



Oncology

Accelerating the future of liquid biopsy

Ultra-low mutation detection solutions
from sample prep to data analysis

The exciting potential of liquid biopsy in oncology research

Currently, the most common strategy for characterizing the genetic makeup of a tumor is the extraction, or biopsy, of a sample of the affected tissue. **Tissue biopsies**, however, can be painful, risky, and, in some cases, not feasible when a tumor is difficult to access. Furthermore, tissue biopsies are not a viable monitoring technique as they cannot be repeated, and they may not be representative of the entire tumor due to tumor heterogeneity.

Liquid biopsy is an emerging area of clinical research, particularly in the context of cancer. As a minimally invasive complementary or alternative approach to tissue biopsies, liquid biopsies are less risky, painful, and costly, and are increasingly being used to analyze biomarkers in liquid samples, such as blood.

Recent studies have shown the utility of liquid biopsies for:



Enhancing understanding of tumorigenesis, metastasis, and therapy resistance



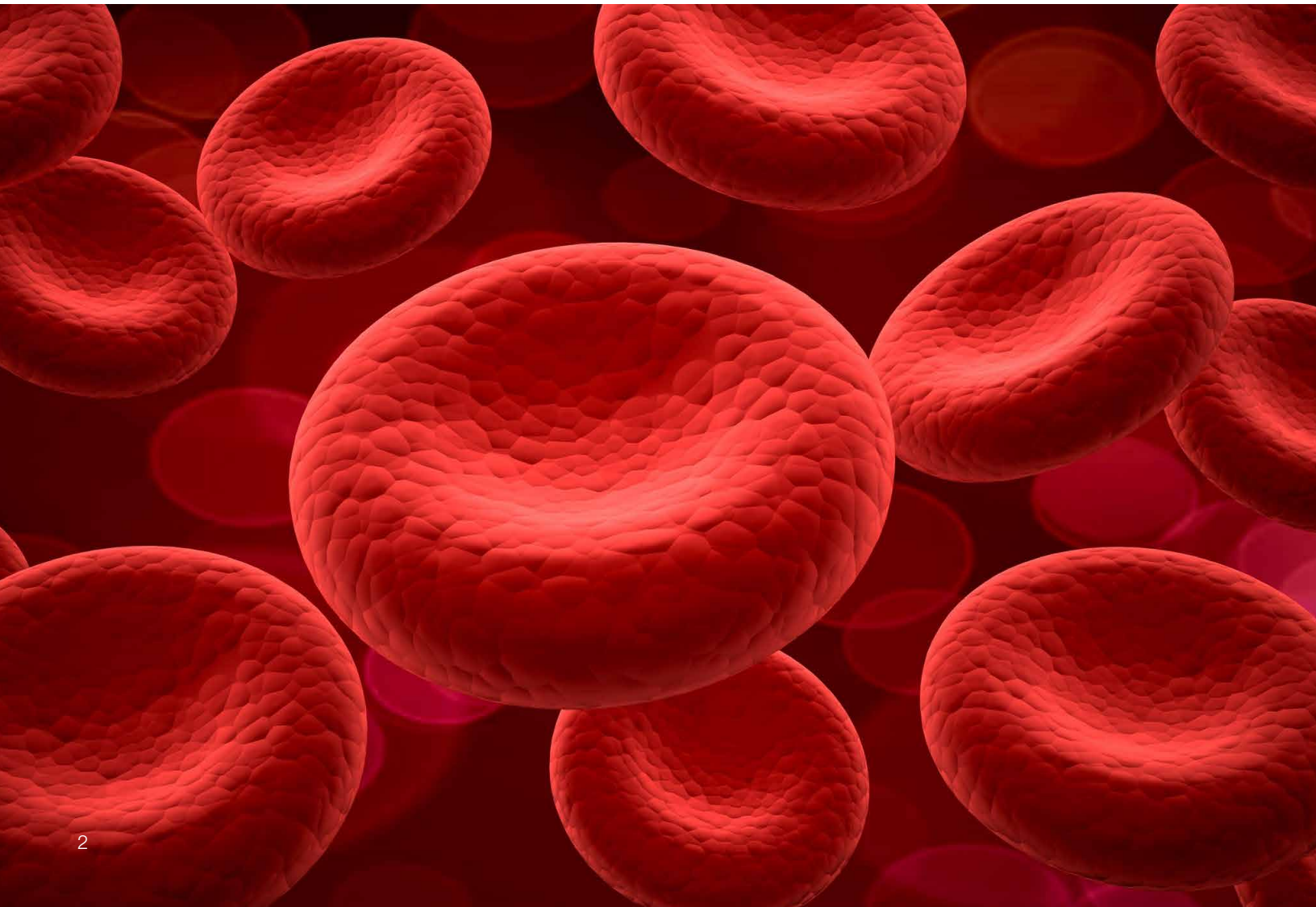
Detection of cancer at early stages when treatment may be most successful



