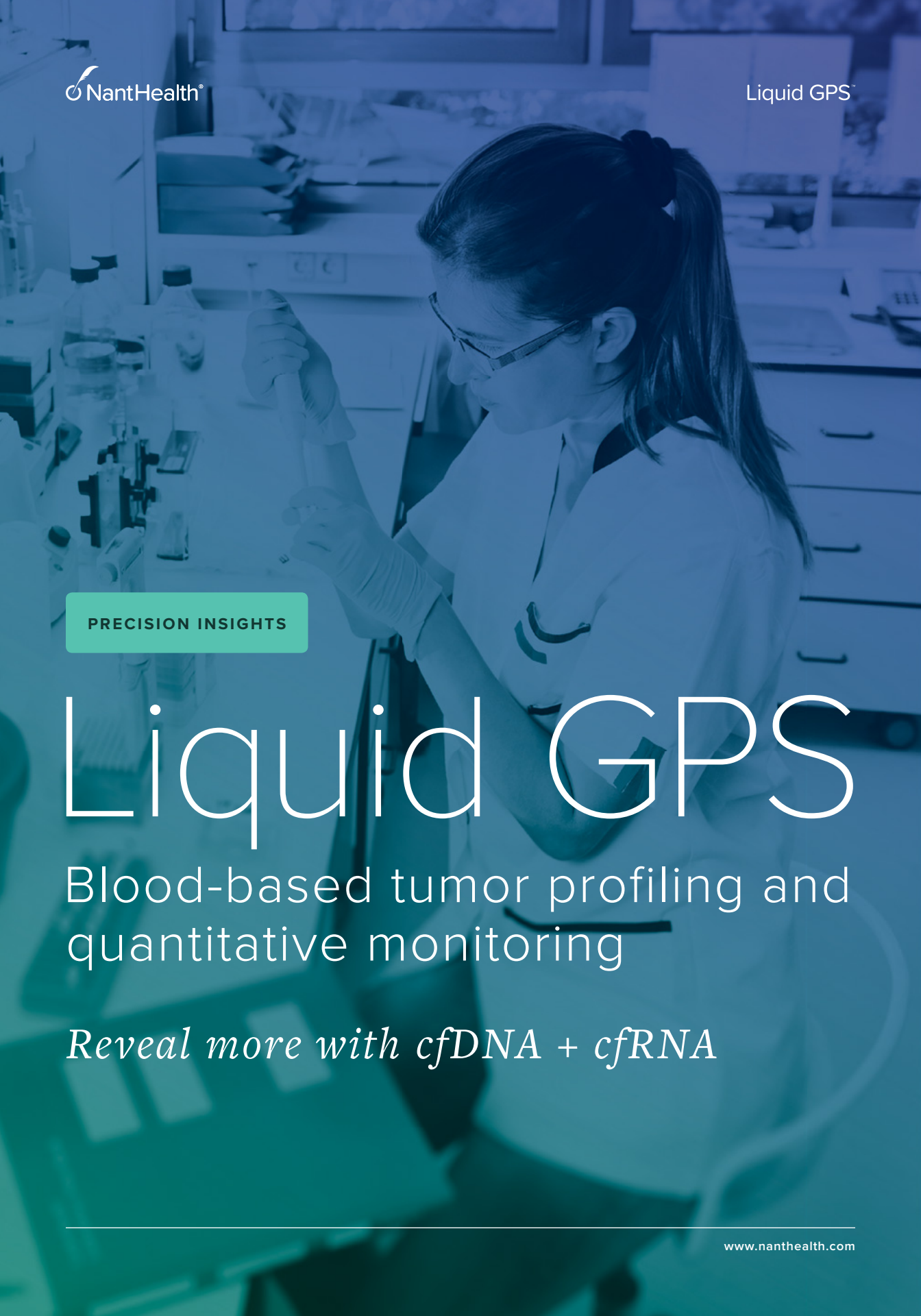


PRECISION INSIGHTS

Liquid GPS

Blood-based tumor profiling and quantitative monitoring

Reveal more with cfDNA + cfRNA

NantHealth®

Why Blood-Based Tumor Profiling?

