GOPATH®
LABORATORIES
Global Pathology Services

ONCOTARGET®
SOLID TUMOR

"The Next Generation in Cancer Diagnostics."

OncoTarget® was created specifically for cancer patients. Every patient's cancer is unique, which is why discovering what makes it unique can be essential for determining how best to treat them. Biomarkers give us insight into exactly why a cancer is taking a certain path. They can also predict how a cancer will respond to a specific therapy. By identifying these genetic mutations, we can determine which targeted therapies or immunotherapies have the best chance of treating a specific cancer, making this an essential tool for creating better treatment plans.

OncoTarget®- 125 is changing the way cancer is being treated. This highly-sensitive, NGS-based testing series examines the full exons of 125 well-characterized cancer genes found in solid tumors for point mutations, copy number alterations, microsatellite instability (MSI), and rearrangements. OncoTarget®- 125 provides oncologists with clinically actionable data including a complete list of all identifiable genetic alterations, relevant FDA-approved drugs and current clinical trials specific to a patient's cancer. The genes tested in OncoTarget®- 125 are of highly clinical and biologic importance and are screened using NGS at extremely high coverage.

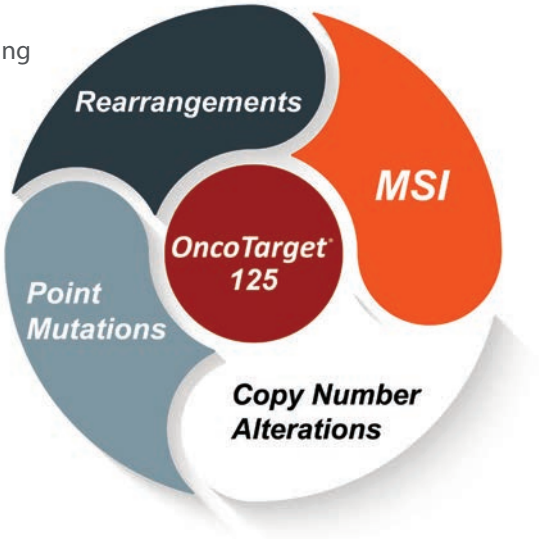


Figure 1. OncoTarget®- 125 Components

OncoTarget®- 48 is a smaller NGS panel created to detect actionable hotspot mutations in the 48 cancer genes most relevant to targeted therapies. With the OncoTarget® series, you'll get results that are right "on target" -- comprehensive, actionable data that will lead to better treatment options for your patients.

Table 1. Genes Evaluated in OncoTarget®- 125

Analysis Type	Genes Evaluated
Full coding analysis in 117 well-characterized cancer genes, as well as ⁺amplification analysis for 41 genes	ABL1 AKT1⁺ ALK⁺ AR⁺ ATM ATRX AXL⁺ BCL2⁺ BRAF⁺ BRCA1⁺ BRCA2 CCND1⁺ CCND2⁺ CCND3⁺ CDK4⁺ CDK6⁺ CDKN2A CHEK2 CREBBP CSF1R⁺ CTNNB1 DDR2 DNMT3A EGFR⁺ EP300 EPHA2 ERBB2⁺ ERBB3⁺ ERBB4 ERCC3 ERG ESR1 EZH2 FANCA FANCD2 FANCG FBXW7 FGFR1⁺ FGFR2⁺ FGFR3⁺ FGFR4⁺ FLT1⁺ FLT3⁺ FLT4⁺ FOXL2 GNA11 GNAQ GNAS HDAC2 HNF1A HRAS IDH1 IDH2 JAK1 JAK2⁺ JAK3 KDR⁺ KEAP1 KIT⁺ KMT2A KRAS⁺ MAP2K1 MAP2K2 MEN1 MET⁺ MLH1 MLH3 MPL MRE11A MSH2 MSH6 MST1R⁺ MTOR MYC⁺ MYCN⁺ MYD88 NBN NF1 NOTCH1 NPM1 NRAS NTRK1⁺ NTRK2⁺ NTRK3⁺ PALB2 PDGFRA⁺ PDGFRB⁺ PIK3CA⁺ PIK3CB⁺ PIK3R1 PMS2 POLD1 POLE PTCH1 PTEN PTPN11 RAD51 RAF1 RARA RB1 RET⁺ RNF43 ROS1⁺ RUNX1⁺ SDHB SMAD4 SMARCB1 SMO SRC STK11 TERT TET2 TP53 TSC1 TSC2 VEGFA⁺ VHL
Rearrangements analyses for selected regions of 29 well-characterized genes	ALK AXL BCR BCL2 BRAF BRCA1 BRCA2 CBFB EGFR ERG ETV1 ETV4 ETV5 ETV6 EWSR1 FGFR1 FGFR2 FGFR3 MYC NTRK1 NTRK2 NTRK3 PDGFRA PDGFRB RAF1 RARA RET ROS1 TMPRSS2
Microsatellite analysis for 5 well-characterized mononucleotide sequences	BAT-25 BAT-26 NR-21 NR-24 MONO-27