Monitoring of cancer development, disease progression, and recurrence



Tracking response or resistance during and after treatment to allow for adjustments in real time



Unlock the potential in your liquid biopsy samples

Cell-free nucleic acid isolation kits



Liquid biopsies most often utilize cell-free DNA (cfDNA) that is derived from both normal and cancerous cells. The tumor-only supply of DNA in the bloodstream is more commonly referred to as circulating tumor DNA (ctDNA), which is loaded with information about a tumor that would otherwise be difficult to access. The first step in obtaining this valuable information is efficient nucleic acid isolation that specifically recovers the fragmented cfDNA while leaving the larger DNA molecules behind. This aspect of enrichment for the cfDNA portion of the total nucleic acid ensures that the shorter ctDNA is concentrated and ready for downstream analysis using real-time PCR (qPCR), digital PCR (dPCR), or next-generation sequencing (NGS).

The Ion Torrent™ Genexus™ Cell-Free Total Nucleic Acid Purification Kit for the Ion Torrent™ Genexus™ Purification System is a set of consumables that enables automated extraction and quantitation of TNA from cell-free plasma, isolated from whole blood.

Applied Biosystems™ MagMAX™ Cell-Free DNA and Cell-Free Total Nucleic Acid Isolation Kits use magnetic bead-based technology to purify enriched cfDNA or cell-free total nucleic acids (including cfRNA), without genomic DNA (gDNA) contamination from plasma, serum, or urine samples.

Genexus Cell-Free Total Nucleic Acid Purification Kit

- Achieve consistent extraction results with MagMAX technology
- Reduce hands-on setup time using prefilled consumables
- Maximize efficiency with automated quantitation using Invitrogen™ Qubit™ devices
- Experience rapid turnaround times of as little as two hours from lysate to quantified nucleic acid

MagMAX Cell-Free DNA Isolation Kit

- Yields cfDNA with no gDNA contamination
- Flexible sample input from 500 µL to 10 mL
- Elution volumes ranging from 15–100 µL
- Phenol-free extraction

MagMAX Cell-Free Total Nucleic Acid Isolation Kit

- Purify free-circulating DNA, RNA, and miRNA with no gDNA contamination
- Flexible sample input from 1–6 mL
- Elution volumes ranging from 15–60 µL
- Phenol-free extraction

Using NGS and dPCR together for improved liquid biopsy analysis

Liquid biopsy analysis requires highly sensitive assays that can detect relatively small quantities of highly fragmented tumor-derived DNA and RNA found in blood. Two of the most common techniques are NGS and dPCR. While each can be an ideal solution under certain circumstances, recent studies suggest they often work better together—the wide-angle view provided by NGS combined with the zoomed-in precise detection of dPCR provides a more complete picture of the cancer genome.

The scientists at Thermo Fisher Scientific are committed to developing high-quality liquid biopsy assays utilizing both dPCR and targeted NGS technologies to enable the identification and monitoring of cancer driver and resistance mutations, as well as recurrence detection. Through the powerful combination of targeted NGS assays, which provide comprehensive detection of cancer-related mutations; and dPCR assays, which offer identification of a targeted set of mutations, liquid biopsies may soon become the standard in cancer management.

