Biopharma and HTG Molecular Diagnostics

Sample Sensitivity Data

Accelerating your success.

Working in harmony with next-generation sequencing (NGS) platforms, HTG's patented chemistry, multiplexed assays and automated platforms offer fast, powerful quantitative gene expression profiling (GEP).

Dedicated to empowering precision medicine, HTG's solutions provide more data from clinically relevant samples.

The HTG team's experience and capabilities in assay development, workflow automation, CDx submissions and global commercialization offer you the security of a clinically deployable technology for your development programs that accelerates your time to market.

Rethink "possible"

HTG's NGS-based nuclease protection chemistry and automation help overcome challenges frequently encountered in biopharma product development.

- *Obtain diagnostic results from FFPE tissues and other clinical samples that would challenge alternative technologies.*
- *Generate comprehensive molecular profiles using HTG's extraction-free chemistry on samples that may be too small or degraded for extraction-based techniques.*
- *Assess tumor microenvironment and systems biology using the enhanced sensitivity of NGS detection.*

HTG offers comprehensive solutions to address your development needs, from translational medicine through clinical development and global commercialization.

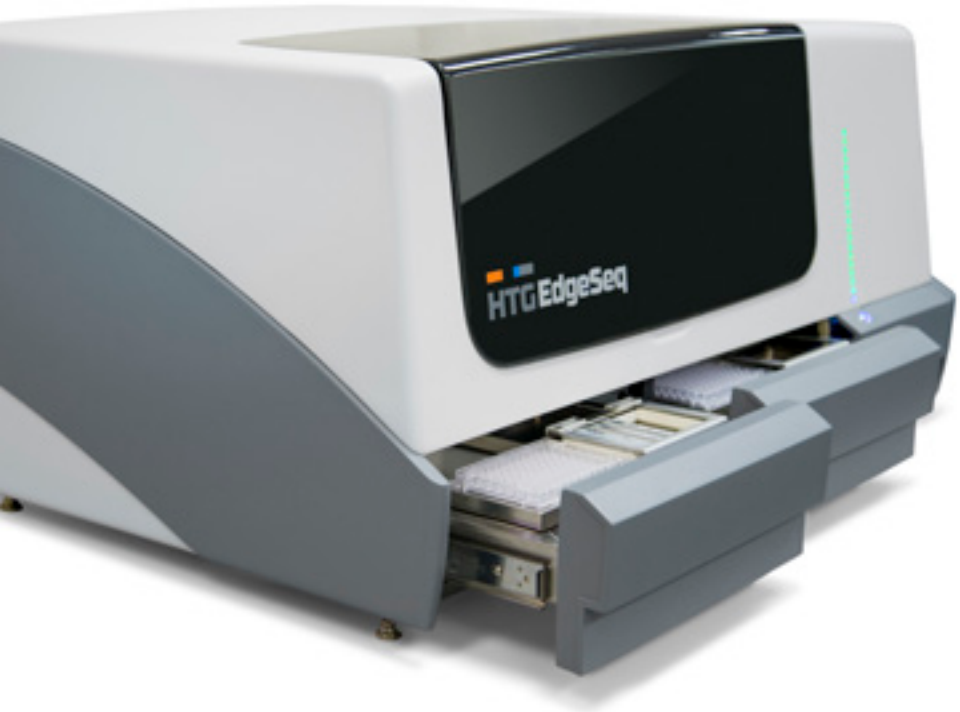
Sample Our technologies offer rich data from clinically relevant samples;

Sensitivity HTG's patented, extraction-free chemistry delivers robust, reproducible data, even for low-expression markers;

Data Unique, multiplexed assays generate more data with less material, enabling comprehensive profiling and analysis.

We offer automated workflow solutions for gene expression profiling that can be deployed to help address the unique needs and challenges through every step of the development process.

HTG succeeds when you succeed. We believe working together accelerates drug development and capture of market leadership.



Sample

Profile challenging sample types, including FFPE tissue, using an extraction-free, automated NGS-based solution.

Sensitivity

Leverage the sensitivity and dynamic range of NGS for comprehensive gene expression profiling.

Data

Deliver actionable results from a platform technology that can be used from translational medicine all the way to the clinic.

