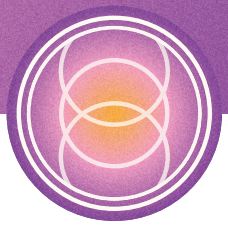
sysmex | Lighting the way with diagnostics

BC-SEQ

Ultra-sensitive mutation detection



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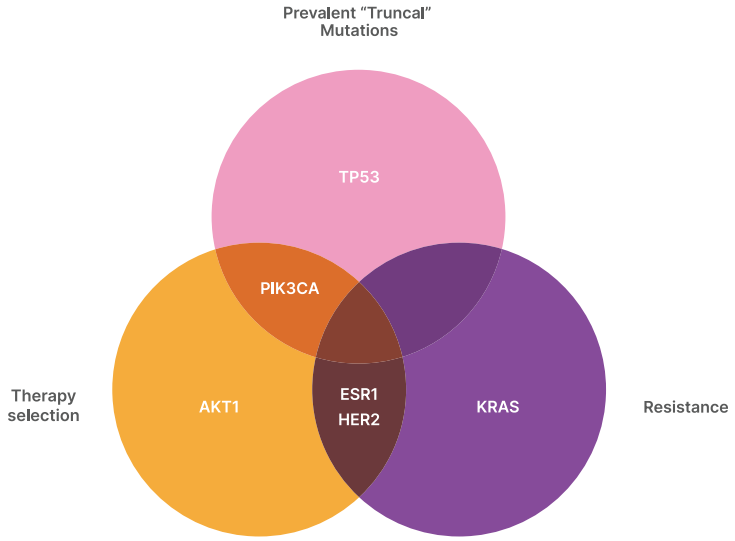
PIK3CA, ESR1, AKT1, ERBB2, TP53, AND KRAS

Reliable detection of low-frequency plasma mutations

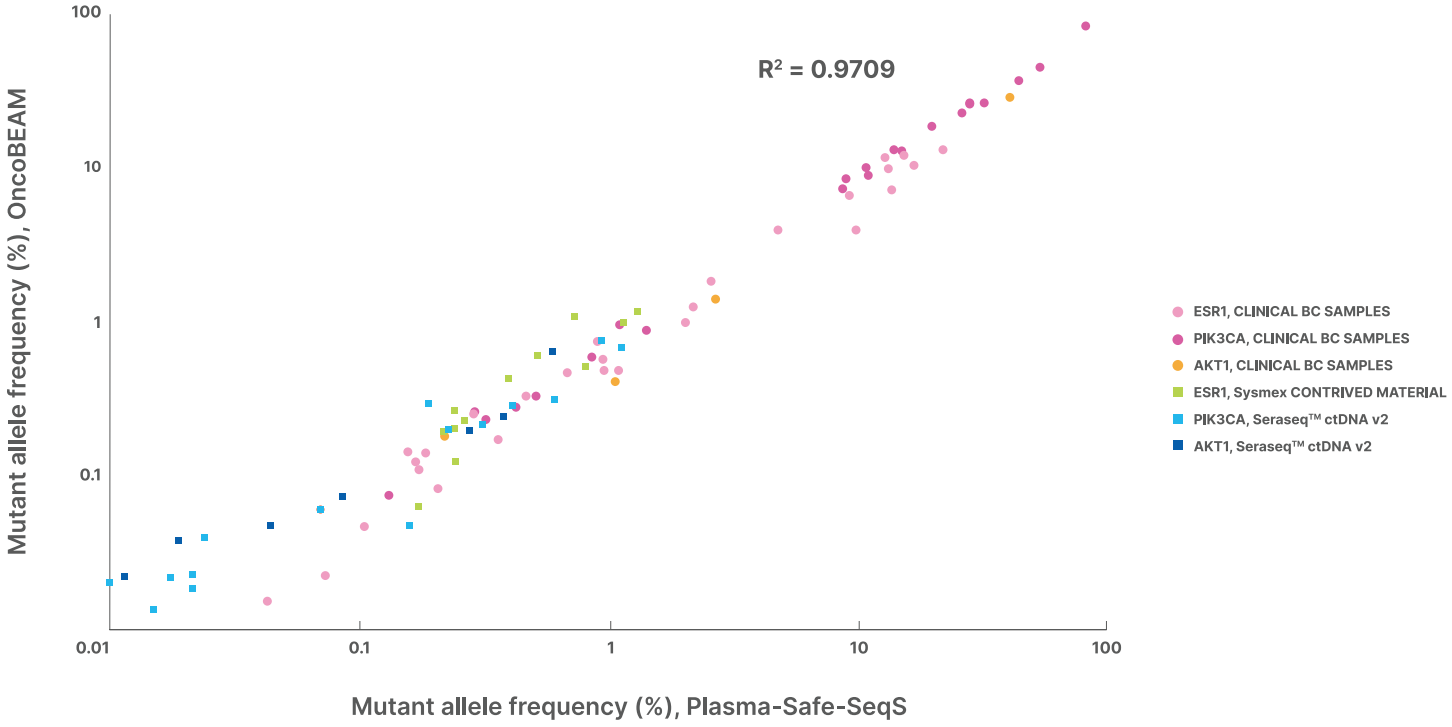
Sysmex's Plasma-Safe-SeqS Breast Cancer Panel is a clinical grade, ultra-sensitive liquid biopsy solution for the identification of gene mutations in PIK3CA, ESR1, AKT1, ERBB2, TP53, and KRAS to detect established and emerging therapeutic indications, resistance mutations, and frequently occurring somatic alterations in breast cancer.