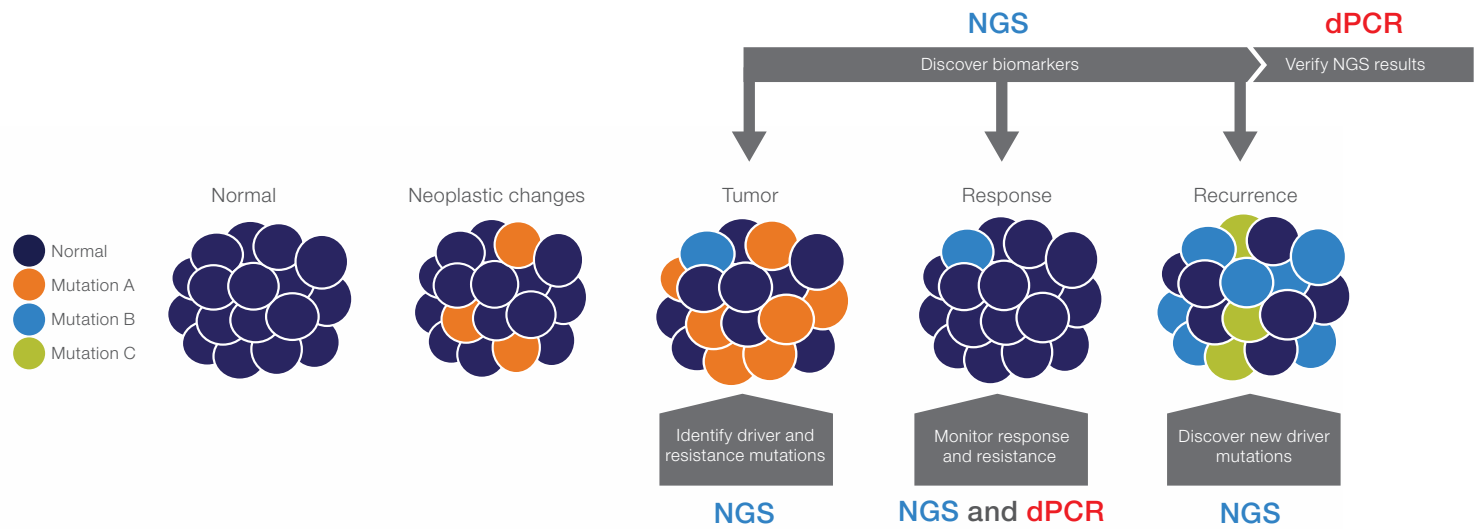


NGS and dPCR liquid biopsy solutions

For discovery and the study of resistance and recurrence

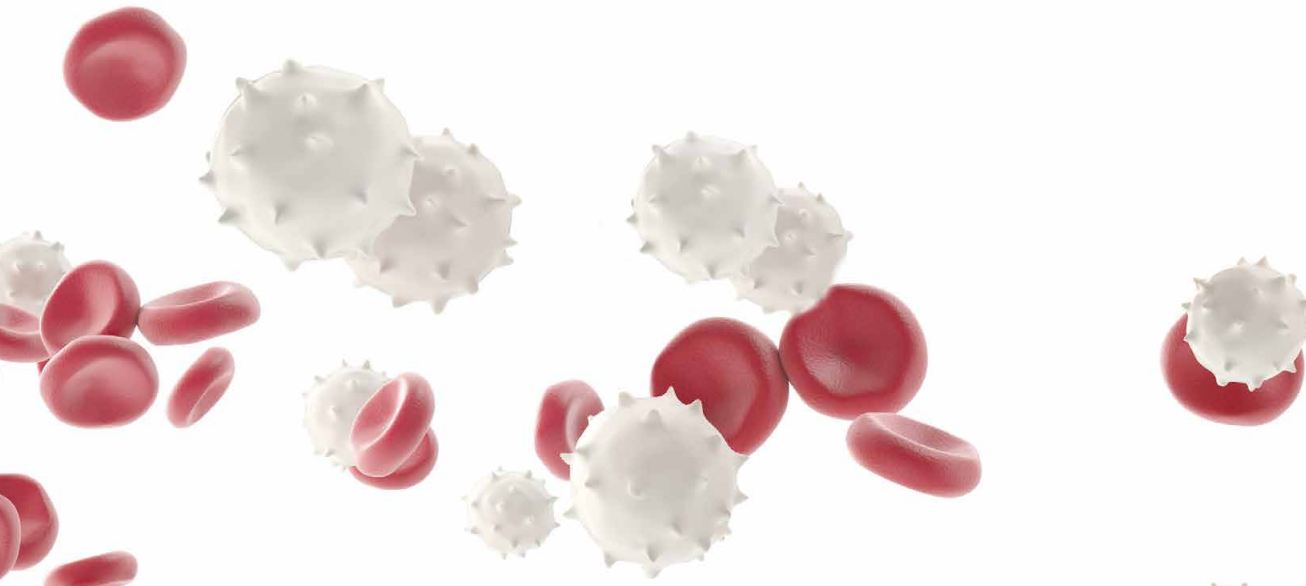
Biomarker discovery and verification

Discovery	Verification
Analyze cfDNA and cell-free RNA (cfRNA) with ultrasensitive, fully customizable panels or predesigned NGS assays to discover potential cancer biomarkers	Orthogonally verify biomarker discovery results using dPCR assays



