Solid Tumor DNA/RNA Profiling

Targeted and Immunotherapy Matching

- Results in 5-10 days
- Detect CNV, indels and fusions
- Low QNS rate of <1%

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.
- Detect Cancer of Unknown Primary (CUP)

The solid tumor profiles provide:

- Targeted and immunotherapy matching
- DNA and RNA profiling
- Tumor Mutation Burden (TMB)
- Microsatellite Instability (MSI)
- Fusion/translocations
- Copy number variation and deletion detection
- HRD/HRR
- Viral HPV testing
- IHC for PD-L1 and FOLR1
- T-cell & B-cell clonality analysis
- HLA genotyping

Solid Tumor Tests

GTC-Solid Tumor Profile PLUS™
DNA/RNA

Liquid Trace™ Solid Tumor
First in class cfDNA/cfRNA

GTC-Solid Tumor Profile™
DNA

GTC-Solid Tumor Profile PLUS™

GTC-Solid Tumor Profile Plus™ tests for abnormalities in 434 DNA genes and >1600 RNA genes

- A pan-tumor assay that can detect all types of cancer
- Includes detection of single nucleotide variation, copy number variation, expression, known and novel fusions, exon skipping, alternative splicing, T-cell & B-cell clonality analysis
- HLA genotyping
- Immunohistochemistry (IHC) testing for PD-L1 and FOLR1 can be complemetary ordered.

Liquid Trace™ Solid Tumor

Liquid Trace™ Solid Tumor is a pan-cancer highly sensitive test evaluating cfDNA and cfRNA

- Can be used for diagnoses, evaluating the host immune response, and identifying biomarkers for predicting response to various therapies.
- Can reduce the need for tissue biopsies for certain cancer patients, especially when obtaining tissue from the tumor is difficult.
- T-cell & B-cell clonality analysis
- HLA genotyping

GTC-Solid Tumor Profile™

GTC-Solid Tumor Profile™ detects the molecular abnormalities in various solid tumors by analyzing the DNA of 434 genes, covering all exons

- Detects microsatellite instability (MSI), tumor mutation burden (TMB) and homologous recombination deficiency (HRD)
- Chromosomal abnormalities
- Results provide prognosis, aid in therapeutic approach and predict response to therapy
- Useful for very small samples

Solid Tumor Tests Comparison Table

Available Tests	GTC-Solid Tumor Profile PLUS™	Liquid Trace™: Solid Tumor	GTC-Solid Tumor Profile™
Genes	**434/>1600**	**284/>1600**	**434**
TAT	**5-10 Days**	**5-7 Days**	**5-7 Days**
Indications	All solid tumors: Detect known (ALK, RET, ROS1, NTRK, etc.) and novel fusions, Exon skipping (MET exon 14), PD-L1 levels, ERBB2 (low HER2) cut-offs and alternative splicing. Chromosomal translocations and amplifications. Viral HPV testing. HLA genotyping. T- & B-cell clonality analysis	All solid tumors: Detect known (ALK, RET, ROS1, NTRK, etc.) and novel fusions, Exon skipping (MET exon 14), PD-L1 levels, ERBB2 (low HER2) cut-offs and alternative splicing. Chromosomal translocations and amplifications. Viral HPV testing. HLA genotyping. T- & B-cell clonality analysis	All solid tumors: Full exon sequencing in 434 genes includes mutations, indels, copy number variation and chromosomal structural abnormalities, TMB, MSI, HRD, HRR
Sample Type	FFPE	Peripheral Blood	FFPE
Sample Requirements	1 H&E slide and 6-8 unstained slides, 5-7 microns of tissue fixed with 10% NBF fixative	Peripheral blood: 8-10 mL. EDTA tube preferred*	1 H&E slide and 6-8 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

Liquid Trace Solid Tumor

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:	C34.90 Malignant neoplasm of unspecified part of unspecified bronchus or lung; C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
Collected Date:	Time: 12:00 AM		
Received Date:	Time: 11:16 AM	Tumor Type:	NSCLC
Reported Date:	Time: 01:20 PM	Stage:	Metastasis