Table 2. OncoTarget®- 125 Key Metrics

Regions Analyzed	Coding regions of 125 genes
Sequencing Method	Illumina next-generation sequencing
Bioinformatics	Patented PARE, Digital Karyotyping and VariantDx
Assay Sensitivity	>99%
Assay Specificity	>99%
Sequencing Coverage	1,250x
Turn-around Time	14 days
Sample Requirements	Tumor only or tumor and matched normal* (optimal results)
Sample Types	FFPE (Formalin-Fixed Paraffin-Embedded) Tissue
DNA Input Required	1ug (minimum 50 ng)

*For maximum ability to differentiate somatic mutations from germline mutations, tumor and matched normal samples are recommended.

Figure 2. Depiction of Next-Generation Sequencing Data for Identifiying Sequence Alterations

Our Proprietary Bioinformatics Algorithm on Targeted Cancer Genes:

- Analyses performed in a CLIA-certified laboratory designed for high-complexity clinical testing
- Analysis using validated approach for optimal sensitivity & specificity
- Detailed inspection and curation of tumor-specific mutations by world-class cancer bioinformatics experts
- Identification of mutated genes with biologic or clinical implications in human cancer
- Proprietary Digital Karyotyping analyses for high-resolution annotation of copy number alterations
- Proprietary PARE translocation analysis algorithms to evaluate tumor-specific rearrangements
- Proprietary analysis algorithms to evaluate genes and pathways enriched for alterations
- Proprietary analysis algorithms to identify bona fide sequence changes and to exclude sequence artifacts
- Proprietary sample preparation methods allow for successful preparation of low abundance, poor quality sample DNA

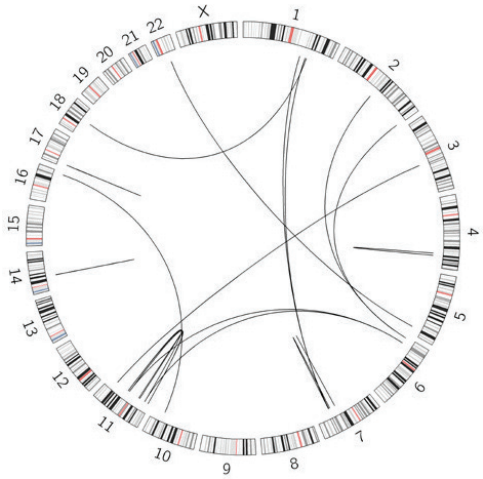


Figure 3. Depiction of NGS Sequencing Data for Identifying Translocations

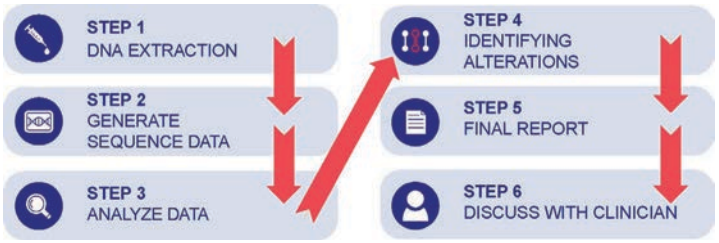
Table 3. Competitor Analysis: OncoTarget®- 125 vs. FoundationOne

