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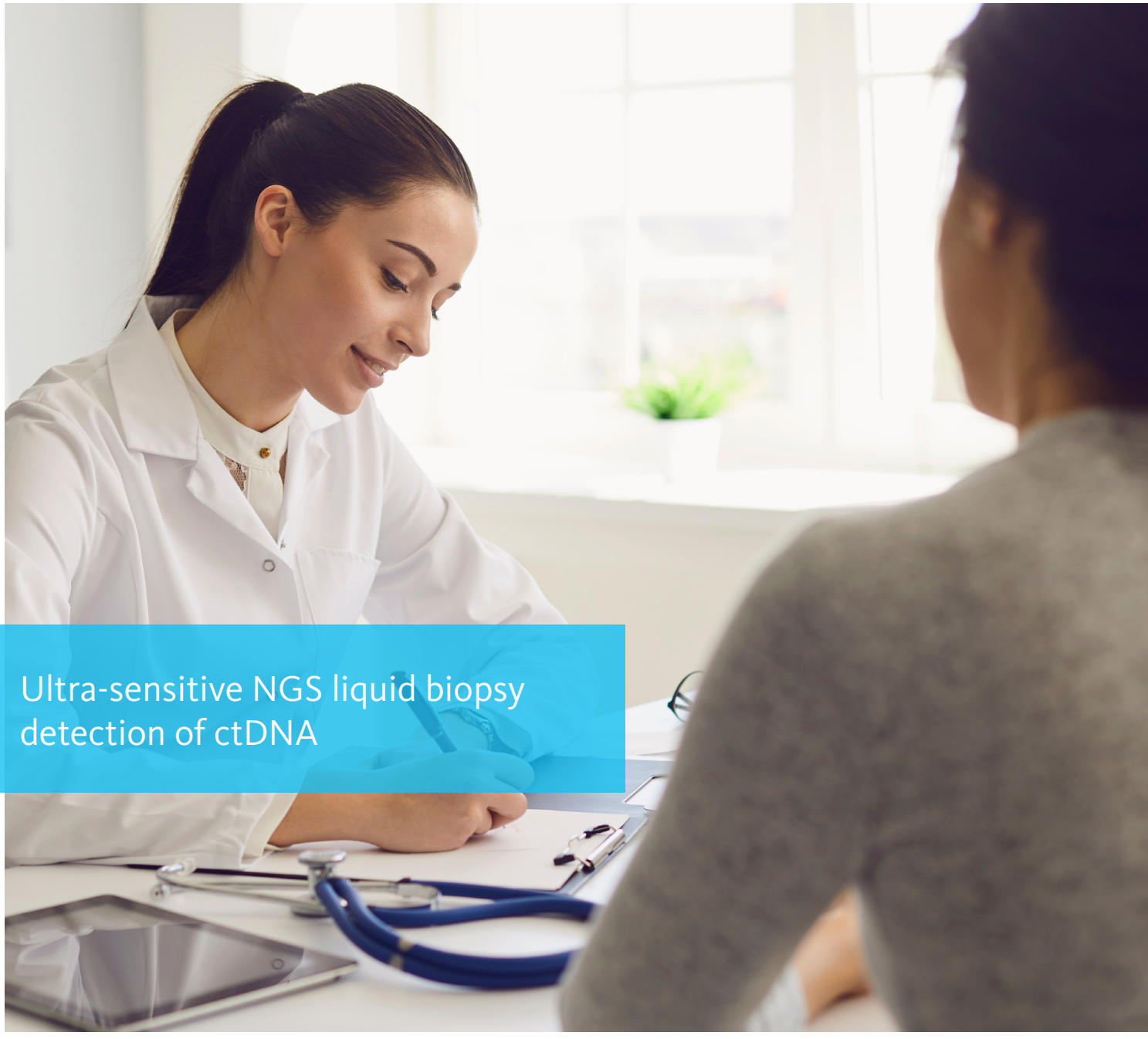
Plasma-Safe-SeqS



Ultra-sensitive NGS liquid biopsy detection of ctDNA

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BIOPHARMA SOLUTIONS

Focused, sensitive genomic sequencing

Focused and sensitive genomic sequencing can expedite oncology studies and provide deeper insights into patient response to new therapies. Driving a new era of optimism, liquid biopsy testing using next-generation sequencing (NGS) is accelerating the pace of drug discovery and therapeutic development, enabling new treatment alternatives, and renewed hope, for cancer patients.