The Plasma-Safe-SeqS Breast Cancer Panel can detect clinically relevant mutations in circulating tumor DNA (ctDNA) from patients with breast cancer across a broader range of genomic regions with a sensitivity equivalent to Sysmex Inostics' OncoBEAM digital PCR liquid biopsy breast cancer test.

The Plasma-Safe-SeqS Breast Cancer Panel is available as a CLIA testing service.



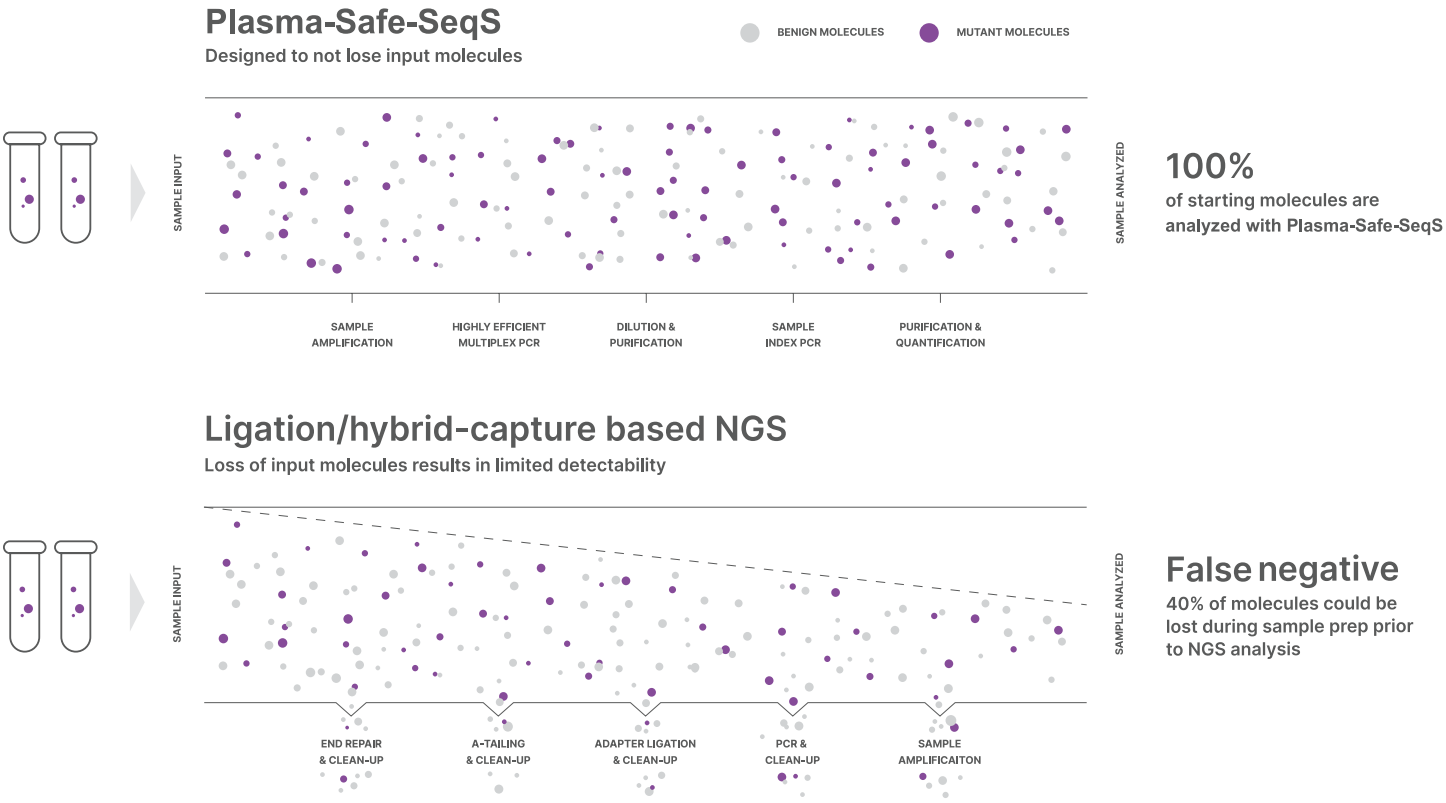
Plasma-Safe-SeqS NGS sensitivity similar to OncoBEAM™