Translational Medicine

Cut to the chase

Translational medicine requires both speed and accuracy. Move too slowly, you lose market leadership. Too quickly, you overlook the next drug candidate. HTG empowers you to cut to the chase and eliminate interference.

Case in Point

In a Phase II study, more than half of the 300 samples run using RNASeq failed to yield interpretable results due to insufficient and/or low-quality materials.

Researchers then ran samples from the same cohort using the HTG EdgeSeq Oncology Biomarker Panel – requiring much lower sample inputs – and produced interpretable results in more than 85% of study samples.

As a result, the company was able to reactivate the development program.

Sample

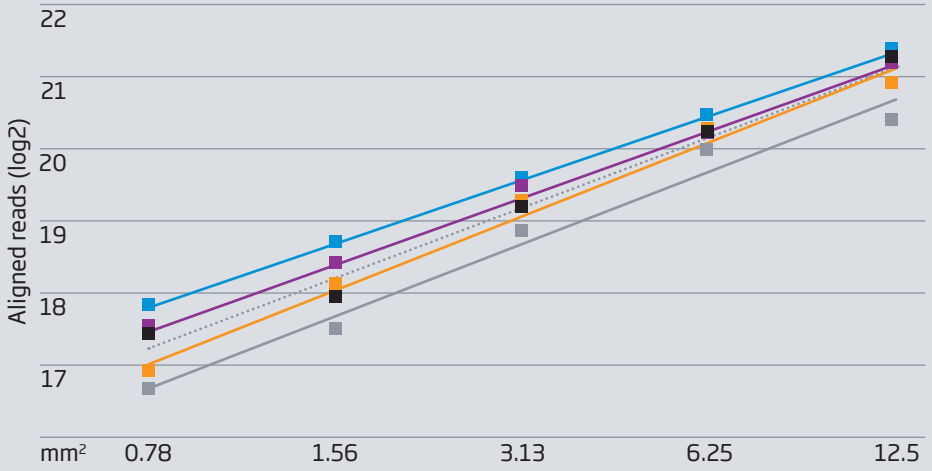
Work with a wide variety of sample types including cell lines, plasma, FFPE tissue, whole blood in PAXgene and extracted RNA.

Sensitivity

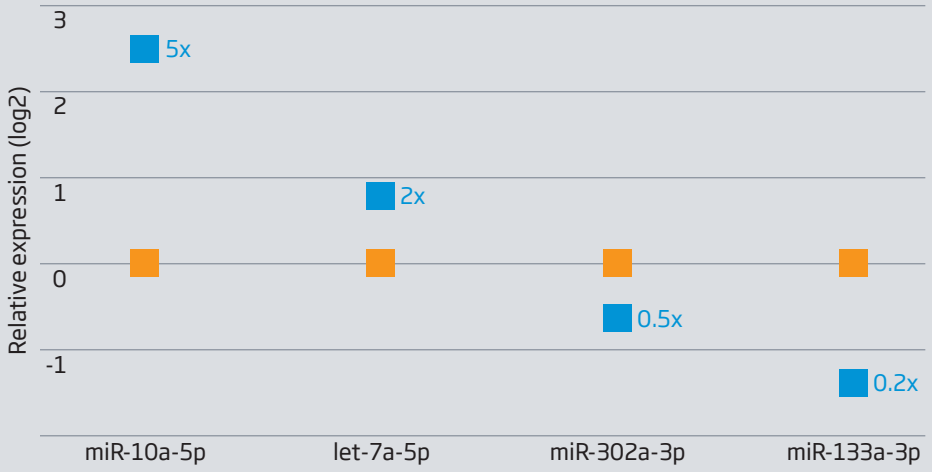
Accurately assess small and large fold changes in highly multiplexed assays.

Data

Reveal systems biology through a comprehensive assessment of signaling pathways in a single panel.



Linearity demonstrated using five different tumor types for sample inputs ranging from 12.5 mm^2 to 0.78 mm^2 of tumor surface area from a single 5 micron FFPE tissue section



Mean expression values for varying concentrations of synthetic miRNAs spiked into a common serum sample

AREG	1,865
IL2	246
PDCD1	976
MLH1	5,870
CD19	3,221
PI3K	127

The HTG EdgeSeq Oncology Biomarker Panel measures the expression of 2,560 genes from a single FFPE tissue section

Biomarker Validation

See what others don't

Failure to see a given result doesn't necessarily mean the markers aren't there. It may just mean you need to use a different lens. HTG provides it, delivering reproducible data on samples failed by or unusable with other testing technologies.