	OncoTarget®- 125	FoundationOne
Sensitivity	>99% at 2% mutant allele frequency for base substitutions and indels	99% for base substitutions at ≥5% mutant allele frequency, 98% for indels at ≥10% mutant allele frequency
Specificity (With Normal)	>99% PPV that mutations called are both present and actually somatic in nature (5% MAF)	Analysis using patient normal not offered (No normal)
Use of Patient Normal to Enhance Results	Yes	No

Next-Generation Sequencing Method & Workflow

Patient samples undergo pathologic evaluations by macroscopic selection of tumor regions, from which DNA is extracted. Next-generation sequencing libraries are constructed from tumor and normal DNA, which are sequenced to 1000x average coverage on Illumina next-generation sequencing systems. After base calling and alignment to the human reference genome, the tumor and normal samples are compared to one another to identify tumor-specific sequence mutations, copy number changes, microsatellite instability (MSI) and rearrangements. The data is then compiled into one comprehensive, actionable report.

Figure 4. Workflow of Next-Generation Sequencing and Analyses



Our Comprehensive Analysis Reporting

OncoTarget®- 125 gives you a comprehensive, specific look at your patient's cancer and what factors are driving its growth. If a relevant mutation is found, the gene and its specific alteration will be listed on the report, along with the significance of this alteration in relation to your patient's tumor.

The OncoTarget® - 125 report includes:

- Pathological evaluation of tumor sample
- Tumor-specific sequence alterations (single base and small index alterations)
- Therapeutic, predictive, and prognostic information and references regarding mutated genes and pathways with biological or clinical significance
- Tumor-specific copy number alterations & translocations
- Description of mutated genes and pathways with biologic or clinical implications
- Annotation of tumor-specific alteration consequences
- Data summary statistics (read data and depth distribution across target regions)


FINAL REPORT

OncoTarget™ – 125 Comprehensive NGS Report

GOPATH LABORATORIES

REPORT SUMMARY

RESULTS

DRUG RESPONSE

OncoTarget®- 48 Hotspot Mutation Analysis

We have also created a smaller NGS-based panel that detects hundreds of actionable hotspot mutations in 48 cancer genes most relevant to targeted cancer therapies. OncoTarget®- 48 analyzes >35 kilobases (kb) of targeted genomic regions by 212 amplicons in both FFPE and fresh tissues. Validation study on more than 40 samples from common cancer types demonstrated that OncoTarget®- 48 is a highly-sensitive, specific, and reproducible NGS assay for the detection of somatic mutations of target cancer genes. The assay provides a high level of uniform coverage across the target genomic regions with >500 average base coverage and >100 minimal base coverage. It has 92% sensitivity and 100% specificity with 91% PPV and 99% NPV for detection of mutations within the genomic sequences covered by the gene panel. Value of limit of detection (LOD) of the assay is ≥3% for mutation detections.

Table 4. Genes Evaluated in OncoTarget®- 48

Analysis Type	Genes Evaluated											
Actionable Hotspot Mutations in 48 Cancer Genes	ABL1	AKT1	ALK	APC	ATM	BRAF	CDH1	CDKN2A	CSF1R	CTNNB1	EGFR	ERBB2
	ERBB4	FBXW7	FGFR1	FGFR2	FGFR3	FLT3	GNA11	GNAQ	GNAS	HNF1A	HRAS	IDH1
	JAK2	JAK3	KDR	KIT	KRAS	MET	MLH1	MPL	NOTCH1	NPM1	NRAS	PDGFRA
	PIK3CA	PTEN	PTPN11	RB1	RET	SMAD4	SMARCB1	SMO	SRC	STK11	TP53	VHL

Providing Suggested Targeted Therapies & Clinical Trials

Discovering what mutations are driving a cancer's growth is an essential part of assessing treatment options. Biomarkers can help determine which targeted therapies may or may not be successful in treating a particular type of cancer. Targeted sequencing and mutation analysis obtained from OncoTarget®- 125 may include prognostic indicators, improved disease classification, additional therapies and relevant clinical trials. This data can help physicians make treatment recommendations that target a cancer's specific genetic mutation and thus rule out treatment options that are likely to be ineffective. The OncoTarget®- 125 report includes a list of FDA-approved drugs and clinical trials that are most relevant to your patient's cancer including somatic vs. germline mutations, microsatellite instability testing, and treatment options based on the patient's specific alterations--information that can be essential for making informed treatment decisions and selecting targeted therapies.