Although tissue-based molecular profiling remains the gold-standard for informing personalized cancer treatment decisions, it is not always feasible. One study identified that 13% of non-small cell lung cancer patients had insufficient tissue available for molecular testing.[1]

Even when tissue testing is feasible to guide initial treatment decisions, cancer is a dynamic disease. It is essential that oncologists have timely insight into how well the patient is responding to treatment. Imaging helps, but is infrequent, expensive, and may show disease progression later than can be seen at a molecular level.[2]

Liquid GPS – Reveal More with cfDNA + cfRNA

Liquid GPS is a blood-based molecular test that provides oncologists with a powerful tool for noninvasive tumor profiling and quantitative monitoring of treatment response. Liquid GPS looks beyond cfDNA to cfRNA, which allows profiling and trending of actionable biomarkers that cannot be assessed through cfDNA alone. In addition to providing molecular insight into key guidelines-based biomarkers (e.g., EGFR, ALK, ROS1, KRAS), this powerful RNA-based approach enables a variety of capabilities and applications not typically available from a liquid biopsy test

Key applications of Liquid GPS

Targeted therapy monitoring – including ALK and ROS1 by cfRNA

In addition to assessing guideline-recommended mutations (e.g., EGFR, BRAF, KRAS, and NRAS), Liquid GPS provides cfRNA-based testing and monitoring for gene fusions and translocations (i.e., ALK, ROS1). RNA has also been shown to be a more accurate indicator of fusions and translocations compared to DNA, which can miss or incorrectly classify gene fusions.[3]

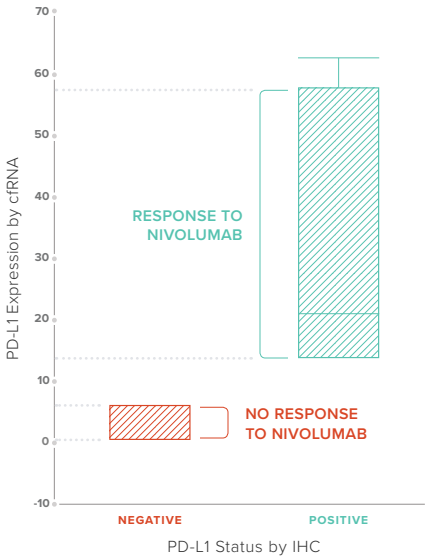
Immunotherapy monitoring – PD-L1, CTLA-4, LAG-3, and TIM-3

With immunotherapy increasingly becoming a central component of care in many cancers, molecular tools are evolving to give oncologists new and earlier insights into their effectiveness in each patient.

Liquid GPS includes 4 analytes associated with approved and investigational immunotherapies – PD-L1, CTLA-4, LAG-3, and TIM-3. PD-L1 via Liquid GPS's cfRNA analysis has been demonstrated to correlate to measurement by IHC, as shown to the right.[4]

Not only can this information inform an oncologist's initial treatment selection, it can also be used to monitor response over time. In fact, blood-based PD-L1 assessment has been shown to objectively differentiate between true progression and pseudoprogression, which may help to avoid erroneously changing treatment due to pseudoprogression.[5]

Concordance between PD-L1 analysis by Liquid GPS cfRNA vs IHC



Chemotherapy monitoring

Liquid GPS includes 11 analytes associated with response or resistance to commonly used chemotherapies, including ERCC1 to inform use of platinums and TUBB3 to inform use of taxanes.

Highlights

Inform and Evolve Treatment

Monitor and inform treatment when tissue is unavailable.

Reveal More Information

Go beyond cfDNA with cfRNA expression.

Easy, Fast, Noninvasive

Get molecular insights in <7 days with a simple blood draw; no special processing at point-of-care – send at room temperature.

Actionable Reports to Inform Oncologists' Treatment Strategies

The Liquid GPS report — accessible through NantHealth's web-based Precision Insights Portal – offers insight into therapies that may have potential benefit and therapies to which the cancer may be resistant.


NantHealth | Liquid GPS

Patient Report

Liquid Analysis — Results

Potentially Effective Drugs — Based Upon

Potentially Ineffective Drugs — Based Upon

Notes from the Medical Director

Based on analysis of cfDNA and cfRNA, the report provides clear information on:

- FDA-approved therapies with potential clinical benefit
- Active clinical trials for investigational therapies
- Therapies to which the tumor may be resistant

Other detailed information within the report includes:

- Trend analysis of analyte levels
- cfRNA level as measured by beta-actin
- Supporting information and references for analyte-drug associations