Case in Point

Pathologists now subtype non-small cell lung cancer (NSCLC) using immunohistochemistry techniques which require multiple sections of tissue from typically small bronchoscopic or needle core biopsies. There is a need for a single, multiplexed solution that preserves these precious specimens for additional characterization.

In collaboration with a leading comprehensive cancer center, HTG developed a custom NGS assay with performance comparable to established microarray-based classifiers.

The HTG custom assay yields highly reproducible data from limited, clinically challenging sample types, including core needle biopsies.

Profiling 62 genes associated with histological markers and associated disease pathways, the HTG custom assay offers a cost-effective solution that dovetails with current clinical workflows and "reclaims" samples otherwise too limited or inferior to analyze via IHC or other molecular technologies.

Sample

Perform extraction-free validation of biomarker hypotheses from FFPE tissues and other clinical sample types.

Sensitivity

Benefit from NGS detection sensitivity and dynamic range to consistently measure small changes in high and low expressing genes.

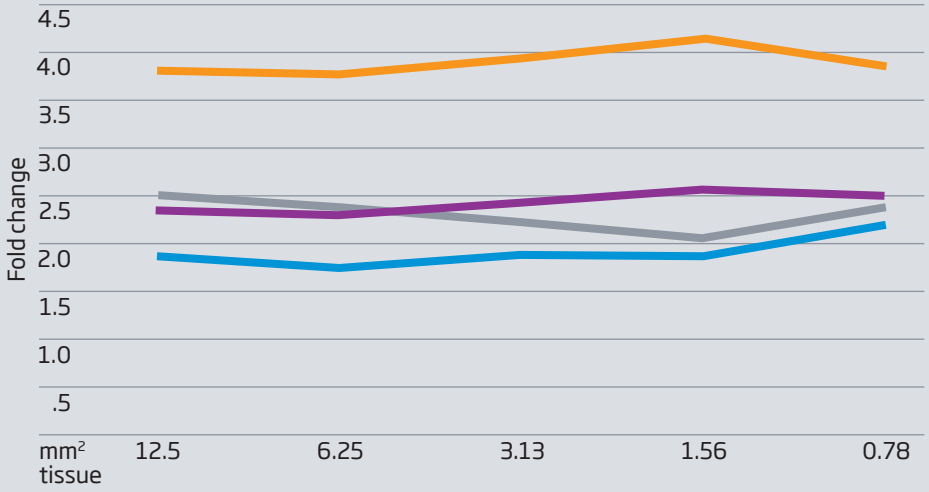
Data

Validate clinically relevant gene expression signatures and classifiers on a deployable, multiplexed platform.

	Sample Input	COO Subtype	Sample Input	COO Subtype
	12.5 mm²	ABC	12.5 mm²	GCB
	6.25 mm²	ABC	6.25 mm²	GCB
	3.13 mm²	ABC	3.13 mm²	GCB
Minimum recommended input	**1.56 mm²**	**ABC**	**1.56 mm²**	**GCB**
	0.78 mm²	ABC	0.78 mm²	GCB
	0.39 mm²	ABC	0.39 mm²	GCB