Detected Genomic Alterations				
Level 1 (FDA-Approved)	Level 2 (Standard of Care)	Level 3 (Clinical Evidence)	Level 4 (Biological Evidence)	Other
KRAS (G12C)	t(4;4)(p16;p16) FGFR3-TACC3 fusion mRNA	TP53 (2 mutations), NFE2L2, TET2	-	-No evidence of chromosomal gain or loss

Results Summary

- **-Low level mutations in TP53 (2 mutations), NFE2L2, KRAS (G12C), and TET2 genes**
  -t(4;4)(p16;p16) FGFR3-TACC3 fusion mRNA
  -No evidence of chromosomal gain or loss
  -EBV not detected
  -HPV not detected

  -These findings are consistent with low-level circulating solid tumor DNA/RNA

  -KRAS (G12C) mutation suggests response to KRAS inhibitors (AMG-510, Sotorasib, Adagrasib).

  -FGFR3 fusion suggests response to FGFR inhibitors (erdafitinib).

e A and Wee1 inhibitors.

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Sample Report Page

Tumor Heterogeneity
There are abnormal low-level clones with TP53 (2 mutations), NFE2L2, KRAS (G12C), and TET2 mutations.

Diagnostic Implications	
TP53 (2 mutations), NFE2L2, KRAS (G12C), TET2, FGFR3-TACC3	These findings are consistent with low-level circulating solid tumor DNA/RNA

FDA-Approved Therapeutics in Other Tumor Types	
KRAS (G12C)	AMG-510, Sotorasib, Adagrasib..

Relevant Alteration Associated with Resistance
TP53 mutation is associated with resistance to therapy.
KRAS mutations suggest resistance to targeted anti-EGFR therapy

Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence)	
TP53	Aurora kinase A inhibitors, Wee1 inhibitors, Chk1 inhibitors, kevetrin, APR-246, nutlins, gene therapy
NFE2L2	Bardoxolone Methyl (NF-?B inhibitor)
KRAS (G12C)	KRAS inhibitors, ERK/MEK inhibitors
TET2	DNA methyltransferase inhibitors

Relevant Genes with NO Alteration		
No evidence of mutation in: NRAS, EGFR, and BRAF	No evidence of: FGFR1, FGFR2, FGFR3, FGFR4, NTRK, ALK, ROS1, RET Fusion	No evidence of MET14 deletion,EGFR Viii

Test Description:

This is a comprehensive molecular profile of cell-free DNA (cfDNA) and cell-free RNA (cfRNA), which uses next generation sequencing (NGS) to identify molecular abnormalities (including SNVs, INDELS, CNVs, EBV and HPV) in DNA of 284 genes and RNA in 1501 genes associated with solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

Biological relevance of detected Alterations

- TP53: This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]

- NFE2L2: This gene encodes a transcription factor which is a member of a small family of basic leucine zipper (bZIP) proteins. The encoded transcription factor regulates genes which contain antioxidant response elements (ARE) in their promoters; many of these genes encode proteins involved in response to injury and inflammation which includes the production of free radicals. Multiple transcript variants encoding

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nt isoforms have been characterized for this gene. [provided by RefSeq, Sep 2015]

This gene, a Kirsten ras oncogene homolog from the mammalian ras gene family, encodes a protein that is a member of the small e superfamily. A single amino acid substitution is responsible for an activating mutation. The transforming protein that results is ated in various malignancies, including lung adenocarcinoma, mucinous adenoma, ductal carcinoma of the pancreas and colorectal oma. Alternative splicing leads to variants encoding two isoforms that differ in the C-terminal region. [provided by RefSeq, Jul 2008]