Dynamic monitoring of tumor progression

Identify driver and resistance mutations	Monitor response and resistance	Discover new driver mutations at recurrence
Analyze cfDNA and cfRNA to identify primary cancer driver and resistance mutations using targeted NGS solutions	Study response and resistance by monitoring cancer driver and resistance mutations using either dPCR (for few mutations) or NGS assays (for many mutations)	Identify new potential cancer driver and resistance mutations related to recurrence using targeted NGS solutions



The power of multibiomarker NGS solutions for liquid biopsy analysis



Ion AmpliSeq HD technology and Oncomine cell-free nucleic acid assays

Ion AmpliSeq™ HD technology uses unique molecular tags, or UMTs, to deliver results with ultrahigh sensitivity. With Ion AmpliSeq HD technology, you have the power to design your own custom gene panels and find variants at very low limits of detection.

- **Low limit of detection**—variant detection down to 0.1%
- **Easy and convenient customization**—flexible panel customization using Ion AmpliSeq™ Designer software
- **Complete 2-day workflow**—fast, targeted NGS workflow from sample to data

Ion Torrent™ Oncomine™ cell-free nucleic acid assays are predesigned, multibiomarker NGS assays that enable the identification and monitoring of cancer driver and resistance mutations from cfDNA and cfRNA simultaneously, down to 0.1% allelic frequency. The high-value gene content includes targets selected and verified by the OncoNetwork consortium and clinical researchers around the world.

- **Optimized content**—SNVs, indels, CNVs, and fusions
- **Low limit of detection**—variant detection down to 0.1%
- **Flexible input amounts**—results enabled from one tube of blood
- **Streamlined workflow**—complete NGS workflow, from sample to data, in just 1–3 days

	Ion Torrent Genexus System	Ion GeneStudio™ S5 System + Ion Chef™ System
		
Assays	Oncomine Precision Assay (GX)	Oncomine cell-free NGS assays
Assay options	Pan-cancer (1)	Tumor type-specific assays (5), pan-cancer (1)
Workflow description	Go from specimen to report with only two user touchpoints and 10 minutes of hands-on time per instrument	Nucleic acid sample-to-report workflow
Turnaround time	1 day	2–3 days
Sample throughput	Up to 4 ctDNA samples and 1 NTC per run on the Ion Torrent GX5™ Chip	<ul style="list-style-type: none"> • Up to 8 pan-cancer samples (ctDNA + RNA) on an Ion 550™ Chip • Up to 24 lung samples (ctDNA + RNA) on an Ion 540 Chip • Up to 20 breast samples (ctDNA v2) on an Ion 540 Chip • Up to 24 colon samples (ctDNA) on an Ion 540 Chip

Tumor-specific assays									
Lung					Breast			Colon	
Oncomine Lung cfDNA Assay		Oncomine Lung Cell-Free Total Nucleic Acid Assay			Oncomine Breast cfDNA Assay v2			Oncomine Colon cfDNA Assay	
ALK	MET	ALK	MET		AKT1	FBXW7	AKT1	ERBB2	NRAS
BRAF	NRAS	BRAF	NRAS		CCND1	FGFR1	APC	FBXW7	PIK3CA
EGFR	PIK3CA	EGFR	PIK3CA		EGFR	KRAS	BRAF	GNAS	SMAD4
ERBB2	ROS1	ERBB2	RET		ERBB2	PIK3CA	CTNNB1	KRAS	TP53
KRAS	TP53	KRAS	ROS1		ERBB3	SF3B1	EGFR	MAP2K1	
MAP2K1		MAP2K1	TP53		ESR1	TP53			

