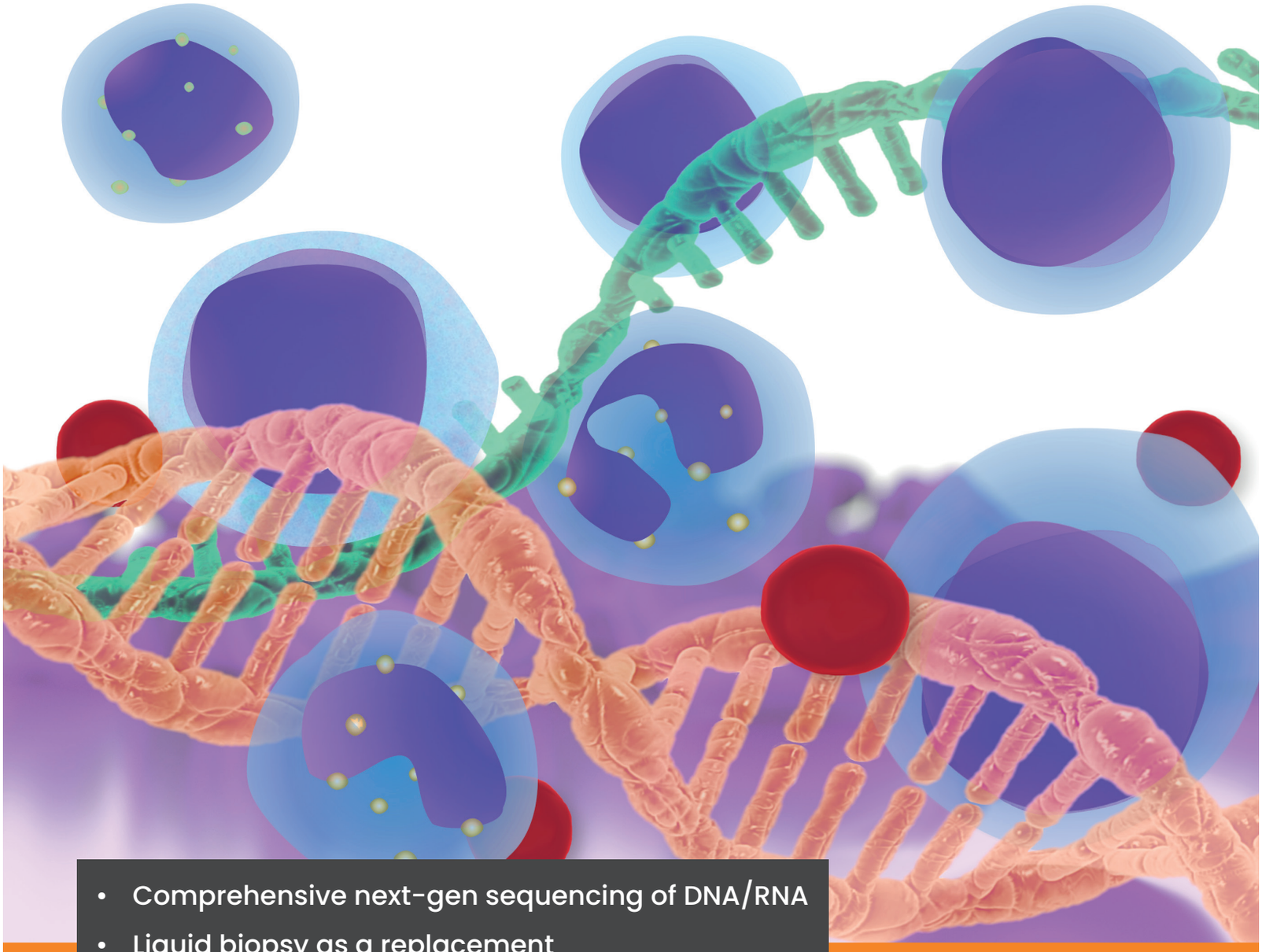
Hematologic Neoplasm Profiling

Precision Diagnosis, Classification and Advanced Treatment



- Comprehensive next-gen sequencing of DNA/RNA
- Liquid biopsy as a replacement for bone marrow biopsy
- Results in 5-10 days