The protein encoded by this gene is a methylcytosine dioxygenase that catalyzes the conversion of methylcytosine to 5-ymethylcytosine. The encoded protein is involved in myelopoiesis, and defects in this gene have been associated with several proliferative disorders. Two variants encoding different isoforms have been found for this gene. [provided by RefSeq, Mar 2011]

formation

first-in-class agent targeting mutant p53. In vitro and in vivo preclinical models have demonstrated that APR-246 has excellent efficacy adenocarcinoma and squamous cell carcinoma) and potently synergises with chemotherapies used in the treatment of OC, restoring chemotherapy-resistant tumours. An initial phase I clinical trial has shown APR-246 to be safe in humans and early results from a ning phase Ib/II trial of APR-246 with carboplatin and liposomal doxorubicin in ovarian cancer have been promising. Together, these a strong rationale for investigating the efficacy of APR246 in OC.

been used in trials studying the treatment of Prostatic Neoplasms, Hematologic Neoplasms, and Platinum Sensitive Recurrent High-s Ovarian Cancer With Mutated p53.

n analogue of PRIMA-1, which modifies the core domain of mutant p53, resulting in restoration of wild-type p53 conformation and of normal p53 function, leading to increased cell cycle arrest and tumor cell death (PMID: 20498645).

lso known as Lumakras, AMG-510) is a first-in-class, orally bioavailable, and selective KRAS G12C covalent inhibitor. AMG-510 nhibits KRAS G12C by locking it in an inactive GDP-bound state. AMG-510 is the first KRAS G12C inhibitor in clinical development and regression of KRAS G12C tumors.

2021, the U.S. Food and Drug Administration approved Lumakras (sotorasib) as the first treatment for adult patients with non-small cell whose tumors have a specific type of genetic mutation called KRAS G12C and who have received at least one prior systemic therapy.

WRTX849) is a KRAS inhibitor being investigated for the treatment of KRAS G12C mutant lung and colon adenocarcinomas. Normally KRAS, activating the protein and promoting effectors to the MAP kinase pathway. GTP is hydrolyzed to GDP, and KRAS is inactivated. mutations impair hydrolysis of GTP, leaving it in the active form.

Sample Report Page

is a reversible inhibitor of mitogen-activated protein kinase 1 (MAPK)/extracellular signal regulated kinase 1 (MEK1) and MEK2.

MEK inhibitor Cobimetinib specifically binds to and inhibits the catalytic activity of MEK1, resulting in inhibition of extracellular signal-related kinase 2 (ERK2) phosphorylation and activation and decreased tumor cell proliferation. Cobimetinib targets kinase activity in the RAS/RAF/MEK/ERK pathway.