Plasma-Safe-SeqS: Ultra-sensitive NGS liquid biopsy detection of ctDNA

Building on the innovative OncoBEAM® technology that powered the liquid biopsy revolution, Plasma-Safe-SeqS provides ultra-sensitive detection of clinically relevant mutations to facilitate the development of novel oncology treatments. Applications of Plasma-Safe-SeqS technology may include:

- Informing therapy selection
- Monitoring tumor response
- Identifying targetable resistance
- Detecting minimal residual disease (MRD)

Plasma-Safe-SeqS is designed specifically for the measurement of ctDNA and gene sequencing panels are developed for particular clinical intended uses where high sensitivity detection may provide unique insights and improve outcomes.

Sensitivity matters

Clinical trial enrollment

Ultra-sensitive technology allows clinical trial sponsors to screen fewer patients to achieve sufficient study enrollment, leading to significantly accelerated clinical trial timelines, reduced costs, and improved trial outcomes.

Treatment response

Detection of somatic mutations enables meaningful comparison of ctDNA levels across timepoints for longitudinal monitoring. Correlating Plasma-Safe-SeqS results with clinical observations may reveal promising opportunities for novel therapeutic strategies.[1]

Minimal residual disease (MRD) detection and recurrence surveillance

Ultra-high sensitivity is essential for reliable detection of extremely small quantities of ctDNA that may be present post-intervention, as well as for early identification of increasing ctDNA levels which may signify relapse.[2]

Maximizing accuracy by minimizing errors

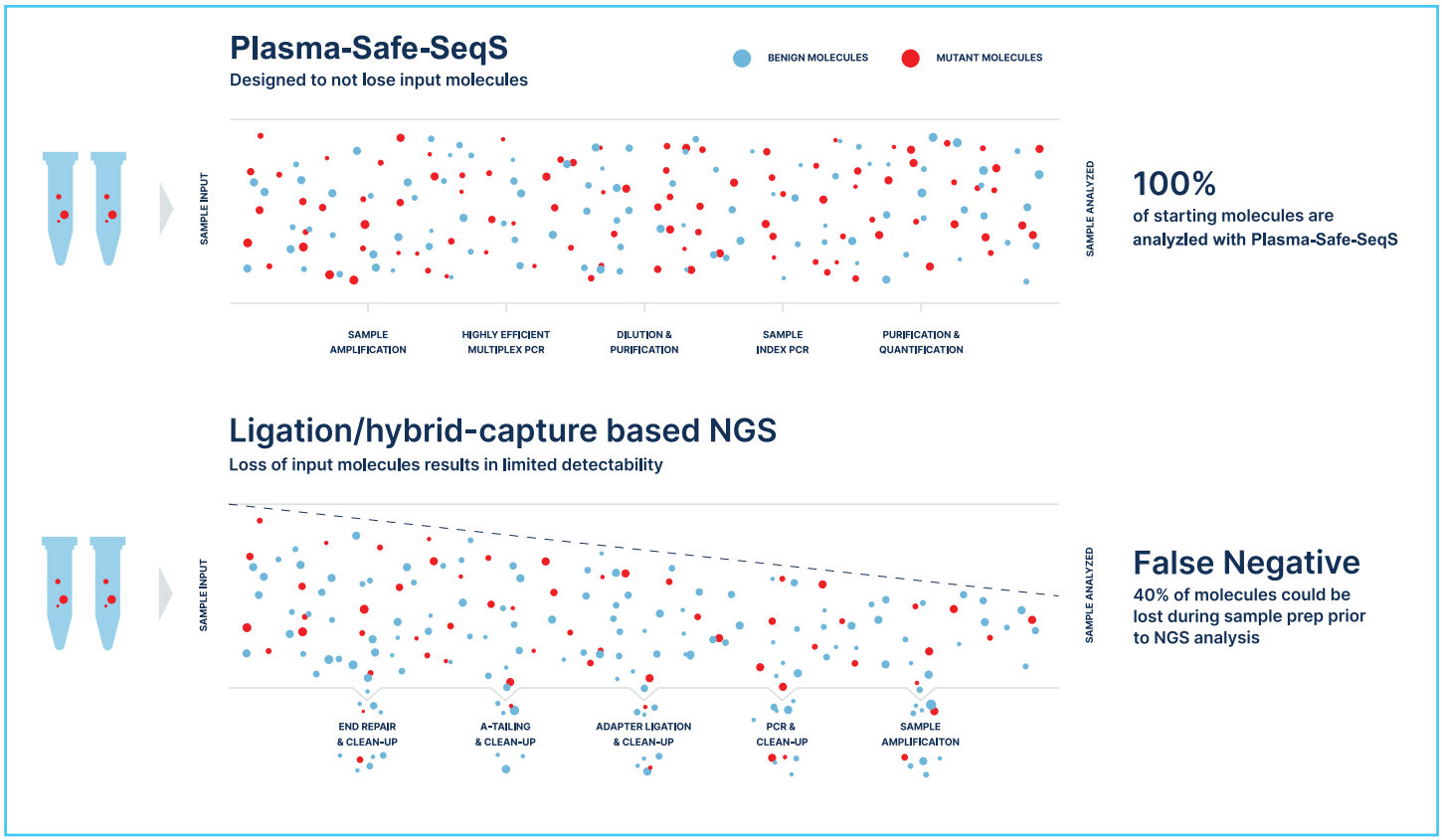
Plasma-Safe-SeqS is a low error rate ("safe") technology, where each DNA molecule is assigned a unique identifier (UID), and UID families are amplified and deep sequenced. The Plasma-Safe-SeqS platform discriminates real mutations from errors potentially introduced during the amplification and sequencing process, resulting in more accurate mutation detection.