GENOMIC® TESTING COOPERATIVE

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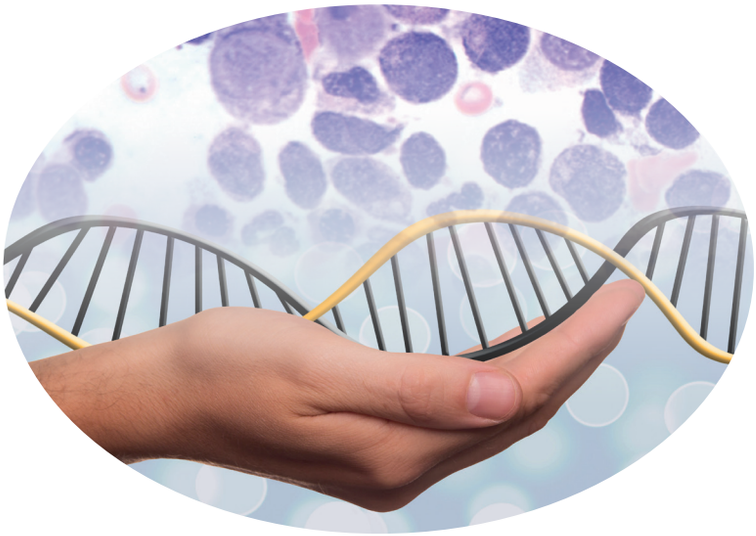
TESTING COOPERATIVE

Don't accept partial results. DNA and RNA provide a complete picture for comprehensive answers.

- GTC's RNA goes beyond just fusion detection, it can also provide immunophenotype, molecular IHC and molecular karyotyping.
- Sophisticated AI systems that help with interpreting and reporting the data to make more accurate diagnoses and subclassifications
- Replacement for bone marrow aspirations and biopsy



The hematology profiles provide:

- Targeted matching
- Fusion/translocations
- DNA and RNA profiling
- Detection of minimal residual disease (MRD)
- Copy number variation and deletion detection
- Precise diagnosis and classification of disease
- RNA expression profiling for molecular immunophenotyping
- Viral EBV testing
- T-cell & B-cell clonality analysis
- HLA genotyping

Hematology Tests

GTC-Hematology Profile PLUS™
DNA/RNA

Liquid Trace™ Hematology
First in class cfDNA/cfRNA

GTC-Hematology Profile™
DNA

GTC-Hematology Profile PLUS™

GTC-Hematology Profile Plus™ combines expression and fusion with mutation analysis in DNA and RNA. This is a comprehensive evaluation of all hematologic neoplasms. However, it is especially recommended for:

- All types of Leukemias
- All types of Lymphomas
- All types of Myelomas
- Includes IgVH mutation status
- Viral EBV testing
- Chromosomal abnormalities, translocations and gene amplifications
- T-cell & B-cell clonality analysis
- HLA genotyping

Liquid Trace™ Hematology

Liquid Trace™ Hematology is a pan-cancer, highly sensitive test evaluating cfDNA and cfRNA

- Replacement for bone marrow aspirations and biopsy
- Can be used for diagnoses, classification of all types of hematological malignancies, evaluating the host immune response, and identifying biomarkers for predicting response to various therapies
- Monitoring therapy and response
- Detection of minimal residual disease (MRD)
- T-cell & B-cell clonality analysis
- HLA genotyping

GTC-Hematology Profile™

GTC-Hematology Profile™ is designed to profile the molecular abnormalities in various hematologic neoplasms including:

- Myelodysplastic Syndrome (MDS)
- Myeloproliferative Neoplasms (MPN)
- Distinguish Clonal Hematopoiesis of Indeterminate Potential (CHIP)
- VEXAS Disease