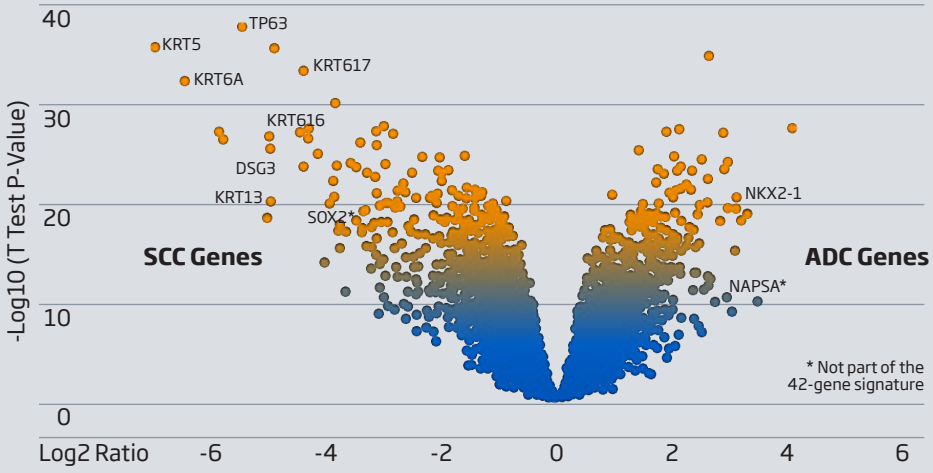
ABC Subtype
GCB Subtype

Consistent DLBCL cell of origin subtype classification was obtained from all titration points when known samples were tested; the recommended sample input is representative of the amount of tissue from a single section of a core needle biopsy, though individual sample input requirements may vary depending on sample quality



FOXP1
CD68
HLA-DRA
CD37

Fold changes in expression between known ABC and GCB type DLBCL tumors across a range of sample input amounts



DOI: 10.1158/1078-0432.CCR-15-2900

An HTG EdgeSeq custom assay was used to develop a classifier using genes originally identified in microarray studies; adenocarcinoma (ADC) and squamous cell carcinoma (SCC) of the lung can be reliably differentiated using this smaller set of genes

Clinical Development

Get on the fast track

At the clinical development stage, it's about getting the right drug to the right patient. Failures or delays due to sample constraints, lack of assay robustness or limited deployability cannot be tolerated. HTG develops automated, NGS-based RUO and IUO assays that help improve patient enrichment in early- and late-phase clinical trials. This helps ensure a smooth transition from biomarker discovery to validation to clinical development and eventual FDA review.

Case in Point

A large biopharma was challenged with developing a GEP-based lymphoma subtyping assay that would be concordant with both IHC and microarray classification for approval and deployment as a companion diagnostic.

HTG used a training cohort with known subtyping as activated B-cell like (ABC) or germinal center B-cell like (GCB) to develop a classification assay and algorithm. The classifier was then validated on a separate cohort, demonstrating excellent concordance to the original microarray classifier.

This assay, using a single FFPE tissue section, is available as a CE-IVD and is being developed as an IUO for accelerated prospective clinical studies.

Sample

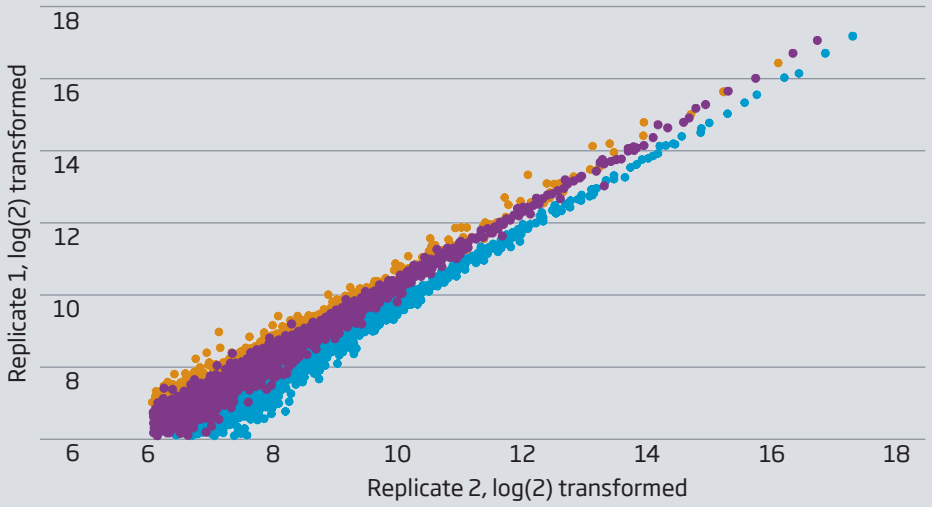
Easily deploy automated, FFPE-based clinical trial assays into CROs and other service laboratories.