Molecular Testing Requisition

GOPATH LABORATORIES

Solid Tumor Requisition

MOLECULAR ONCOLOGY

1351 Barclay Blvd., Buffalo Grove, IL 60089
Tel: 855.467.2849 Fax: 224.588.9941
www.gopathlabs.com

PATIENT INFORMATION (Please print) | ORDERING PHYSICIAN / LAB INFORMATION (Please print)

Name (Last, First) | Facility Name
Address | Name (Last, First)
City, State, Zip | Address
Female ☐ Male ☐ Date of Birth (M/D/Y) | City, State, Zip
SSN# (Optional) | Phone# Fax# E-Mail:
Phone# | Ordering Physician (M/D/Y)
Diagnosis: | NPI#: Treating Physician:
Report Delivery: Fax ☐ E-Mail ☐ Mail ☐ Website Only ☐

CODING INFORMATION | COMMON ICD-10 CODES

Diagnosis Code/ICD-10 Code (Required):
The physician is required to document all applicable ICD codes or descriptions for all tests ordered supporting medical necessity which shall be used in patient plan of care. Example: ICD-10: C73 (Malignant neoplasm of thyroid gland)

Bladder: C67 Breast: C50.411, C50.412, C50.419, C50.811, C50.812, C50.819 Brain: C71.9, C79.31 Colon: C18.2, C18.7, C18.9 GIST: C49 Lung: C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90 Melanoma: C43.9 Ovarian: C56 Prostate: C61 Stomach: C16.9 Thyroid: C73

BILLING INFORMATION (Please provide copy of insurance card) | SPECIMEN INFORMATION (Please provide copy of pathology report)

Primary Insurance: | Pathology Department:
Bill: ☐ Insurance ☐ Medicare ☐ Medicaid ☐ Hospital ☐ Client ☐ Self Pay | Phone#: Fax#:
Secondary Insurance: ☐ Yes ☐ No *If yes, please attach secondary insurance form* | Specimen Block ID/#:
Secondary Insurance: | Collection Date (M/D/Y):
Place of Service: | Type: ☐ Slides ☐ Block | Archived Specimen: ☐
☐ 21 - Inpatient Hospital ☐ 22 - Outpatient Hospital ☐ 24 - Ambulatory Surgery Ctr | Body Site: | Primary ☐ Metastatic ☐

MOLECULAR ONCOLOGY - SOLID TUMOR

IHC: ☐ Global (With Interpretation) ☐ Tech-Only (Without Interpretation) FISH ☐ Global (With Interpretation) ☐ Tech-Only (Without Interpretation)

LUNG CANCER
☐ Driver Profile: EGFR MUTATION, ALK (FISH), ROS1 (FISH), PDL1 (IHC)
☐ Expanded Driver Profile: EGFR MUTATION, ALK (FISH) and ROS1 (FISH), PDL1 (IHC), BRAF, MET (FISH) and RET (FISH)
Individual Markers:
☐ EGFR ☐ BRAF ☐ PDL1 (IHC) ☐ ALK (FISH) ☐ MET (FISH) ☐ ROS1 (FISH) ☐ RET (FISH)
☐ EGFR by Peripheral Blood (Liquid Bx)
☐ EGFR T790M Drug Resistance: ☐ Solid Tumor ☐ Liquid Biopsy
☐ ALK (FISH) by Peripheral Blood (CTCs): The detection of circulating tumor cells (CTCs) in the peripheral blood followed by genetic analysis of ALK by FISH