Hematology Tests Comparison Table

Available Tests	GTC-Hematology Profile PLUS™	Liquid Trace™: Hematology	GTC-Hematology Profile™
Genes	**284/>1600**	**284/>1600**	**284**
TAT	**7-10 Days**	**5-7 Days**	**5-7 Days**
Indications	All hematologic neoplasms including lymphomas, myelomas, and leukemias Includes IgVH Chromosomal abnormalities, translocations and gene amplifications Viral EBV testing. HLA genotyping. T- & B-cell clonality analysis	All hematologic neoplasms including lymphomas, myelomas, leukemias, VEXAS syndrome, and EBV Chromosomal abnormalities, translocations and gene amplifications Replacement for bone marrow aspirations and biopsy, Monitoring therapy and response, Detection of minimal residual disease (MRD), HLA genotyping, T- & B-cell clonality analysis	Detects various abnormalities in hematologic neoplasms including: Chromosomal abnormalities, Myelodysplastic Syndrome (MDS), Myeloproliferative Neoplasms (MPN), Distinguish Clonal Hematopoiesis of Indeterminate Potential (CHIP) VEXAS Disease
Sample Type	Bone marrow, Peripheral blood, Fresh tissue	Peripheral Blood	Bone marrow, Peripheral blood, Fresh tissue
Sample Requirements	Bone marrow: 2mL. Peripheral blood: 5 mL. EDTA tube preferred FFPE: 1 H&E slide and 6-10 unstained slides, 5-7 microns of tissue fixed with 10% NBF fixative	Peripheral blood: 8-10 mL. EDTA tube preferred* **Samples received beyond 72 hours may include only DNA results**	Bone marrow: 2mL. Peripheral blood: 5 mL. EDTA tube preferred FFPE: 1 H&E slide and 6-10 unstained slides, 5-7 microns of tissue fixed with 10% NBF fixative
Results Reported	DNA + RNA	DNA + RNA	DNA

*Important: cfRNA stability is optimal 48-72 hours from blood draw. cfDNA stability is 7 days from blood draw. Samples received beyond 72 hours may include only cfDNA results.

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CLIA # 05D2111917 CAP # 9441574

Hematology Profile Plus

Sample Report Page

Patient Name:		Ordering Physician:	
Date of Birth:		Physician ID:	
Gender (M/F):		Accession #:	
Client:		Specimen Type:	
Case #:		Specimen ID:	
Body Site:			
MRN:		Indication for Testing:	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites (C85.89)
Collected Date:	Time: 12:00 AM		
Received Date:	Time: 11:33 AM	Tumor Type:	Lymphoma
Reported Date:	Time: 02:23 PM		

Detected Genomic Alterations				
CD79B	ETV6 (2 mutations)	MYD88	KMT2D	PBRM1
TBL1XR1	IDH1	Chromosomal structural analysis shows: 3p-, 8q-, +9 with bi-allelic deletion of CDKN2A/B), +12, +13, +16, 18q+, and +21.	Expression profiling suggests ABC cell of origin, more aggressive subtype.	

Results Summary

- **-Mutations in CD79B, ETV6 (2 mutations), MYD88, KMT2D, PBRM1, TBL1XR1, and IDH1 genes**
  -Chromosomal structural analysis shows: 3p-, 8q-, +9 with bi-allelic deletion of CDKN2A/B), +12, +13, +16, 18q+, and +21.
  -Increased B-cell markers
  -No significant increase in BCL1, BCL2, or MYC mRNA.
  -Expression profiling suggests ABC cell of origin, more aggressive subtype.

  -These findings are consistent with diffuse large B-cell lymphoma, ABC cell of origin, more aggressive

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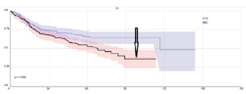
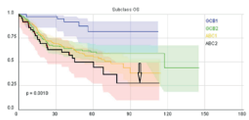


Predicted overall survival based on cell of origin classification as ABC.



Predicted overall survival based on cell of origin subclassification as ABC2.