Sensitivity

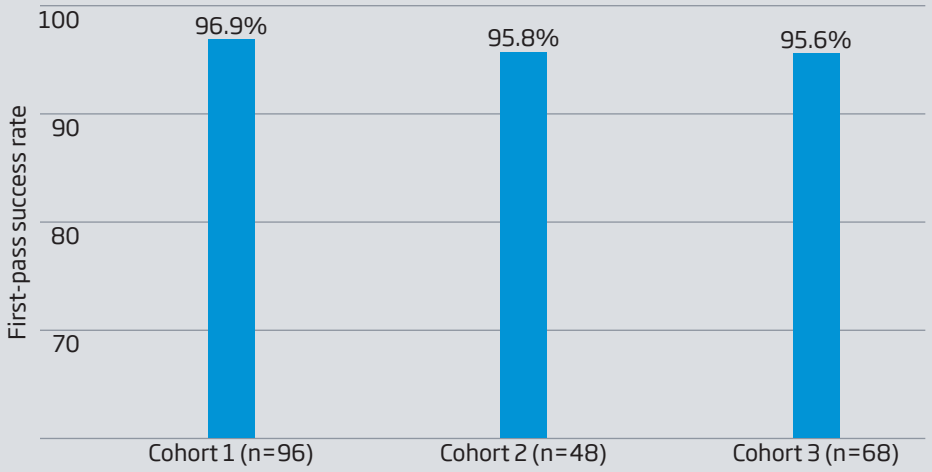
Build robust, extraction-free, NGS-based assays that work with real-world samples such as a single section from a core needle biopsy.

Data

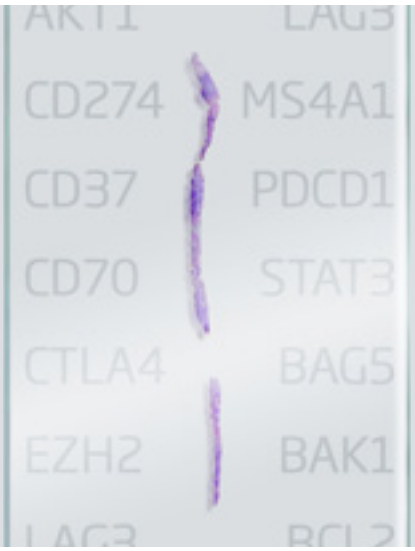
Improve patient enrichment and help identify durable response without the sample and workflow limitations of other technologies.



Sequential FFPE tissue sections from a melanoma were processed at three customer sites using the HTG EdgeSeq Oncology Biomarker Panel



A 96.2% first-pass success rate was achieved from 212 DLBCL cases from three clinical trial cohorts using the HTG EdgeSeq DLBCL Cell of Origin Assay



DLBCL Classification Result:

Activated B-Cell (ABC) Type

HTG EdgeSeq DLBCL Cell of Origin Assay measures the expression of 93 genes from a single 5 micron FFPE tissue section

DMPK

Stay ahead

Current FDA draft guidance for drug interaction studies requires assessment of CYP1A2, CYP2B6 and CYP3A4 induction. Testing for additional induction effects, such as CYP2C8, CYP2C9 and CYP2C19 may be added in the future, making traditional and complex qPCR testing even more cumbersome.

The HTG Edge DMPK Core CYP Assay measures the expression of the CYP1A2, CYP2B6, CYP3A4, CYP2C8, CYP2C9 and CYP2C19 in a single well, no RNA extraction required, allowing you to scale to new guidelines as they emerge without developing new assays, adding staff or increasing workload.

In addition to the Core CYP genes, the HTG Edge DMPK Comprehensive Assay also measures the expression of Phase 2 UGT as well as transporter genes.

The HTG Edge system and associated DMPK assays are fully automated, require less than 30 minutes of hands-on time and reduce total turnaround time, as compared to qPCR, by as much as 50%. The HTG solution delivers all of this with robust results that correlate well with traditional qPCR methods.