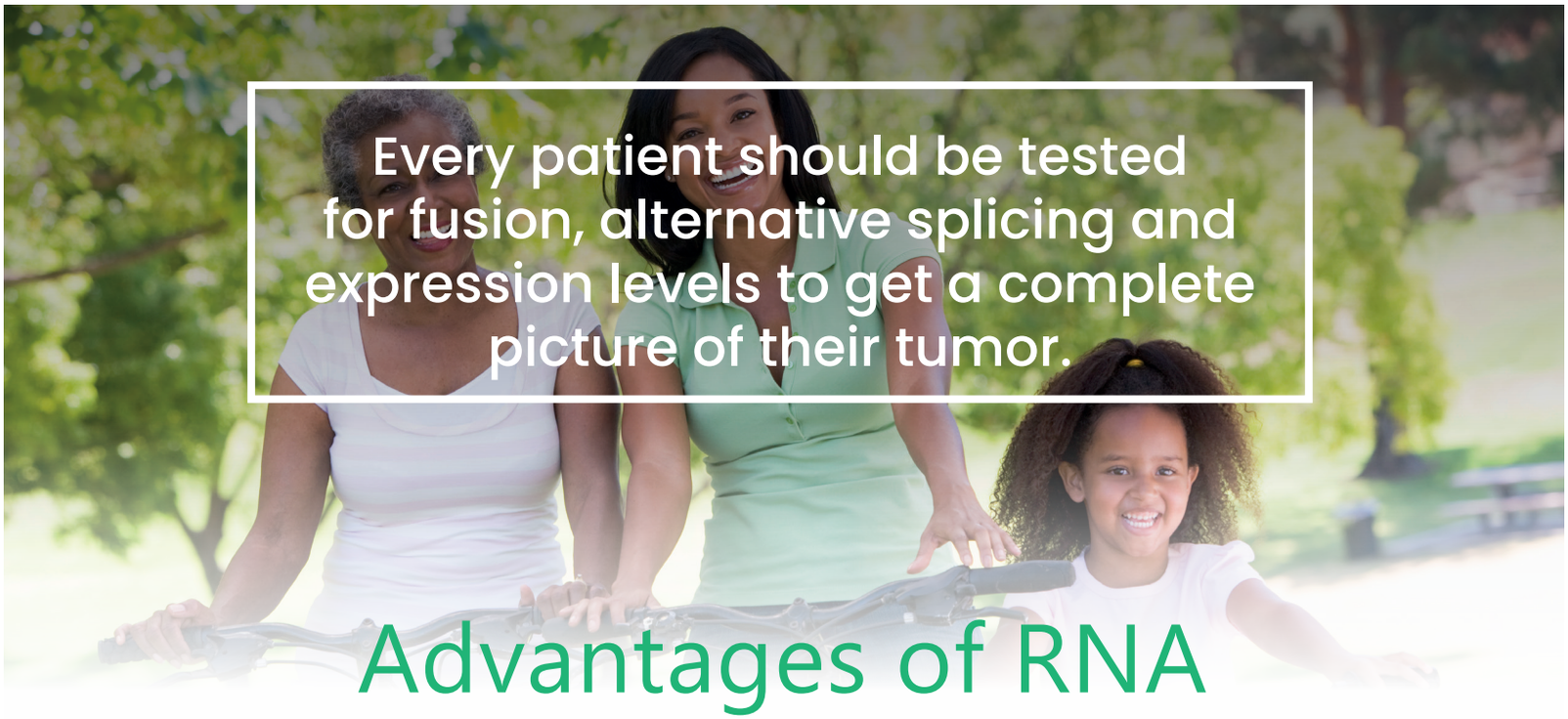
Trametinib

Trametinib is an orally bioavailable inhibitor of mitogen-activated protein kinase kinase (MEK MAPK/ERK kinase) with potential antineoplastic activity. Trametinib specifically binds to and inhibits MEK 1 and 2, resulting in an inhibition of growth factor-mediated cell signaling and cellular proliferation in various cancers. MEK 1 and 2, dual specificity threonine/tyrosine kinases often upregulated in various cancer cell types, play a key role in the activation of the RAS/RAF/MEK/ERK signaling pathway that regulates cell growth.

Azacitidine

Azacitidine is a pyrimidine analogue that inhibits DNA methyltransferase, impairing DNA methylation. It is also an antimetabolite of cytidine, incorporated primarily into RNA. Azacytidine has been used as an antineoplastic agent.

Azacitidine for injection is a nucleoside metabolic inhibitor indicated for the treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome (MDS) subtypes: Refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in



Every patient should be tested for fusion, alternative splicing and expression levels to get a complete picture of their tumor.