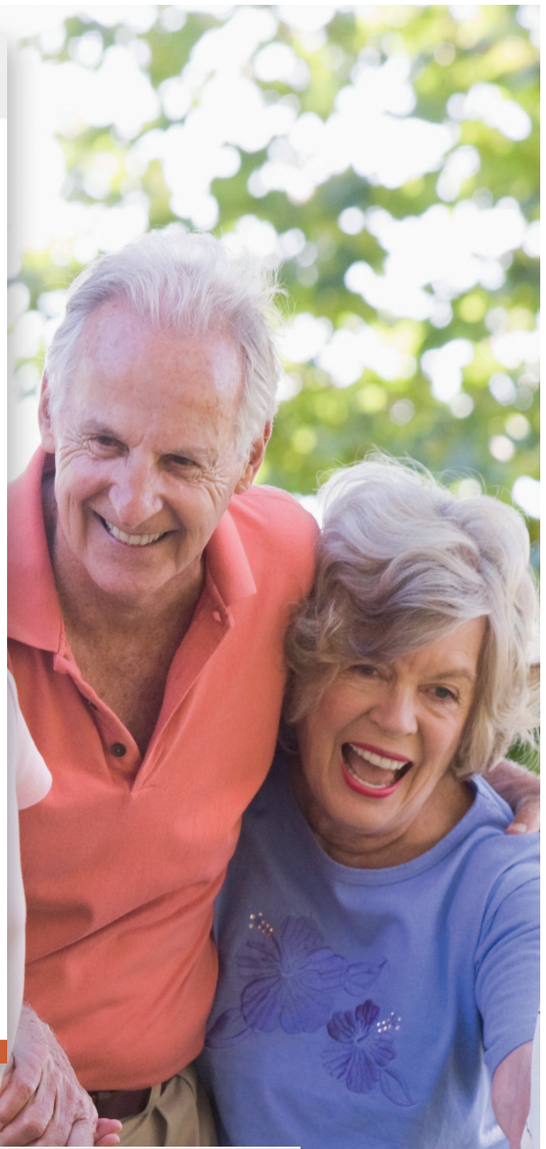
Heterogeneity
There is a dominant abnormal clone with CD79B mutation. The ETV6 (2 mutations), MYD88, and KMT2D mutations are detected in subclones. There are abnormal low-level clones with PBRM1, TBL1XR1, and IDH1 mutations.

Expression	
Increased B-cell markers	No significant increase in BCL1, BCL2, or MYC mRNA

Diagnostic Implications	
CD79B, ETV6 (2 mutations), MYD88, KMT2D, PBRM1, TBL1XR1, IDH1	These findings are consistent with diffuse large B-cell lymphoma (see results summary).

Therapeutic Implications	
MYD88	BTK inhibitors
IDH1	IDH1 inhibitors

Prognostic Implications	
CD79B	Unknown
ETV6 (2 mutations)	Unknown
MYD88	Poor
KMT2D	Unknown
PBRM1	Unknown
TBL1XR1	Unknown
IDH1	Neutral



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Genes with NO Alteration
nce of mutation in: NOTCH, SF3B1, TP53

scription:

omprehensive molecular profile which uses next generation sequencing (NGS), Sanger ig and fragment length analysis testing to identify molecular abnormalities (including SNVs, NVs, and IgVH) in DNA of 179 genes and RNA in 1408 genes associated with hematologic s, including leukemia, lymphoma, myeloma, and MDS. Whenever possible, clinical relevance and ns of detected abnormalities are described.

al relevance of detected Alterations

The B lymphocyte antigen receptor is a multimeric complex that includes the antigen-specific component, surface immunoglobulin face Ig non-covalently associates with two other proteins, Ig-alpha and Ig-beta, which are necessary for expression and function of the ntigen receptor. This gene encodes the Ig-beta protein of the B-cell antigen component. Alternatively spliced transcript variants g different isoforms have been described. [provided by RefSeq, Jul 2008]

his gene encodes an ETS family transcription factor. The product of this gene contains two functional domains: a N-terminal pointed omain that is involved in protein-protein interactions with itself and other proteins, and a C-terminal DNA-binding domain. Gene t studies in mice suggest that it is required for hematopoiesis and maintenance of the developing vascular network. This gene is o be involved in a large number of chromosomal rearrangements associated with leukemia and congenital fibrosarcoma. [provided by Sep 2008]