Sample

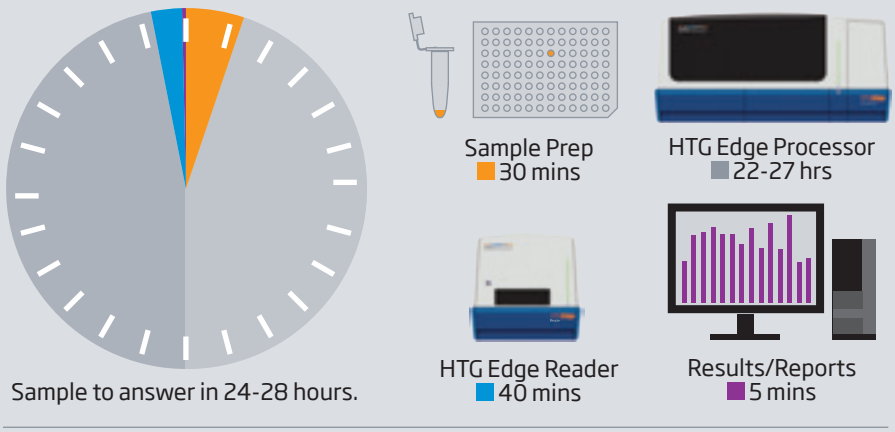
Identify p450-inducing compounds in hepatocyte studies using a fully automated platform.

Sensitivity

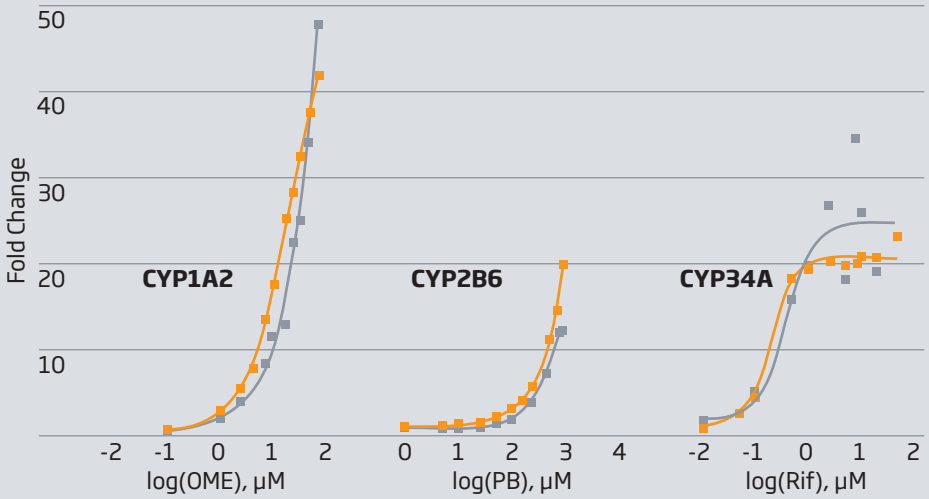
Routinely assess dose-response curves and determine EC_{50} in an automated workflow.

Data

Reproducibly meet existing and emerging FDA guidelines today using a single panel.



HTG Edge DMPK assays can be processed on the fully automated HTG Edge system in about 28 hours, requiring only 30 minutes of hands-on time



HTG Edge DMPK Core CYP Assay results are comparable to RT-qPCR testing of prototypical compounds and appropriate p450 genes

Correlations between all pair-wise replicates by processor

Assay	Treatment	Proc 23 vs 31	Proc 28 vs 23	Proc 28 vs 31
Core	DMSO	0.98	0.98	0.98
	OME	1.00	0.99	1.00
	PB	1.00	0.99	0.99
	RIF	1.00	0.98	0.99

Correlations between all pair-wise replicates by day

Assay	Treatment	Day 1 vs 2	Day 1 vs 3	Day 2 vs3
Core	DMSO	0.98	0.99	0.97
	OME	1.00	1.00	0.99
	PB	0.99	1.00	0.99
	RIF	0.99	1.00	0.99

Pearson correlations from test replicates demonstrate reproducibility across multiple instruments and different days