Thirty-five clinical samples (2 ml plasma) and replicate testing (3x/method) of contrived material using Plasma-Safe-SeqS and OncoBEAM Breast Cancer Tests.[2]

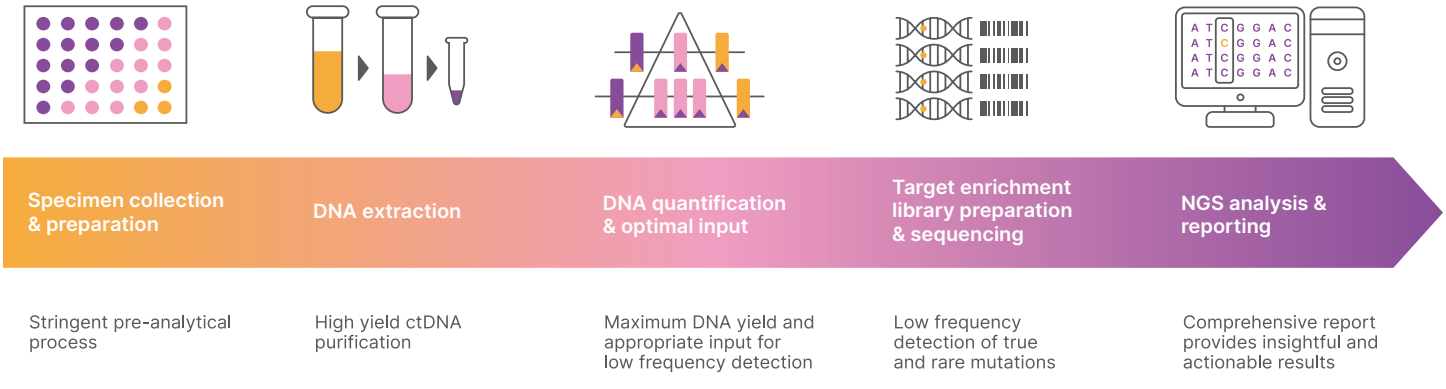
No molecule left behind

Plasma-Safe-SeqS technology was designed not to lose mutant molecules throughout the workflow. 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.



Plasma-Safe-SeqS workflow

The Plasma-Safe-SeqS workflow delivers exquisite performance for ctDNA analysis through optimization of all steps, from pre-analytics through data analysis and reporting.



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

Panel features

Ultra-high sensitivity coverage of the most relevant targets for HR+ breast cancer yields more information, with greater efficiency.