This gene encodes a cytosolic adapter protein that plays a central role in the innate and adaptive immune response. This protein s as an essential signal transducer in the interleukin-1 and Toll-like receptor signaling pathways. These pathways regulate that n of numerous proinflammatory genes. The encoded protein consists of an N-terminal death domain and a C-terminal Toll-interleukin1 domain. Patients with defects in this gene have an increased susceptibility to pyogenic bacterial infections. Alternate splicing results le transcript variants. [provided by RefSeq, Feb 2010]

The protein encoded by this gene is a histone methyltransferase that methylates the Lys-4 position of histone H3. The encoded proteir f a large protein complex called ASCOM, which has been shown to be a transcriptional regulator of the beta-globin and estrogen genes. Mutations in this gene have been shown to be a cause of Kabuki syndrome. [provided by RefSeq, Oct 2010]

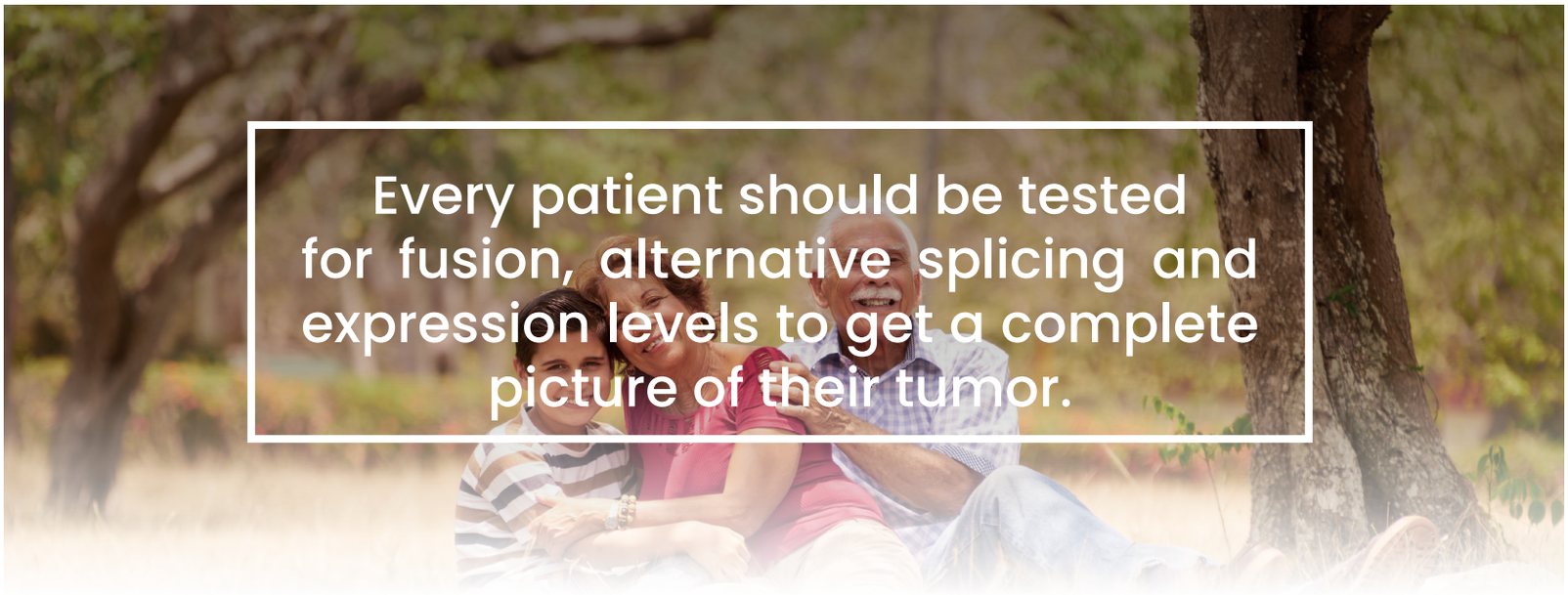
(POLYBROMO 1) gene encodes a subunit of ATP-dependent chromatin-remodeling complexes. The encoded protein has been identifiec egral component of complexes necessary for ligand-dependent transcriptional activation by nuclear hormone receptors. Mutations at s have been associated with primary clear cell renal cell carcinoma, but can be seen in other types of tumors. No targeted therapy is e.