Pan-cancer									
Oncomine Precision Assay (GX)									
DNA hotspots					CNVs		Inter-genetic fusions		Intra-genetic fusions
AKT1	CHEK2	FGFR3	KIT	NTRK3	ALK	FGFR1	ALK	NTRK1	AR
AKT2	CTNNB1	FGFR4	KRAS	PDGFRA	AR	FGFR2	BRAF	NTRK2	EGFR
AKT3	EGFR	FLT3	MAP2K1	PIK3CA	CD274	FGFR3	ESR1	NTRK3	MET
ALK	ERBB2	GNA11	MAP2K2	PTEN	CDKN2A	KRAS	FGFR1	NUTM1	
AR	ERBB3	GNAQ	MET	RAF1	EGFR	MET	FGFR2	RET	
ARAF	ERBB4	GNAS	MTOR	RET	ERBB2	PIK3CA	FGFR3	ROS1	
BRAF	ESR1	HRAS	NRAS	ROS1	ERBB3	PTEN	MET	RSPO2	
CDK4	FGFR1	IDH1	NTRK1	SMO			NRG1	RSPO3	
CDKN2A	FGFR2	IDH2	NTRK2	TP53					

Oncomine Pan-Cancer Cell-Free Assay										
Hotspot genes					Tumor suppressor genes		CNV genes		Gene fusions	
AKT1	EGFR	FLT3	KRAS	PDGFRA	APC		CCND1	ERBB2	ALK	FGFR3
ALK	ERBB2	GNA11	MAP2K1	PIK3CA	FBXW7		CCND2	FGFR1	BRAF	MET
AR	ERBB3	GNAQ	MAP2K2	RAF1	PTEN		CCND3	FGFR2	ERG	NTRK1
ARAF	ESR1	GNAS	MET	RET	TP53		CDK4	FGFR3	ETV1	NTRK3
BRAF	FGFR1	HRAS	MTOR	ROS1			CDK6	MET	FGFR1	RET
CHEK2	FGFR2	IDH1	NRAS	SF3B1			EGFR	MYC	FGFR2	ROS1
CTNNB1	FGFR3	IDH2	NTRK1	SMAD4						
DDR2	FGFR4	KIT	NTRK3	SMO						

Content in Oncomine cell-free nucleic acid assays. Select from five focused, tumor-specific assays predesigned with key gene content, or between two pan-cancer assays. The Oncomine Precision Assay (GX) runs on the Genexus System, while all other assays listed above run on the Ion GeneStudio S5 system.

Use dPCR to study response and resistance

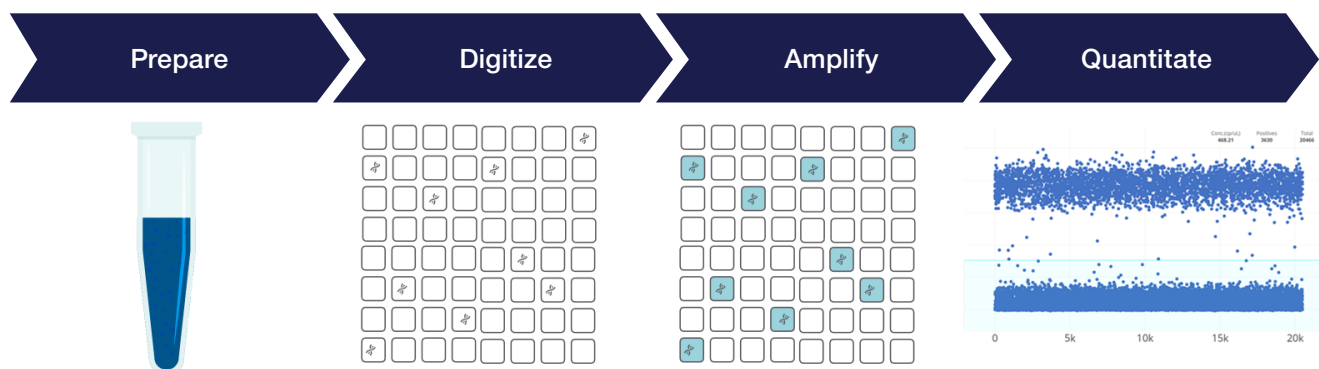
Absolute Q™ Liquid Biopsy digital PCR assays

Applied Biosystems Absolute Q Liquid Biopsy dPCR assays provide a precise, cost-effective, and rapid method for the detection and quantification of common cancer driver and resistance mutations, making them ideal for the study of response and resistance. They have been wet lab-verified and are guaranteed* to perform on the Applied Biosystems QuantStudio Absolute Q Digital PCR System.



- **Optimized dPCR performance**—wet lab-verified Absolute Q assays targeting common cancer mutations, including markers for non-small cell lung cancer (NSCLC), breast cancer, and colorectal cancer (CRC)
- **Highly sensitive**—detect and quantify rare mutant prevalence down to 0.1%
- **Cost-effective, single-tube assay**—single-tube format includes both wild-type and mutant alleles
- **Guaranteed performance**—backed by the Absolute Q assay performance guarantee*
- **Streamlined analysis**—enhanced bioinformatics tools for better quantification of rare mutations

* Terms and conditions apply. To see full details of the guarantee, go to thermofisher.com/absoluteqassayguarantee.