Routine clinical testing: Plasma-Safe-SeqS vs pan-cancer NGS

	Plasma-Safe-SeqS (NGS)	Other ctDNA NGS
Sensitivity	MAF >0.03%	MAF <0.5-1.0%
Sample Volume	2x10mL tubes of whole blood	≥2x10mL tubes of whole blood
Gene Coverage	Clinically-relevant, adjustable coverage	Indiscriminate, fixed coverage of 40+ genes
Customizable	High fidelity	Low capability to customize
Cost	Efficient	High

No molecule left behind

Plasma-Safe-SeqS technology is designed to preserve mutant molecules throughout the workflow, leaving a more robust sample to identify patients even with extremely low-level ctDNA. Other assays, particularly broad, hybrid-capture-based pan-cancer panels, are known to lose up to 40% of all input DNA during sample prep, which decreases reliable detection of ctDNA.[3]



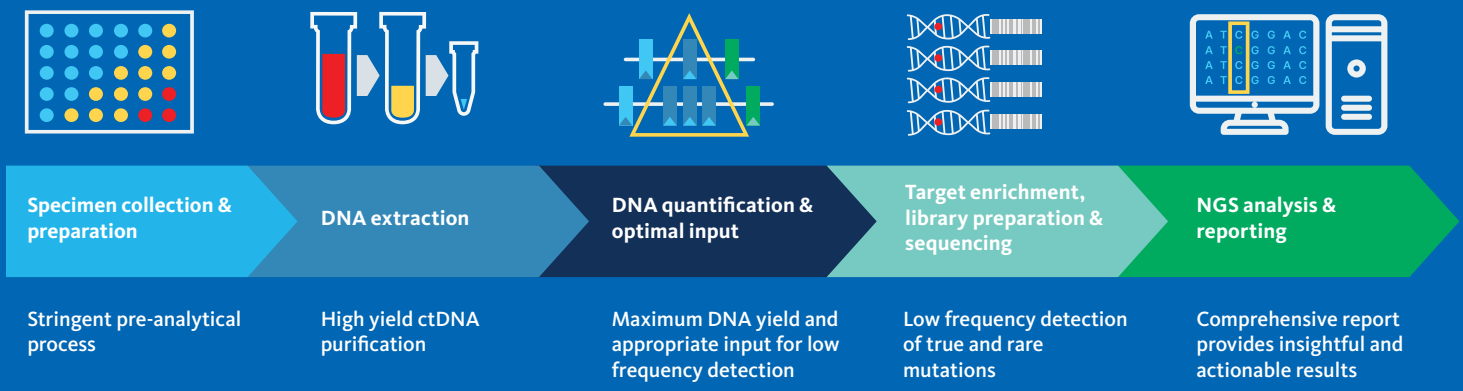
Flexible, focused gene coverage

When it comes to tumor profiling, dynamic NGS technology is vital to delivering useful clinical information. With traditional broad panel NGS testing, sample-input DNA often limits assay sensitivity and results in increased costs since fixed pan-cancer NGS assays expend sequencing power on unnecessary gene regions.

By accurately identifying ctDNA across various tumor types, Plasma-Safe-SeqS's best-in-class sensitivity can expedite and improve advanced therapeutic clinical development. Built-in workflow optimizations and conservation of input DNA molecules ensure efficient ctDNA detection for clinically relevant targets.

Optimized workflow for ultra-sensitive ctDNA detection

Plasma-Safe-SeqS is expertly designed to ensure low-frequency mutant molecule detection with high specificity and efficiency. The Plasma-Safe-SeqS workflow delivers best-in-class performance for ctDNA analysis by optimizing all steps, from pre-analytics through data analysis and reporting.