BREAST CANCER
☐ Reflex to HER2 (FISH) if HER2 (IHC) is: ☐ 0 ☐ 1+ ☐ 2+ ☐ 3+
Individual Markers:
☐ HER2/neu (FISH) ☐ Ki-67 (IHC) ☐ HER2/neu (IHC) ☐ PTEN (IHC) ☐ ER (IHC) ☐ PIK3CA (Molecular) ☐ PR (IHC)
☐ HER2 (FISH): by (CTCs) ONCOCEE-BR™
☐ PROSIGNA: Breast Cancer Gene Assay
The Prosigna Breast Cancer Prognostic Gene Signature Assay is an in vitro diagnostic assay that is performed on the NanoString nCounter® DX Analysis System using FFPE breast tumor tissue previously diagnosed as invasive breast carcinoma. (Send out)

COLON CANCER
☐ Colon Profile: KRAS, BRAF, NRAS, PIK3CA
Individual Markers:
☐ KRAS (exons 2, 3 and 4) ☐ BRAF ☐ NRAS (exons 2, 3 and 4) ☐ PIK3CA

LYNCH SYNDROME/HNPCC
☐ MMR (IHC) (MLH1, MSH2, MSH6, PMS2)
☐ Reflex to MSI (PCR) when MMR intact
☐ If loss of MLH1 by IHC reflex to MLH1 - Methylation (MethyTek™) - GoPath's proprietary, quantitative methylation-specific PCR assay
☐ BRAF reflex to MLH1 - Methylation (MethyTek™)
☐ Microsatellite Instability (MSI)

ONCOOEFENDER™-CRC
☐ OncoDefender™
OncoDefender™-CRC is a molecular test that can predict risk of recurrence for early stage colorectal cancer (Stage I/II)

GASTRIC CANCER
☐ HER2/neu (IHC)
☐ Reflex to HER2 (FISH) if HER2 (IHC) is: ☐ 0 ☐ 1+ ☐ 2+ ☐ 3+
☐ HER2/neu (FISH)

DISTAL ESOPHAGEAL CANCER
☐ HER2/neu (IHC)
☐ Reflex to HER2 (FISH) if HER2 (IHC) is: ☐ 0 ☐ 1+ ☐ 2+ ☐ 3+
☐ HER2/neu (FISH)

NEXT-GENERATION SEQUENCING:

ONCOTARGET®
☐ Robust and powerful hybrid capture NGS panel detecting mutations, rearrangements, copy number and MSI

ONCO-TRACKING™
☐ Molecular Targeting & Monitoring for early signs of cancer recurrence and metastasis via solid tumor and liquid biopsy

THYROID CANCER
☐ Dx
BRAF, KRAS, NRAS
(Sensitivity is 2-1%)
Individual Markers:
☐ BRAF ☐ KRAS ☐ NRAS
☐ Thyroid FISH ☐ RET

PROSTATE CANCER
Prostate Cancer Prognostic Panel
PTEN (FISH) & ERG (FISH)
☐ PTEN (FISH) ☐ PCA3 ☐ ERG (FISH) ☐ ERG (IHC)

BLADDER CANCER
☐ Urine FISH
(reflex on atypical urine cytology)
☐ CytoSnap™ - GoPath's proprietary, highly sensitive molecular mutational analysis for bladder cancer in the urine
☐ Urine FISH reflex to CytoSnap™

BRAIN CANCER
☐ Brain Profile: 1p/19q Deletion-FISH IDH1/IDH2, MGMT Promoter Methylation
Individual Markers:
☐ 1p/19q Deletion FISH ☐ IDH1/IDH2 ☐ MGMT Promoter Methylation

MELANOMA CANCER
☐ Melanoma Profile: BRAF, PDL1 (IHC), NRAS, cKIT
Individual Markers:
☐ BRAF ☐ NRAS ☐ PDL1 (IHC) ☐ cKIT

GIST
☐ GIST Profile: cKIT (for GIST tumors), PDGFR, BRAF
Individual Markers:
☐ cKIT (for GIST tumors) ☐ PDGFR ☐ BRAF

OVARIAN CANCER
☐ BRAF ☐ KRAS ☐ PIK3CA

TUMOR OF UNKNOWN PRIMARY
☐ Cancer Type ID (Send out)

Special Instructions / Add On Tests / Stand Alone / Other Tumor Types:

Preparing Samples (Solid Tumor)
FFPE tissue blocks are preferred. Blanks at 4 µm for 10 slides or at 8 µm for 5 slides are acceptable when blocks cannot be provided. Specimen types include: endoscopic biopsies, excisional biopsies, core needle biopsies, surgical resections and cell blocks (pleural effusions, ascites). Use GoPath Labs kit for transport. Ship at room temperature. Include copy of this requisition.