Plasma-Safe-SeqS Breast Cancer Panel coverage

GENE	TRANSCRIPT	AMINO ACIDS COVERED	EXAMPLE VARIANTS WITH KNOWN CLINICAL RELEVANCE
AKTI	ENST00000554581	17–23	c.49G>A (p.E17K)
ERBB2	ENST00000269571	303–315, 754–769, 770–786	c.929C>T (p.S310F), c.929C>A (p.S310Y), c.2301C>G (p.I767M), c.2313_2324dup (p.V772_A775dup), c.2314_2325dup (p.V772_A775dup)
ESR1	ENST00000440973	370–381, 460–473, 529–538	c.1138G>C (p.E380Q), c.1387T>C (p.S463P), c.1607T>G (p.L536R), c.1607T>C (p.L536P), c.1607T>A (p.L536H), c.1607_1608delinsAG (p.L536Q), c.1607_1608delinsAT (p.L536H)
KRAS	ENST00000256078	4–14	c.34G>A (p.G12S), c.34G>C (p.G12R), c.34G>T (p.G12C), c.35G>A (p.G12D), c.35G>C (p.G12A), c.35G>T (p.G12V)
PIK3CA	ENST00000263967	86–92, 111–117, 119–122, 345–352, 363–371, 418–421, 450–462, 538–553, 714–728, 1040–1056	c.263G>A (p.R88Q), c.353G>A (p.G118D), c.1633G>A (p.E545K), c.1633G>C (p.E545Q), c.1634A>C (p.E545A), c.1634A>G (p.E545G), c.3127A>G (p.M1043V), c.3129G>A (p.M1043I), c.3129G>C (p.M1043I)
TP53	ENST00000269305	49–77, 99–125, 126–141, 151–179, 192–219, 233–260, 262–285, 297–306, 308–331, 332–360	c.488A>G (p.Y163C), c.524G>A (p.R175H), c.817C>T (p.R273C), c.818G>A (p.R273H)

Performance specifications

Analytical sensitivity and specificity of the Plasma-Safe-SeqS Breast Cancer Panel

# OF ctDNA MOLECULES	MUTANT ALLELE FREQUENCY (MAF)*	ANALYTICAL SENSITIVITY	ANALYTICAL SPECIFICITY	REPORTING THRESHOLD
20	0.10%	100%	100%	6 ctDNA molecules (0.030% MAF)
10	0.050%	98%		
5	0.025%	94%		
3	0.015%	78%		

*Based on cell-free DNA input of 66ng. Analytical sensitivity and specificity cited above is for targeted, clinically important regions.
Reporting Threshold is set above LoD95.

Plasma-Safe-SeqS comparison to the gold-standard OncoBEAM technology

OncoBEAM set the gold standard for ctDNA analysis being the most sensitive digital PCR approach available. It has been used to detect subclonal resistance mutations, such as those in ESR1 for breast cancer patients on adjuvant aromatase inhibitor therapy who demonstrate endocrine resistance.[1] With robust detection as low as 0.02% mutant allele frequency (MAF), OncoBEAM ensures reliable molecular information for real-time therapy selection as well as monitoring of tumor response.

The figure to the left shows the robust accuracy at low allelic frequencies observed for Plasma-Safe-SeqS and demonstrates reliable detection of ctDNA across a broad dynamic range, which can provide new insights into tumor response and resistance as well as expedite validation of biomarker hypotheses.[2]

