RET	Fusion	Fusion
MET	Fusion	Fusion

Table 5. Oncomine Dx Express Test—concordance

	Alteration type	Percent agreement (%)	95% CI
PPA	SNVs and fusions	100.00% (51/51)	(93.02%, 100.00%)
NPA	SNVs and fusions	99.98% (56,272/56,282)	(99.97%, 99.99%)



Limit of blank study

The limit of blank was established by profiling cfTNA extracted from 30 blood plasma samples from healthy donors confirmed to be variant-negative by a reference method. The study included:

- **2 replicates per sample**
- **2 reagent lots**

For all 30 samples, the false positive rate was determined to be 0.20% for SNVs, 0% for indels, and 0% for fusions. By definition of CLSI EP17-A2, the limit of blank is zero.

Limit of detection (LoD) study

The LoD was evaluated with 11 representative SNVs, indels, CNVs, and RNA fusions detected by the Oncomine Dx Express Test in clinical plasma samples. The LoD is defined as the lowest variant level that can be detected at least 95% of the time.
The study included:

- **6 titration levels**
- **2 reagent lots**
- **10 replicates per sample blend**
- **2 cfTNA input levels: 5 ng and 30 ng**

Based on a representative variant approach, the LoDs for SNVs and indels range from 0.65% to 1.82% allelic frequency (mean = 1.9% allelic frequency) for the 5 ng input level. The LoDs for SNVs and indels at the 30 ng input level ranged from 0.31% to 0.42% allelic frequency (mean = 0.36% allelic frequency).

The LoDs for RNA fusions at the 5 ng input level ranged from 9.9 to 19.6 molecular counts (median = 14.3 molecular counts). The LoDs for RNA fusions at the 30 ng input level ranged from 6.4 to 8.0 molecular counts (median = 7.5 molecular counts).

Precision study

The repeatability and reproducibility were evaluated using contrived cfTNA plasma samples prepared by blending cfTNA extracted from variant-positive cell lines and cfTNA from healthy donor plasma.

Three sites, with 2 operators and instruments per site, were used for the study. Site 1 had 4 instruments, and sites 2 and 3 had 2 instruments each.

The mean call rates excluding no-calls were 99.86%, and 99.25% for variant-positive SNVs/indels and fusions, respectively. The mean call rates excluding no-calls was 100% for wild-type DNA (negative-calls) and wild-type RNA.

For details, see the Oncomine Dx Express Test User Guide.

Oncomine Dx Express Test

The following reagents and supplies are available for order as needed. For detailed contents and storage information, see the Oncomine Dx Express Test User Guide.

Ordering information

Product	Cat. No.
Genexus Dx Integrated Sequencer	A53579
Genexus Dx Barcodes 1-32 HD	A54104
Genexus Dx Pipette Tips	A54105
Genexus Dx Library Strips 1 and 2-HD	A50430
Genexus Dx GX5 Chip and Genexus Coupler	A54106
Genexus Dx Templating Strips 3-GX5 and 4	A50431
Genexus Dx Sequencing Kit	A50432
Oncomine Dx Express Test Panel	A54103
Oncomine Dx Express Test FFPE DNA and RNA Control Kit	A52167
Oncomine Dx Express Test Plasma cfTNA Control Kit	A52168
Oncomine Reporter Dx, one-year license	A54966

Learn more at **thermofisher.com/oncomine-dxexpress**

Abbreviated Intended Use: The Oncomine Dx Express Test is a qualitative *in vitro* diagnostic test that uses targeted next-generation sequencing (NGS) technology, the Ion Torrent Genexus Dx System to detect deletions, insertions, substitutions and copy number gain present in 42 genes and fusions in 18 genes from DNA and RNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples. Oncomine Dx Express Test also detects deletions, insertions, substitutions in 42 genes and fusions in 7 genes from cfTNA extracted from plasma samples. The Oncomine Dx Express Test is intended to provide clinically relevant tumor mutation profiling information to be used by qualified health care professionals in accordance with professional guidelines as an aid in therapy management of cancer patients with solid malignant neoplasms using FFPE samples and as an aid in therapy management of cancer patients with non-small cell lung cancer using plasma samples. It is not conclusive or prescriptive for labeled use of any specific therapeutic product.