. This gene is a member of the WD40 repeat-containing gene family and shares sequence similarity with transducin (beta)-like 1X-linked (TBL1X). The protein encoded by this gene is thought to be a component of both nuclear receptor corepressor (N-CoR) and histone deacetylase 3 (HDAC 3) complexes, and is required for transcriptional activation by a variety of transcription factors. Mutations in these gene have been associated with some autism spectrum disorders, and one finding suggests that haploinsufficiency of this gene may be a cause of intellectual disability with dysmorphism. Mutations in this gene as well as recurrent translocations involving this gene have also been observed in some tumors. [provided by RefSeq, Mar 2016]

- IDH1. Isocitrate dehydrogenases catalyze the oxidative decarboxylation of isocitrate to 2-oxoglutarate. These enzymes belong to two distinct subclasses, one of which utilizes NAD(+) as the electron acceptor and the other NADP(+). Five isocitrate dehydrogenases have been reported: three NAD(+)-dependent isocitrate dehydrogenases, which localize to the mitochondrial matrix, and two NADP(+)-dependent isocitrate dehydrogenases, one of which is mitochondrial and the other predominantly cytosolic. Each NADP(+)-dependent isozyme is a homodimer. The protein encoded by this gene is the NADP(+)-dependent isocitrate dehydrogenase found in the cytoplasm and peroxisomes. It contains the PTS-1 peroxisomal targeting signal sequence. The presence of this enzyme in peroxisomes suggests roles in the regeneration of NADPH for intraperoxisomal reductions, such as the conversion of 2, 4-dienoyl-CoAs to 3-enoyl-CoAs, as well as in peroxisomal reactions that consume 2-oxoglutarate, namely the alpha-hydroxylation of phytanic acid. The cytoplasmic enzyme serves a significant role in cytoplasmic NADPH production. Alternatively spliced transcript variants encoding the same protein have been found for this gene. [provided by RefSeq, Sep 2013]

Drug Information

Sample Report Page



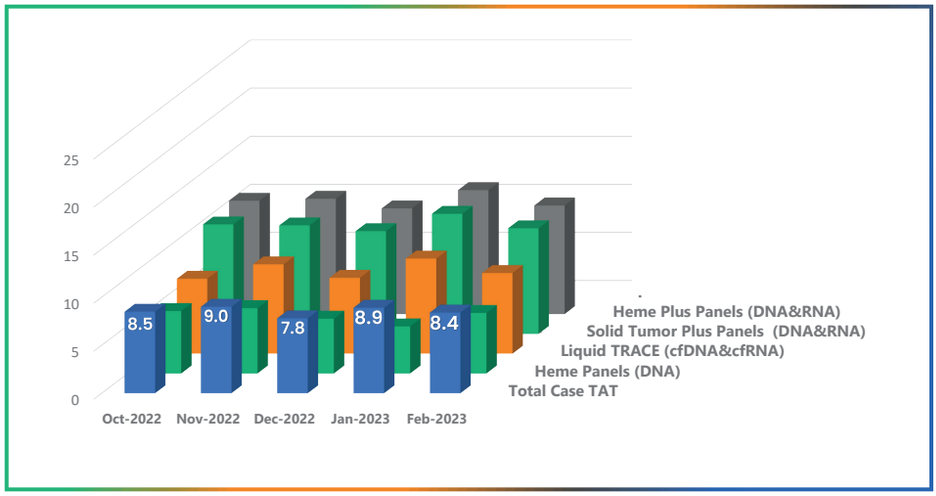
Advantages of RNA

GTC RNA results are compared with thousands of cases with expression levels, then run through our sophisticated AI systems that provide a summary of the findings for each patient.