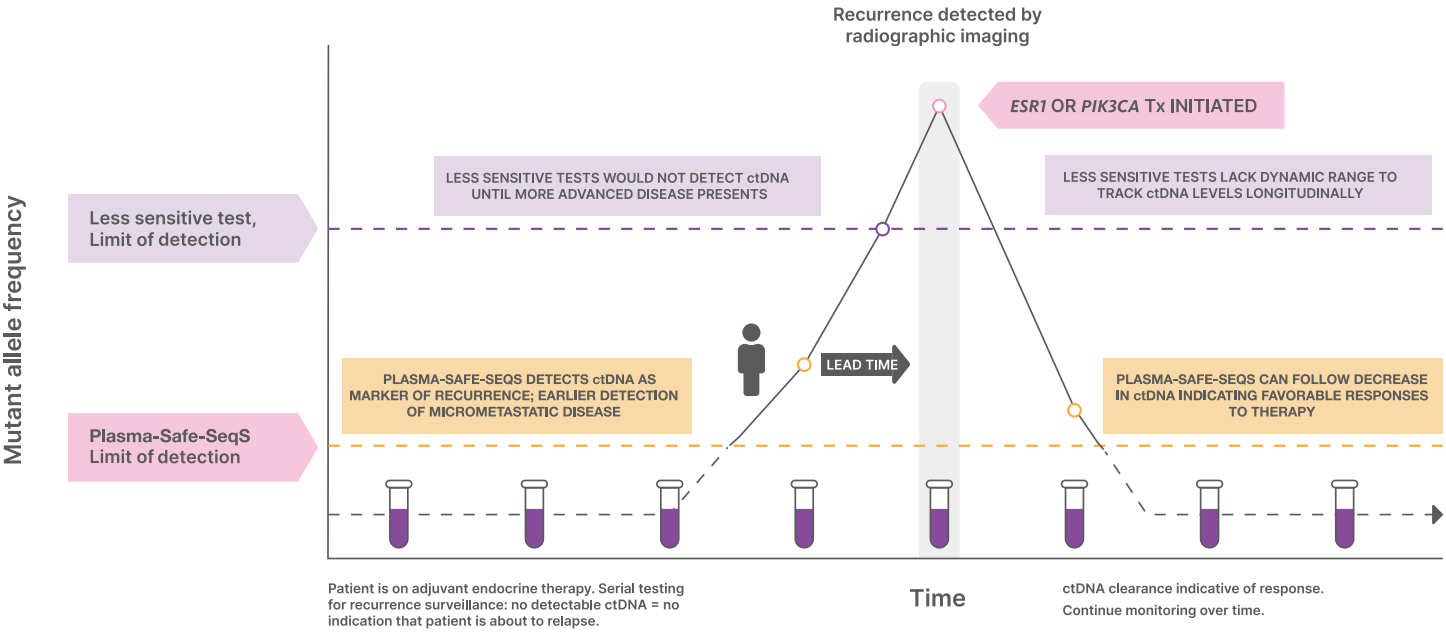
Clinical relevance

Therapeutic selection: Enables maximum identification of biomarker-positive patients eligible for therapy. Less sensitive technologies can miss a significant subset of patients who may benefit from targeted therapy.

- **PIK3CA**—Identifying patients with PIK3CA mutations who derive benefit from PI3K-targeted therapy could help to guide treatment decisions. The BELLE-2 trial showed that a non-invasive ctDNA technique, such as Plasma-Safe-SeqS, can be used for detection of PIK3CA mutations in plasma and may provide a more accurate measure of mutational status over time and treatment, compared with archival tumor tissue.[3]

- **ESR1**—Mediated resistance to endocrine therapy—Plasma-Safe-SeqS overcomes the challenges of detecting subclonal ESR1 mutations, a primary mechanism of resistance to aromatase inhibitors. These mutations are particularly difficult to detect since local biopsy of heterogeneous tissue may fail to capture ESR1-mutant tumor cells; additionally, ctDNA carrying ESR1 mutations is present at very low levels in circulation, making detection using less-sensitive methods very difficult.[1]

- **AKT1**—Ultra-sensitive detection of the activating mutation E17K as well as other rare mutations ensures robust and efficient investigation into the efficacy of novel therapies targeting this PI3K signaling pathway member.[4]



Monitor treatment response: Quantitative 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.[5]

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 herald relapse.[6]

Sample requirements and processing time

Sample specification

2×10mL tubes of whole blood

Pre-analytical sample handling

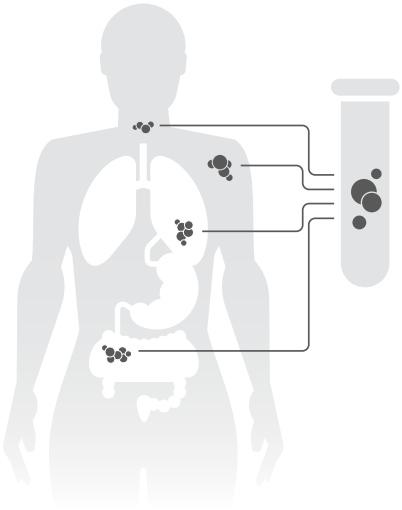
Sysmex Inostics' validated shipping kits and temperature loggers ensure sample stability

Result turnaround time

7 – 10 business days

PLASMA-SAFE-SEQS TECHNOLOGY

Ultrasensitive across a large genomic area



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

Plasma-Safe-SeqS is an order of magnitude more sensitive than other liquid biopsy NGS methods to accelerate trial enrollment and evaluate biomarker hypotheses with greater power.

Coverage of a larger genomic area, with sensitivity and specificity equivalent to our digital PCR platform OncoBEAM, yields unique information that can accelerate clinical studies

Have a question about BC-SEQ?
Visit: **sysmex-inostics.com/oncology/bc-seq#contact**

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