Absolute Q Liquid Biopsy dPCR assays enable absolute quantification of target alleles. To perform dPCR, a nucleic acid mixture is digitized into many microchambers, such that some wells receive a target molecule and some do not. Microreactions are subjected to standard PCR before identifying microchambers that have not received target molecules. A standard statistical correction model accounts for microchambers that may have received more than a single target molecule, and a final concentration value is produced.

Find out more at thermofisher.com/digitalpcr

Liquid biopsy solutions

Ordering information

Product	Cat. No.
Sample preparation	
MagMAX Cell-Free Total Nucleic Acid Isolation Kit	A36716
MagMAX Cell-Free DNA Isolation Kit	A29319
Absolute Q DNA Digital PCR Master Mix (5X)	A52490
Genexus Cell-Free Total Nucleic Acid Purification Kit	A45542
Mutation detection	
QuantStudio Absolute Q Digital PCR System	Please inquire
Ion AmpliSeq HD Made-to-Order Panels	Design on ampliseq.com
Oncomine Pan-Cancer Cell-Free Assay	A37664
Oncomine Lung Cell-Free Total Nucleic Acid Research Assay	A35864
Oncomine Lung cfDNA Assay	A31149
Oncomine Breast cfDNA Research Assay v2	A35865
Oncomine Colon cfDNA Assay	A31182
Ion GeneStudio S5 Prime System	A38196
Ion GeneStudio S5 Plus System	A38195
Ion GeneStudio S5 System	A38194
Ion Chef Instrument	4484177
Liquid biopsy solutions on the Genexus System	
Oncomine Precision Assay GX	A46291
Genexus Purification System	A48148
Genexus Integrated Sequencer	A45727
GX5 Chip and Genexus Coupler	A40269
Genexus GX5 Starter Pack-AS	A40279
Data analysis and reporting	
QuantStudio Absolute Q Digital PCR Analysis Software	Access online
Ion Reporter Server System	4487118

Ordering information

Gene	Amino acid mutation	CDS mutation	COSM ID	Cat. No.
Absolute Q Liquid Biopsy digital PCR assays				
BRAF	p.V600K	c.1798_1799delinsAA	473	A52769
	p.V600E	c.1799T>A	476	A52743
EGFR	p.L747_A750delinsP	c.2239_2248delinsC	12382	A52777
	p.E746_S752delinsV	c.2237_2255delinsT	12384	A52787
	p.L747_P753delinsQ	c.2239_2258delinsCA	12387	A52795
	p.E746_T751del	c.2236_2253del	12728	A52796
	p.L861Q	c.2582T>A	6213	A52762
	p.E746_A750del	c.2235_2249del	6223	A52756
	p.L858R	c.2573T>G	6224	A52747
	p.E746_A750del	c.2236_2250del	6225	A52770
	p.G719S	c.2155G>A	6252	A52765
	p.G719C	c.2155G>T	6253	A52797
	p.L747_S752del	c.2239_2256del	6255	A52780
IDH1	p.R132C	c.394C>T	28747	A52772
JAK2	p.V617F	c.1849G>T	12600	A52746
KIT	p.D816V	c.2447A>T	1314	A52757
	p.A146V	c.437C>T	19900	A52781
KRAS	p.G12C	c.34G>T	516	A52750
	p.G12S	c.34G>A	517	A52760
	p.G12V	c.35G>T	520	A52753
	p.G12D	c.35G>A	521	A52745
	p.G13C	c.37G>T	527	A52782
NPM1	p.W288Cfs*12	c.860_863dup	17559	A52751
NRAS	p.G12D	c.35G>A	564	A52766
	p.Q61K	c.181C>A	580	A52771
PIK3CA	p.H1047R	c.3140A>G	775	A52749
	p.H1047L	c.3140A>T	776	A52761
TP53	p.R273H	c.818G>A	10660	A52767
	p.R248Q	c.743G>A	10662	A52768
	p.R273L	c.818G>T	10779	A52779
Custom dPCR assay				Please inquire

 Learn more about our complete suite of liquid biopsy solutions
at thermofisher.com/liquidbiopsy