NantHealth Precision Insights

GPS Cancer
Precise and comprehensive tissue-based profiling

Liquid GPS
Blood-based tumor profiling and quantitative monitoring

Precision Insights Portal
Bringing precision insights to evidence-based care

Current Analytes

	TARGETED THERAPY MARKERS			CHEMOTHERAPY MARKERS			IMMUNOTHERAPY MARKERS	
RNA EXPRESSION	EGFR	AR / AR-V7	ROS1 fusion	ERCC1	hENT1	TOP1	PD-L1	CTLA-4
	HER2	c-MET	ALK fusion	XRCC1	TP	TOP2A	TIM-3	LAG-3
				MGMT1	RRM1	TOP2B		
				TUBB3	TS			
DNA MUTATIONS	KRAS	BRAF		*Liquid GPS also reports on cell-free RNA level as measured by beta-actin.*				
	EGFR	NRAS						

AR-V7 testing in prostate cancer

Pill-based, androgen-directed therapies abiraterone and enzalutamide are increasingly used by both medical oncologists and urologists to manage patients with metastatic castration-resistant prostate cancer (mCRPC). In fact, these two drugs are often used sequentially. How do you know if your patient is unlikely to respond? AR-V7 has been shown to strongly predict resistance to both abiraterone and enzalutamide.[6]

AR-V7 positive patients are unlikely to respond to these drugs, and may be more likely to benefit from other treatment strategies, such as taxane chemotherapy.[7] Up to 12% of mCRPC patients are AR-V7 positive prior to therapy with either abiraterone or enzalutamide, and therefore, likely to be resistant. Up to 25% are AR-V7 positive after treatment with one of these drugs.

Liquid GPS is the only liquid biopsy that assesses AR-V7 via cfRNA. Compared to assessing AR-V7 in circulating tumor cells (CTCs), analysis through cfRNA has demonstrated improved sensitivity, and may allow detection in less advanced disease, prior to the point when CTCs are detectable in the blood (e.g., tumors confined to bone metastases).[8]

References

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[5] Lee JH, Long GV, Menzies AM, et al. Association Between Circulating Tumor DNA and Pseudoprogression in Patients With Metastatic Melanoma Treated With Anti–Programmed Cell Death 1 Antibodies. JAMA Oncol. Published online February 08, 2018. doi:10.1001/jamaoncol.2017.5332

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[7] Scher et al. Association of AR-V7 on Circulating Tumor Cells as a Treatment-Specific Biomarker With Outcomes and Survival in Castration-Resistant Prostate Cancer. JAMA Oncol. 2016 Nov 1;2(11):1441-1449.

[8] Cho WJ et al. Gene expression analysis of bone metastasis and circulating tumor cells from metastatic castrate-resistant prostate cancer . J Transl Med. 2016; 14: 72.

Variants for Selected Analytes

GENE	VARIANTS
KRAS	G12C
	G12D
	G12A
	G12V
	G12S
	G12R
	G13D
	Q61H

GENE	VARIANTS
EGFR	L858R
	L861Q
	G719S
	Ex19Del
BRAF	V600E

GENE	VARIANTS
NRAS	G12D
	Q61K
	Q61L
	Q61R
EML4-ALK	V1
	V2
	V3
	V5a

GENE	VARIANTS
ROS-1	CD74-ROS1 V1
	CD74-ROS1 V2
	CD74-ROS1 V3
	EZR-ROS1 V1
	EZR-ROS1 V2

All other analytes are expression assays.

Specifications

Method

cfDNA and cfRNA by rt-PCR

Sample requirements

Two 10 ml tubes of peripheral whole blood

Turn-around time

< 7 days from receipt of specimen

	MAF/TUMOR FRACTION	SENSITIVITY	POSITIVE PREDICTIVE VALUE (PPV)
MUTATIONS BY cfDNA (EGFR, KRAS, NRAS, BRAF)	≥ 0.4%	95.7% - 99.9% (varies by biomarker)	94.0 - 99.9% (varies by biomarker)

	ALLELE FRACTION	SENSITIVITY	POSITIVE PREDICTIVE VALUE (PPV)
ALK FUSIONS BY cfRNA	> 0.4%	99.9%	≥ 99.9%
ROS1 FUSIONS BY cfRNA	> 0.4%	96.0%	≥ 99.9%

Expression assays by cfRNA	LIMIT OF DETECTION (in 10mL of peripheral blood)	SENSITIVITY	POSITIVE PREDICTIVE VALUE (PPV)
PD-L1	27 copies	99.9%	≥ 99.9%
AR-V7	13 copies	100.0%	≥ 90.0%
C-MET	12 copies	92.0%	≥ 92.0%
ALL OTHER EXPRESSION ASSAYS	1-2 copies	N/A	N/A

NantHealth®

ABOUT NANTHEALTH

NantHealth's Mission is to improve the delivery of healthcare and optimize patient outcomes by leveraging the latest advancements in precision medicine and software technologies to enable true value based care.

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