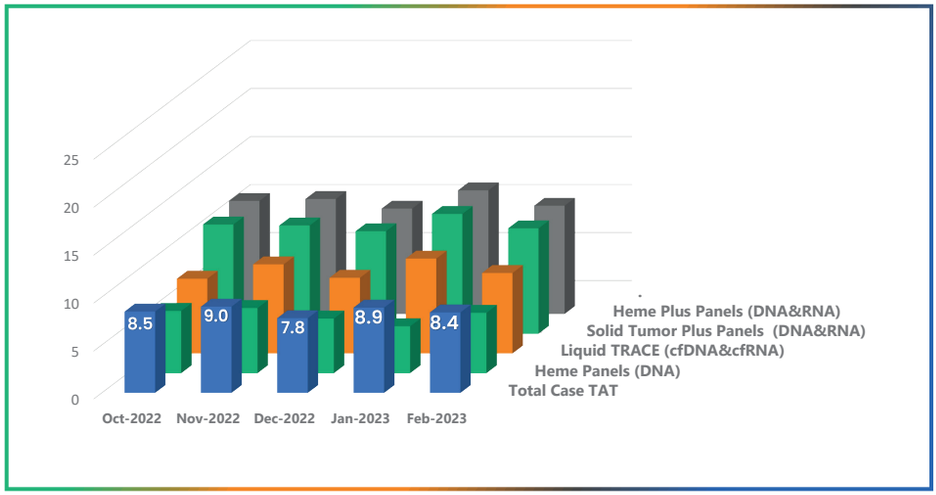
Advantages of RNA

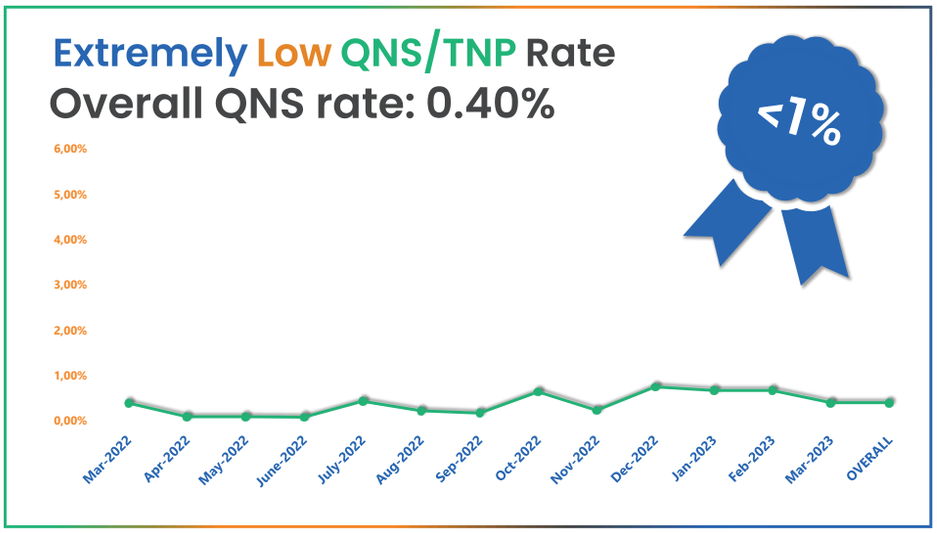
GTC RNA results are compared against thousands of cases with expression levels, then run through our sophisticated AI systems that provide a summary of the findings for each patient.

- RNA can detect all possible translocations that may involve ALK, ROS1, RET, NTRK and FGFR.
- Our NGS assay will detect MET exon 14 skipping, which is also currently in NCCN guidelines and responds very well to capmatinib (TABRECTA™).
- With RNA testing we can evaluate the microenvironment, immune response, PD-L1, PD-L2, PD-1, CD8, etc., and determine the MET exon 14 skipping and various alternative splicing, expression and amplification of ERBB2 (HER2), MET and EGFR.
- Our NGS can detect all NTRK (1,2,3) fusions, which are also in current NCCN guidelines and patients will be eligible for NTRK inhibitors such as entrectinib (ROZLYTREK®) and larotrectinib (VITRAKVI®).
- Our assay can detect the ALK, ROS1, and RET fusions at significantly higher sensitivity than FISH and will require no additional tissue.
- Our NGS can detect the presence of ERBB2 (HER2) amplification/ overexpression, which is present in 5% of lung cancer and is within NCCN guidelines.
- Viral HPV testing is useful for screening head and neck cancer, plus staging/screening for cervical lesions.

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.





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 large labs benefit from 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. The informatics tools we use utilize 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.

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