- RNA Expression/Fusion profiling provides data on alternative splicing and levels of expression which helps in classification of genes
- RNA sequencing offers a superior method to identify gene fusion variants known to have prognostic and predictive significance in treatment.
- Measuring of cytokines, chemokines and interleukins
- Prediction of fusions in hematologic diseases
- Complete immunophenotying
- Prediction of clinical behavior
- Alternative splicing
- Viral EBV testing

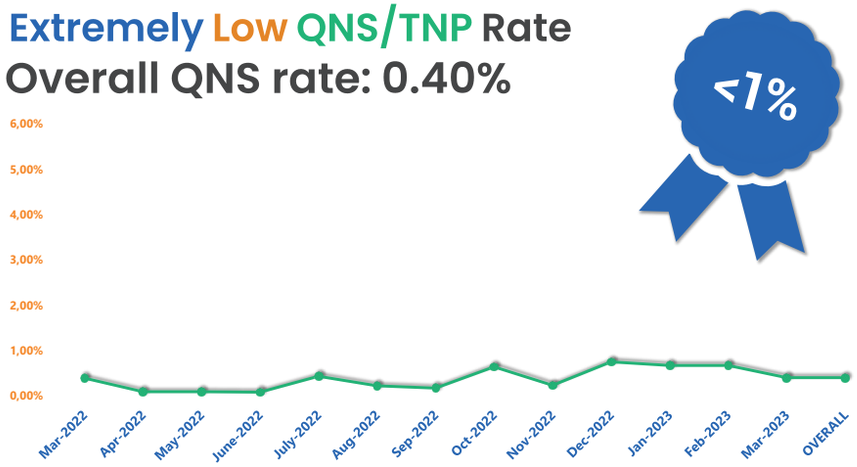
GTC provides a 5-10 day turnaround time for all our tests

GTC is committed to helping physicians and patients get answers fast. GTC consistently delivers results in 5-10 days.



Extremely Low QNS/TNP Rate

Overall QNS rate: 0.40%



Don't let QNS/TNP fears stop you from ordering comprehensive genomic profiling.

Using innovative chemistry helps reduce QNS and TNP rates.

GTC's QNS rate is currently less than 1%.

The Co-Op model

- Enables local labs to offer a comprehensive molecular testing menu to support their own communities.
- Provides economies of scale that benefit large labs with sophisticated technology at a local level.
- Reduces overhead costs (staffing, capital equipment, billing, etc.).

About GTC

GTC offers advanced genomic testing to communities everywhere at an affordable price.

Genomic Testing Cooperative (GTC) is a different kind of cancer diagnostic laboratory.

Our cooperative model allows us to partner with laboratories, hospitals, oncology practices and medical professionals to share resources which create efficiencies in cost, turnaround time and quality. In creating a network of Co-Op partners, we help get results to physicians faster, share knowledge and generate better outcomes for patients.

Our testing is focused on comprehensive profiling of DNA and RNA in hematologic neoplasms and solid tumors, embracing the latest sequencing technology and informatics tools, thereby providing better insights into the patient's tumor signature. Our RNA sequencing capabilities go beyond just the detection of fusions and include alternative splicing, gene expression and prediction. Our RNA profiling can be used to complement flow cytometry and immunohistochemistry (IHC) testing. GTC's capabilities include liquid biopsy testing that give physicians testing options when tissue or bone marrow specimens are not available. Our informatics tools use artificial intelligence with sophisticated algorithms to interpret complex data sets; these informatics tools are unmatched anywhere on the market today.

GTC was founded in 2018 by Maher Albitar, MD, who has held senior roles at numerous diagnostic laboratories and was a tenured professor at MD Anderson Cancer Center. He has committed his life to helping cancer patients by advancing cancer diagnostics and democratizing testing. Dr. Albitar founded GTC because he had a vision to revolutionize diagnostics and scientific discovery by improving access to comprehensive genomic profiling with next generation sequencing to all patients. He believes every cancer patient should have access to comprehensive genomic profiling. Dr. Albitar is regularly published in the top medical journals in oncology with over 300 publications to date, and has authored over 50 patents.

GTC-Heme v3.1 09.23

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