Products

Make success possible

HTG EdgeSeq Immuno-Oncology Assay		
Illumina	916-005-208	HTG EdgeSeq Immuno-Oncology Assay ILM (2x8)
	916-005-008	HTG EdgeSeq Immuno-Oncology Assay ILM (4x8)
	916-005-224	HTG EdgeSeq Immuno-Oncology Assay ILM (1x24)
	916-005-024	HTG EdgeSeq Immuno-Oncology Assay ILM (4x24)
	916-005-096	HTG EdgeSeq Immuno-Oncology Assay ILM (1x96)
Ion Torrent	916-005-308	HTG EdgeSeq Immuno-Oncology Assay IT (2x8)
	916-005-108	HTG EdgeSeq Immuno-Oncology Assay IT (4x8)
	916-005-324	HTG EdgeSeq Immuno-Oncology Assay IT (1x24)
	916-005-124	HTG EdgeSeq Immuno-Oncology Assay IT (4x24)
HTG EdgeSeq Lymphoma Panel		
Illumina	916-007-208	HTG EdgeSeq Lymphoma Panel ILM (2x8)
	916-007-008	HTG EdgeSeq Lymphoma Panel ILM (4x8)
	916-007-224	HTG EdgeSeq Lymphoma Panel ILM (1x24)
	916-007-024	HTG EdgeSeq Lymphoma Panel ILM (4x24)
	916-007-096	HTG EdgeSeq Lymphoma Panel ILM (1x96)
Ion Torrent	916-007-308	HTG EdgeSeq Lymphoma Panel IT (2x8)
	916-007-108	HTG EdgeSeq Lymphoma Panel IT (4x8)
	916-007-324	HTG EdgeSeq Lymphoma Panel IT (1x24)
	916-007-124	HTG EdgeSeq Lymphoma Panel IT (4x24)
HTG EdgeSeq miRNA Whole Transcriptome Assay		
Illumina	916-001-208	HTG EdgeSeq miRNA WTA ILM (2x8)
	916-001-008	HTG EdgeSeq miRNA WTA ILM (4x8)
	916-001-224	HTG EdgeSeq miRNA WTA ILM (1x24)
	916-001-024	HTG EdgeSeq miRNA WTA ILM (4x24)
	916-001-096	HTG EdgeSeq miRNA WTA ILM (1x96)
Ion Torrent	916-001-308	HTG EdgeSeq miRNA WTA IT (2x8)
	916-001-108	HTG EdgeSeq miRNA WTA IT (4x8)
	916-001-324	HTG EdgeSeq miRNA WTA IT (1x24)
	916-001-124	HTG EdgeSeq miRNA WTA IT (4x24)
HTG EdgeSeq Oncology Biomarker Panel		
Illumina	916-002-208	HTG EdgeSeq Oncology Biomarker Panel ILM (2x8)
	916-002-008	HTG EdgeSeq Oncology Biomarker Panel ILM (4x8)
	916-002-224	HTG EdgeSeq Oncology Biomarker Panel ILM (1x24)
	916-002-024	HTG EdgeSeq Oncology Biomarker Panel ILM (4x24)
	916-002-096	HTG EdgeSeq Oncology Biomarker Panel ILM (1x96)
Ion Torrent	916-002-308	HTG EdgeSeq Oncology Biomarker Panel IT (2x8)
	916-002-108	HTG EdgeSeq Oncology Biomarker Panel IT (4x8)
	916-002-324	HTG EdgeSeq Oncology Biomarker Panel IT (1x24)
	916-002-124	HTG EdgeSeq Oncology Biomarker Panel IT (4x24)
HTG EdgeSeq DLBCL COO Assay		
Illumina	CE-003-008	HTG EdgeSeq DLBCL COO Assay CE-IVD (4x8)
	CE-003-024	HTG EdgeSeq DLBCL COO Assay CE-IVD (4x24)
	CE-003-096	HTG EdgeSeq DLBCL COO Assay CE-IVD (1x96)
HTG Edge DMPK Assays		
Core CYP	816-103-040	4 pack (full-plate) assay kit
Comprehensive	816-092-040	4 pack (full-plate) assay kit
HTG Edge and HTG EdgeSeq Systems		
	HTG EDGE-SQ-100	HTG EdgeSeq system
	HTG EDGE-SQ-100E	HTG EdgeSeq system CE-IVD
	HTG EDGE-SP-010	HTG EdgeSeq processor
	HTG EDGE-SY-100	HTG Edge system
	HTG EDGE-PR-010	HTG Edge processor
	HTG EDGE-RD-010	HTG Edge reader
	HTG EDGE-PC-001	HTG Edge system PC, algorithm, accessories

VERI/O Lab Services

Our in-house VERI/O laboratory services support biomarker research and companion diagnostic development using HTG's extraction-free technology and evolving portfolio of profiling assays. Planned services will also include direct sequencing of genetic variants.