Overview of the Plasma-Safe-SeqS Workflow in Sysmex Inostics' CLIA-certified Laboratory.

Plasma-Safe-SeqS ultra-sensitive assay portfolio[4]

The Plasma-Safe-SeqS portfolio of CLIA-validated panels addresses the needs of biopharma sponsors seeking ultra-sensitive detection of circulating DNA to support clinical development. All Plasma-Safe-SeqS testing is performed in the Sysmex Inostics CLIA lab in Baltimore, Maryland.

Plasma-Safe-SeqS CLIA-validated panel	Clinically relevant gene regions	Clinical intended uses	Limit of detection (95% CI)	DNA input levels tested	Corresponding MAF for 20,000 copies (~66 ng DNA)
RAS-RAF pathway (RAS-RAF-SEQ)	BRAF, KRAS, NRAS, AKT1, PIK3CA	■ Therapy selection ■ Therapeutic monitoring	7 mutant molecules	5,000-10,000 GE	0.035% MAF
HPV-related cancers (HPV-SEQ)	HPV 16, HPV 18	■ Therapy selection ■ Therapeutic monitoring ■ Recurrence surveillance	2 mutant molecules	1,000-20,000 GE	0.035% MAF
Breast cancer (BC-SEQ)	AKT1, ERBB2, ESR1, KRAS, PIK3CA, TP53	■ Therapy selection ■ Therapeutic monitoring ■ Recurrence surveillance	6 mutant molecules	1,000-30,000 GE	0.030% MAF
AML MRD (AML-MRD-SEQ)	FLT3, IDH1, IDH2, NPM1, BCOR, BRAF, CEBPA, GATA2, JAK2, KIT, KRAS, NRAS, PRPF8, PTPN11, SETBP1, SF3B1, SRSF2, TP53, U2AF1, ZRSR2	■ Therapy selection ■ Therapeutic monitoring ■ MRD detection ■ Recurrence surveillance	7 mutant molecules	1,000- 20,000 GE	0.035% MAF

Sample requirements and processing time

Sample specification

2x10mL tubes of whole blood

Pre-analytical sample handling

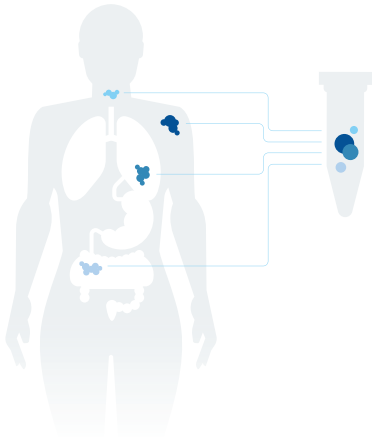
Sysmex Inostics' validated shipping kits and temperature loggers ensure sample stability

Result turnaround time

7 – 10 business days

PLASMA-SAFE-SEQS TECHNOLOGY

Ultra-sensitive across clinically relevant genomic regions



Sysmex Inostics' Plasma-Safe-SeqS technology offers highly sensitive mutation detection across the most clinically relevant gene targets. Plasma-Safe-SeqS is designed specifically for the measurement of ctDNA and panels are developed for particular clinical intended uses where high sensitivity detection may provide unique insights and improve outcomes.

Plasma-Safe-SeqS demonstrates equivalent performance to OncoBEAM digital PCR and is 10 times more sensitive than other liquid biopsy NGS Methods. This level of sensitivity allows clinical trial sponsors to accelerate trial enrollment and evaluate biomarker hypotheses with greater power.

Have a question about the Plasma-Safe-SeqS technology?

Please visit www.sysmex-inostics.com/products/Plasma-Safe-SeqS

REFERENCES

1 Dawson, S.J. et al. (2013) Analysis of circulating tumor DNA to monitor metastatic breast cancer. N Engl J Med. 368:1199-209. doi:10.1056/NEJMoa1213261.

2 Rodriguez, et al. (2019) Detection of TP53 and PIK3CA mutations in circulating tumor DNA using next-generation sequencing in the screening process for early breast cancer diagnosis. J Clin Med. 8(8), 1188.doi: 10.3390/jcm8081183.

3 Aigrain, L., Gu, Y., & Quail, M. A. (2016). Quantitation of next generation sequencing library preparation protocol efficiencies using droplet digital PCR assays - a systematic comparison of DNA library preparation kits for Illumina sequencing. BMC Genomics, 17(1), 458.

4 Internal validation data on file, Sysmex Inostics, Inc., 2021.

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