A signature certifies that he/she is licensed to order the test(s) listed above and that tests ordered are necessary for the treatment of the above patient. Authorized Signature Date:

To view reports, please visit www.gopathlabs.com and click Online Reporting

GP-10-01-1017

Our requisition is easy-to-read with clearly-defined categories listed by cancer type, which makes for easy test ordering. All of our requisitions are also available online and can be customized with your office's information to streamline the ordering process.

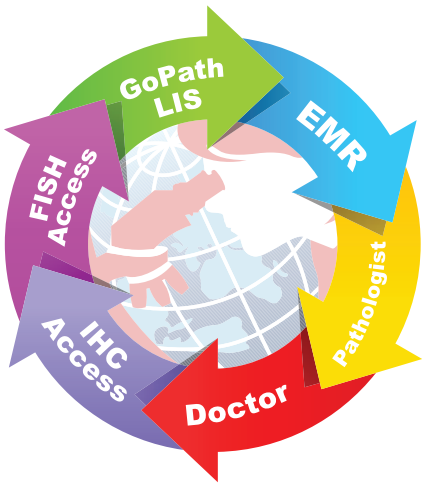
OncoTarget® - 125 Specimen Requirements

Preparation of normal and tumor genomic DNA can be extracted from FFPE block, or alternately, from saliva or blood for matched normal. The DNA is subsequently subjected to quantification, DNA fragmentation and library preparation procedures. Table 5 describes the collection amount required for OncoTarget®- 125 testing. GoPath Laboratories will provide the corresponding DNA collection kit depending on the collection sample.

Table 5. OncoTarget®- 125 Samples Required

Specimen	Quantity
Tumor Tissue FFPE	10-15 5 µm blanks
Non-Tumor Tissue FFPE	10-15 5 µm blanks
Saliva, Blood	For matched normal, as specified
Shipping Conditions	Room temperature for FFPE; Cold pad for saliva or blood

GoPath Connect™: Stay Connected to Your Patients' Reports 24/7



GoPath Connect™ makes it easy to connect to your patients' pathology reports anytime, from anywhere. With a wide range of test ordering and result retrieval options, as well as cloud-based solutions, GoPath Connect™ works seamlessly with your existing platform and workflow and connects you with your patient's reports and images in real-time from any device that is connected to the internet.

- Virtual pathology resources
- All data accessible from our website
- View high quality images
- Email/fax report notification
- Time-saving & secure e-requisitions
- Safe, encrypted data environment
- One-click report printing
- Optional remote auto-faxing
- Web-based & paper ordering
- EMR/PMS interfacing

GoPath Laboratories' Client Services

Let Us Help You Get Started

Providing appropriate information saves valuable time, eliminates confusion, limits phone calls & shortens turnaround time.

- Indicate Billing
- Patient's Legal Name
- Patient's DOB and Gender
- Date of Service / Collection
- Patient's Address and Phone Number
- Ordering Physician's Name, Facility and NPI
- ICD10-CM Codes

Account Set Ups

- Immediate
- Customized Requisitions
- Personalized In-Service and Training
- Convenient Supply Ordering
- Specialized Account Set Up Team

Office Pickup Options

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- FedEx Express
- FedEx Same Day City

Billing Capabilities

Billing shouldn't frustrate your patients or distract your staff. We offer the following billing solutions:

- In-Network Lab Accepting All Government Insurances
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- Convenient Client Billing
- Dedicated Billing Support
- Technical and Professional Model Billing also Available
- Tech-Only Services

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- Test Supply Order Forms
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GOPATH® LABORATORIES
Global Pathology Services

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