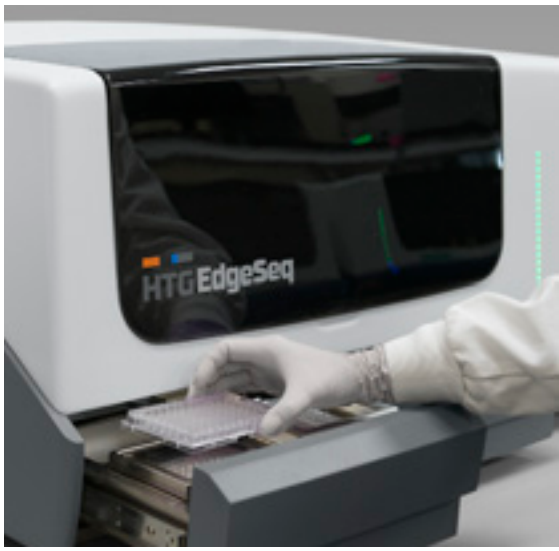
CLIA-Certified Partners

For prospective research, HTG has partnered with several CLIA-certified laboratories that provide profiling services using HTG systems and assays. Contact your HTG representative for more information.

New problems demand new solutions. Challenge HTG to develop custom assays to overcome the hurdles in your path.

Leverage HTG technology without capital investment by shipping your samples to our in-house VERI/O lab or one of our CLIA-certified lab partners.

The HTG EdgeSeq system and assays allow you to leverage the global installed base of NGS systems.



Bases Covered

Partner with HTG

Commitment

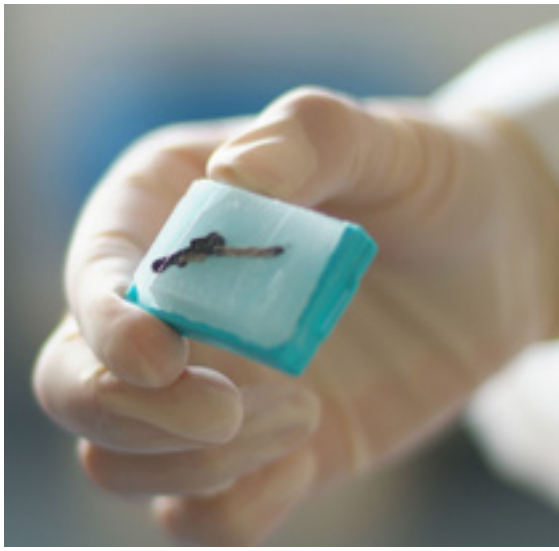
Comprehensive, NGS-based molecular profiling is a critical tool that enables your success in biomarker discovery and drug development. HTG is a committed partner every step of the way: from discovery through clinical development and commercial deployment.

Expertise

The HTG team has a track record of success in leveraging its experience and capabilities in assay development, workflow automation, CDx submissions and global commercialization.

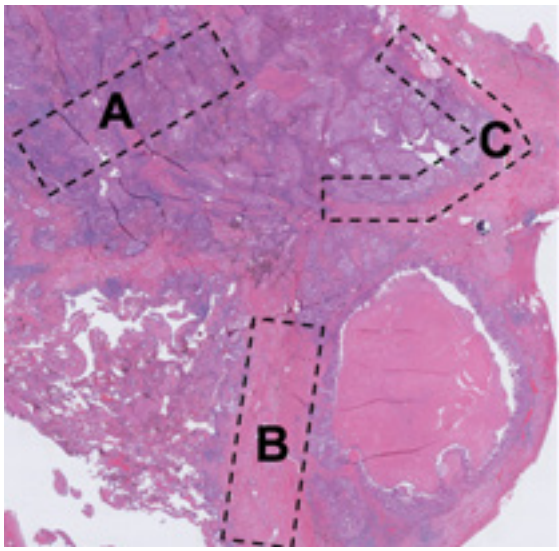
Technology

HTG's extraction-free technology platforms and assays adapt to existing NGS workflows, providing automated solutions that are easily deployed to support your therapeutic and CDx objectives. HTG's solutions are simple, cost-effective, and generate actionable results from clinically relevant samples, especially FFPE tissue.



Re-think possible.

Discover how HTG technology can de-risk the development process and accelerate your time to market.



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HTG Edge and HTG EdgeSeq processors are CE-marked and CSA-certified.

For Research Use Only. Not for use in diagnostic procedures.

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